Abstract Booklet

ISSP2021

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ORAL PRESENTATIONS

ORAL PRESENTATION #1

Implications of a diagnosis of Atypical Small Acinar Proliferation and High Grade Prostatic Intraepithelial Neoplasia on prostate biopsy

O'Connor, E., Dowling, C., Casey, M., O'Connor, D., McHale, T.

Introduction: Prostate cancer is the most frequently diagnosed non-cutaneous cancer of men in Western Europe. However, mortality rates have been declining. While this decline may be affected by improvements in treatment, it is also likely due, in large part, to PSA-driven increased detection of T1/T2 disease. In the era of active surveillance of low-risk prostatic cancer, reconsideration of the implications of a biopsy report of ASAP and HGPIN may be timely. Aims: We examined the biopsy follow-up of patients with ASAP and HGPIN biopsy diagnoses over a 5-year period. Results: A biopsy diagnosis of ASAP carried a significantly higher risk of prostate cancer on re-biopsy (20% v 5.9%, p=0.009) and ≥GG2 prostate cancer (11.4% v 2.9%, p=0.037) compared to a benign biopsy. HGPIN also carried an increased risk of prostate cancer (14.8% v 5.9%, p=0.005) and a ≥GG2 prostate cancer (11.1% v 2.9%, p=0.001) compared to a benign biopsy. Concomitant ASAP+HGPIN carried the highest risk of prostate cancer (50%) and ≥GG2 prostate cancer (29%) on re-biopsy compared to a benign diagnosis (p<0.001). There was no significant difference in the rates of re-biopsy in ASAP (54.2%) and HGPIN (37%) (p=0.079). There was no significant difference in PSA values between the 3 diagnostic groups at the time of initial biopsy (p=0.206). Discussion: The frequency of re-biopsy of HGPIN cases is comparable to ASAP, though HGPIN is generally not considered an indication for repeat biopsy while ASAP is. This suggests that factors other than histologic diagnosis play a significant role in the decision to re-biopsy (PSA level/velocity, PSA density, mpMRI, age, patient preference). A combination of ASAP+HGPIN on biopsy carried the highest risk of detecting a clinically significant cancer on re-biopsy.

ORAL PRESENTATION #2

Assessing the impact of COVID-19 related disruption to cancer screening services on the stage of colorectal cancer

Andrea Hennessy, Fergus MacSweeney

Aim The COVID-19 pandemic resulted in the delay or cancellation of elective procedures such as screening colonoscopies to diagnose colorectal cancer. In Ireland, screening colonoscopy services were disrupted between March 2020 and August 2020. The aim of this study is to assess the impact of COVID-19 related delay in diagnoses on the stage of colorectal cancers at the Histopathology Department of Waterford University Hospital (UHW). Methods A comparison was made between the stage of colorectal cancers reported between the years 2019 and 2020 using the TNM 8 staging system. (1) All colorectal cancers reported at UHW between January 2019 and December 2020 were reviewed. In total there were 257 colorectal cancer specimens reported within this period (132 in 2019, 125 in 2020). All cases had SNOMED codes. Data was collected on depth of local invasion and maximum distance of extramural spread, lymph node status (total number examined and number involved), and histologically confirmed metastases. Data was also collected to include venous, lymphatic and perineural invasion, and tumour deposits in accordance with core data items from the Dataset for Histopathological Reporting of Colorectal Cancer (2018) published by the Royal College of Pathologists (RCPath). (2) Results There were 20 stage I cancers reported in 2019 compared to 8 in 2020, representing a decrease in stage I cancer diagnoses of 60 percent. However, in 2020 an increase in stage III cancers by 28 percent was observed (53 in 2019 compared to 68 in 2020). The frequency of extramural venous invasion was increased in 2020 compared to 2019 (29% and 18% respectively). Lymphatic invasion and perineural invasion were also increased in 2020. Conclusion This study demonstrates an increase in stage III cancers and a decrease in earlier stage cancers, which could reflect delayed detection in the context the COVID-19 pandemic. However, a significant decrease in stage IV cancer was also seen. A broader range of data to include the period January to August 2021 would likely prove useful in accounting for a lag period between service disruption and case detection. References 1. Brierley, J.D., Gospodarowicz, M.K. and Wittekind, C. eds., 2017. TNM classification of malignant tumours. John Wiley & Sons. 2. Loughrey, M.B., Quirke, P. and Shepherd, N.A., 2018.

ORAL PRESENTATION #3

WT1 POSITIVE OVARIAN ENDOMETRIOID TUMOURS: OBSERVATIONS FROM CONSULT CASES AND STRATEGIES FOR DISTINGUISHING FROM SEROUS NEOPLASMS.

Simon Rajendran, W Glenn McCluggage.

Ovarian endometrioid carcinoma, more than any other type of ovarian epithelial malignancy, demonstrates a varied morphology which can cause problems in diagnosis. In tubo-ovarian tumour pathology, WT1 is a commonly used marker as it is consistently expressed in low-grade and high-grade serous carcinomas (LGSC and HGSC) and is often considered a specific marker of a serous phenotype. However, ovarian endometrioid neoplasms may also express WT1 which may contribute to misdiagnosis. We report our experience with 23 ovarian endometrioid neoplasms (4 borderline tumours, 19 carcinomas), mainly received in consultation, which were WT1 positive (diffuse in 11 cases) which often contributed to misdiagnosis. Endometriosis was identified in the same ovary in 6 cases and squamous elements in 7. We describe strategies for distinguishing such neoplasms, which may exhibit morphological overlap with serous tumours, from LGSC and HGSC and stress that a diagnosis of HGSC is unlikely with two grossly and histologically normal fallopian tubes. We also stress that a panel of markers should always be used rather than relying on a single marker and that when the morphology is classical of an endometrioid carcinoma, diagnostic immunohistochemistry is not needed given the potential for confusion in cases showing “aberrant” staining. We also discuss the phenomenon of “aberrant” immunohistochemical staining in endometrioid carcinomas which appears more common than in other ovarian carcinomas.

ORAL PRESENTATION #4

Title: Rates of sentinel lymph node positivity in patients with microinvasive ductal carcinoma in situ (DCIS); a single institution experience.

Ward C, Walsh S, Mahon S.

Objective: To assess the rates of sentinel lymph node (SLN) positivity in patients with microinvasive ductal carcinoma in situ (DCIS). Background: Staging of the axilla via SLN biopsy, although not routinely performed in DCIS, is mandatory in invasive ductal carcinoma. The role of SLN biopsy in microinvasive DCIS is less well-defined [1]. Rates of SLN positivity in microinvasive DCIS are low, ranging from 2-20% [2, 3]. Many of these cases include micrometastasis (0.2-2mm) or isolated tumour cells, the clinical significance of which is believed to be comparable to node-negative disease [1]. Additionally, there remains an appreciable morbidity associated with SLN biopsy. Axillary staging in clinically node-negative microinvasive DCIS is therefore uncertain owing to the low risk of lymph node metastasis, favorable overall prognosis and the morbidity associated with surgical intervention in the axilla. Methods: We collected data on all patients diagnosed with microinvasive DCIS on core biopsy in our institution (MMUH) over a 5-year period (2016-2020) to evaluate the rates of sentinel lymph node positivity in this patient cohort. Of 617 patients with DCIS, 56 had microinvasion on core biopsy. Of these, 37 had purely microinvasive DCIS following surgery, 16 had foci of invasive cancer, while 3 patients were lost to follow-up. All patients underwent SLN biopsy, of which 2 had a lymph node macrometastasis (3.8%), while a single patient had a micrometastasis (1.9%). There were no instances of isolated tumour cells. Most cases were associated with high-grade DCIS (83%). Oestrogen receptor (ER) status was assessed in 40 patients, the majority of which were positive (n=31). Rates of HER2 positivity were lower (10/31 tested). Conclusions: Microinvasion is associated with high-grade DCIS in the majority of cases and is most commonly ER-positive. Although rates of lymph node positivity were low (5.7%), comparable to those reported in the literature, this remains appreciably significant in terms of a patients' prognosis and subsequent management to warrant staging of the axilla in such cases. References: 1. Cardoso, F., et al., Ann Oncol, 2019. 30(10): p. 1674. 2. Magnoni, F., et al., Br J Surg, 2019. 106(4): p. 375-383. 3. Fan, B., et al., Ann Surg Oncol, 2020. 27(11): p. 4468-4473.

ORAL PRESENTATION #5

Association between histological subtypes of lung adenocarcinoma and KRAS mutations, with an emphasis on G12C mutations: a pilot study

Keogh A, O'Brien C, Ward R, Murchan P, Baird AM, Gray SG, Finn SP

Lung adenocarcinoma (LUAD) is considered one of the most heterogenous cancer types. Multiple studies have demonstrated that different histological subtypes of LUAD are associated with distinct molecular profiles. KRAS mutations in LUAD, specifically G12D and G12V mutations, are associated with invasive mucinous subtypes. However, G12C mutations, representing approximately 40% of the KRAS mutated subgroup of LUADs, are less well-defined and are also known to have a particularly poor prognosis. KRAS has historically been coined "undruggable" however, FDA has recently approved Sotorasib, a targeted therapy for KRAS G12C mutations in NSCLC, making this group of LUADs of special interest. Aims: Identify the prevalence of KRAS mutated LUADs in Ireland. Compare clinicopathological and histological features of KRAS LUADs to wild type (wt) LUADs Methods All advanced lung carcinomas at St. James's Hospital (SJH) from 2016 (n=422) who had undergone molecular testing were examined. Of these 128 harboured a KRAS mutation and were selected for analysis. Histological subtypes were analysed on resected specimens of which there were three groups: KRAS G12C (n=21), non-G12C KRAS (n=14) and wt LUADs (n=81). We reviewed histopathology reports to obtain both clinicopathological and histological information. Results The prevalence of KRAS mutations in our cohort was 30% (128/422). The most common KRAS mutations were G12C, G12D, and G12V representing 48%, 14% and 13% of cases respectively. Clinicopathological characteristics such as sex , age, nodal status, size, pleural invasion, stage, and LVI were similar in all groups. Solid predominant subtype was present in 48% of KRAS G12C LUADs (10/21) compared to 21% in non-G12C (3/14) and 21% in wt LUADs (17/81). Invasive mucinous subtype was present in 9.5%, 21%, and 1% of G12C (2/21), non-G12C (3/14) and wt (1/81) LUADs respectively. Conclusion This pilot study highlights the association of molecular phenotype and morphology in LUADs. KRAS G12C mutations were associated with solid predominant subtype. This subtype of LUAD is associated with aggressive behaviour which may explain the adverse clinical outcome observed in KRAS G12C mutated LUADs. Additional specimens are being accrued to formally validate this finding

ORAL PRESENTATION #6

Precision vs Accuracy in Digital Pathology: A Morphomolecular Analysis

Authors: May Almezen, Dr. Allan O'Keeffe, Sinead Conneely, Prof Grace Callagy, Dr. Sean O. Hynes

OBJECTIVE: Quantifying tumour nuclear content in a sample is vital for molecular tests such as Single Gene Testing and Next Generation Sequencing. These tests inform clinical decisions therefore accurate quantification is imperative. Tight thresholds govern these tests and suitable tumour content needs to be ascertained to receive accurate results. The aim of our study was to train an algorithm in QuPath to be able to accurately assess tumour nuclear content in slide images based off manual training. METHODS: For this study, four anonymized colorectal cases were analysed. Each had 12 sections cut over a space of 36 microns with H&E staining applied at levels 1,4,8 and 12. Images at level 1 and 8 were manually assessed through cell counting and identification. This manual analysis was used to train 2 different algorithms using an open source image analysis software application called QuPath; each algorithm was trained from 24 images. One algorithm was trained to only detect tumour, apoptotic bodies and stromal cells in an image (#1). A 2nd was trained to differentiate all cells in an image including tumour, epithelium, inflammatory cells etc (#2). The detections the algorithms made were compared to manual decisions to assess accuracy and precision. RESULTS: #1 had the least amount of misidentification with the highest being 20 errors in a single image. Whereas #2 misidentified 200+ cells of various types especially tumour and fibroblasts across many images. For tumour content, #1 matched manual percentages within a range of 5% in 8 of the 24 images. The #2 algorithm matched only 4 out of 24 images in a 5% range. In addition, both algorithms struggled with 'illusion cells' (detecting cells that were not present) which appears to parameter based. Both were also consistent in demonstrating that tumour percentages can vary between levels. For instance, cases 1 and 3 had a difference of >10% between levels 1 and 8 while case 4 had a difference of >20%. CONCLUSIONS: This study demonstrates that an algorithm can be trained to be precise in its identifications whereas accuracy remains an issue. Furthermore, the differences in tumour content between levels in a single case is important to address as the percentage differences can be significant enough to affect molecular testing suitability.

Histopathology Trainee Abstracts Research and Audits

POSTER PRESENTATION #1

ER, PR and HER2 assessment in a population-representative Northern Irish contralateral breast cancer cohort using digital image analysis

Louisa Miller, Stephanie Craig, Colin McIlmunn, Kris McCombe, Christine Greene, Stephen McQuaid, Barry McGinn, Kienan Savage, Stuart McIntosh, Jacqueline James

Abstract: Breast cancer is the most common cancer in the UK. Whilst survival has been steadily increasing, so has the risk of developing a second cancer in the other breast, collectively referred to as contralateral breast cancers (CBC). Currently identified risk factors for CBC include younger age at first diagnosis, lobular histology, family history and hormone receptor (HR) status. Recent identification of a large CBC cohort (N=403) in NI provided a foundation on which to begin researching risks factors and prognosis associated with CBC's. Initial findings are similar to previously published work, with a mean time between diagnoses of 7.6 years and increased mortality ratio of 6.5 when compared to the matched control. Unfortunately, it was not possible to fully investigate the HR status of these patients, as many predated the routine use of such analyses. ER/PR status of both primary and CBC tumours was only available for 30.3% (122/403) of patients and showed an increase in ER negative (ER-) CBC's compared to primary tumours. This study aims to assess the value of digital image analysis in the automated assessment of tumour HR status in the CBC cohort. Tissue microarrays were produced from both primary and CBC tumours for 30 randomly selected patients, 4µm sections were taken and stained for ER, PR and HER2 using a Leica Bond RX. Stained slides were scanned at 40X magnification on an Aperio AT2 scanner and digital slides initially assessed manually for ER/PR/HER2 by a trainee histopathologist using QuPath v.0.2.3 as a slide viewer only. Slides were subsequently scored using QuPath to perform automatic cell detection, object classification and positive cell detection. QuPath was deemed reliable for assessing ER, PR and HER2 status in breast cancers with manual and digital results agreeing in over 90% of cores assessed. However, the process of digital image analysis was inefficient for routine use. In particular, image pre-processing was labour intensive and time consuming. Subsequently we establish that digital image analysis does not significantly improve HR status assessment for these particular biomarkers and recommend the current gold standard approach of manual scoring.

POSTER PRESENTATION #2

Uroplakin 2 antibody staining patterns in variants of primary bladder urothelial carcinoma

Dr Brian Pierce, Stephen Power, Dr Nick Mayer. Cork University Hospital

Background Urothelial carcinoma (UC) comprises a spectrum of disease with respect to genetics as well as morphology. Variant morphology is present in 25% of UCs often being associated with more aggressive disease and the recognition of these variants is important as it increasingly may influence treatment. Furthermore, some variants mimic the morphology of tumours from outside the bladder and need to be distinguished from metastatic disease. Although less sensitive than GATA3, antibodies to uroplakin II (UPII) have shown high specificity as a UC marker. In this study, UPII has been evaluated with respect to its sensitivity and staining characteristics (proportion of tumour cells and intensity) in 11 UC variants. Methods Variants of UC of the bladder diagnosed between 2013 and 2018 were retrospectively identified from the surgical pathology database in Cork University Hospital (85 cases identified). Following immunostaining, the variant component was scored with regard to intensity (0 (none) to 3 (strong)) and proportion of variant tumour cells stained. Results UPII immunoreactivity was identified in 66/85 (78%) of total UC variant cases: 15/15 micropapillary (100%), 13/13 clear cell (100%), 6/6 nested (100%), 2/2 pleomorphic giant cell (100%), 1/1 lipid cell (100%), 7/8 glandular differentiation (88%), 19/25 squamous differentiation (76%), 1/2 rhabdoid (50%), 1/4 small cell neuroendocrine (25%). No immunoreactivity was detected in the sarcomatoid (n=6) or lymphoepitheliomatous (n=3) variants. The average staining proportion across all the groups was 63%. Of note the squamous differentiation group showed only weak and focal staining. Conclusion There is considerable variation in the sensitivity and staining characteristics of UPII with different UC variants. Although the case numbers are low, we found no or limited staining in the sarcomatoid and small-cell neuroendocrine variants (in keeping with previous studies), and the lymphoepitheliomatous variant. Pathologists need to be aware of this variation especially in the setting of metastatic disease and ideally use this antibody as part of a panel with, for example, GATA-3.

POSTER PRESENTATION #3

Provision of a telepathology solution for a specialist liver histopathology service – a tale of two viruses.

Laoise Coady, Tom Crotty, Aurelie Fabre, Niamh Nolan

The National Liver Unit is based in St Vincent's University Hospital. It carries out approximately 65 liver transplants (OLTs) per year. All of these surgeries involve routine histopathological assessment of the donor liver by examination of a wedge of the donor organ, usually taken at the time of re-perfusion. In about 30% of cases, a frozen section is requested to confirm the clinical suspicion of severe fatty liver, or to evaluate the nature of a lesion in either the donor or (in the case of suspected metastatic neoplasm) the recipient. COVID-19 has impacted every aspect of the healthcare environment leading to significant pressure on the health service, which in turn has been exacerbated by staff shortages due to illness and redeployment and unplanned consultant absences. This, coupled with a deficit in consultant on call cover in the unit, resulted in the acquisition of a single slide digital scanner in late April 2021. The implementation of the service was almost immediately delayed by the arrival of the second virus: the HSE -wide effect of the cyber-attack. Digital pathology is an emerging field, which, in recent years has been increasingly used for both diagnostics and educational purposes. The Royal College of Pathologists recommends methods to validate digital systems prior to going 'live'. To evaluate the accuracy of remote diagnosis by telepathology a series of 20 consecutive frozen sections from the Hepatobiliary service were scanned and identified as FS 1, FS 2, etc by LC. The three consultants providing the on-call service were provided with the clinical diagnoses given at the time of the original frozen. Each then logged on to the scanner remotely and provided a report for each frozen. This report was then compared to both the original report and the paraffin section report. Service will commence with the satisfactory performance of the digital reports. Telepathology provides a means of sustaining an urgent service despite staffing constraints. It also allows for training and the provision of second opinions. As telepathology depends on the internet, a virus free environment with ICT support is also essential.

POSTER PRESENTATION #4

Primary Cutaneous Melanoma and Sentinel Lymph Node Biopsy: a 6-year retrospective study from University Hospital Waterford

1Hannigan, C.E. 2MacSweeney, F, 1Department of Histopathology, Beaumont Hospital 2Department of Histopathology, University Hospital Waterford

Introduction The incidence of primary cutaneous melanoma (CM) in Ireland has continued to increase year-on-year since the early 1990's. Cork, Waterford and Wexford are considered the most affected counties. Each of those three counties has a standardised incidence ratio of at least 1.16 over the national average for CM over this period of time. Surgical excision remains the main treatment option for CM, however the use of sentinel lymph node biopsy assists in the surgical planning of and patient selection for radical node dissection. Methods Data was retrospectively obtained from a generalised electronic histopathology log which detailed all primary CM cases presenting to University Hospital Waterford (UHW) between January 2015 and December 2020. From that cohort, each CM case with a sentinel lymph node biopsy (SLNB) was quantified and further studied. The data collected included patient demographics, site, Breslow depth, Clarke's level, and SLNB result. All referred, external cases were excluded from this study. Results In total, 585 cases of CM presented to UHW during the study period. Of these, 118 cases (20.1%) underwent a SLNB in UHW. Females (53%) made up the majority of the study cohort, and age at presentation for both sexes was 56.6 years on average. Sentinel lymph node biopsy positivity was 25/118 (21.1%), markedly reduced from 37.8% reported for the period 2010-2014 in the same centre where less (103) biopsies were carried out. The most commonly affected site was the upper limb (31.3%), followed by the lower limb (27.1%) and the back (25.4%). The average Breslow depth was 2.76mm with a corresponding average Clarke's level of III. Conclusion There has been a slight decrease (-1.2%) in the overall number of primary CM presentations to UHW over the study period as compared to the period 2010-2014. Sentinel lymph node biopsies and positivity have decreased during the study period compared to 2010-2014. This finding could be explained by earlier stage of disease at presentation, increased surveillance and high quality patient information.

POSTER PRESENTATION #5

Title: Colorectal Carcinoma Dataset Reporting at the Beacon Hospital in 2020

Reddy PWH, Jeffers M.

Introduction: The Royal College of Pathology (RCPath) has recommended audit criteria to monitor the reporting of colorectal carcinoma specimens. The aim of this audit was to review the pathological reporting of colorectal carcinoma in our institution and compare this with the college's recommended standard. Methods: Colorectal cancer cases were retrieved from our hospital LIS system following a search using the hospital's codes for colon and rectal cancers. Only primary colorectal carcinomas were included. Pathological reports were reviewed, and the data extracted to our data spreadsheet in accordance with the RCPath audit criteria. Results: Our department met 2 out of 3 of the recommended criteria as set out by the RCPath. The median number of lymph nodes harvested per case was 13, above the recommended standard of 12. The percentage of peritoneal involvement in colon cases was 23%, greater than the advised standard of 20%. Unfortunately, vascular invasion was only reported in only 25% of cases, below the recommended standard of >30%. Conclusion: Our audit demonstrates reassuring results when compared with the RCPath recommended standard. While lymph node medians met the college's criteria, there were individual cases where lymph counts were significantly below this standard. We intend to review these cases to identify any specific issues. We will review our MDT process to ensure additional sampling is undertaken in cases of low lymph node counts. With regards to venous invasion our department did not meet the recommended standard. We plan to raise within the department and stress the importance of reporting venous invasion. Finally, we will widen our audit to reach at least 100 cases.

POSTER PRESENTATION #6

Audit of Outcomes of B1 Breast Biopsies in a Breast Screening Unit in Ireland

Ryan S, D'Arcy C, McNally S

Merrion Breast Screening Unit, St Vincent's University Hospital, Dublin 4 Introduction: The aim of breast screening is to detect cancer at an early stage, improve outcomes and reduce mortality. If an abnormality is detected on a screening mammogram the patient will be recalled for further investigation (either further imaging or biopsy). Breast core biopsy pathology should always be interpreted in the context of the radiological findings and discussed at a multidisciplinary meeting (MDM). The aim of our audit was to document follow up of patients with breast biopsies classified as B1, normal tissue. We aimed to ensure discussion at an MDM occurred, and to document the final outcome including radiological concordance or requirement for repeat imaging or further tissue sampling. Method: A list of all breast biopsies designated as B1 from January 2018 to December 2019 was generated from internal databases at the Merrion Breast Screening Unit Dublin. We retrospectively examined the radiological, clinical and pathological reports for all biopsies including initial recall reason, biopsy type, MDM outcome and further investigations. Results: A total of 93 B1 biopsies from 90 patients were identified. Over the two years the B1 biopsy rate was 6.4% (93/1449). All of the B1 biopsies were discussed at an MDM (100%). The outcomes from the MDM were return to routine recall (48/93, 51.6%), early recall for repeat imaging (20/93, 21.5%), further assessment (21/93, 22.6%), diagnostic surgery (3/91,3.2%) and therapeutic surgery (1/93, 1.1%). Following further work-up (either repeat imaging or further tissue sampling), the majority of patients were reassured, with a final histology of B1 or B2, and returned to routine screening. Two patients had a final pathological diagnosis of atypia and were referred for follow up in the symptomatic breast clinic with annual mammograms. Five patients had a final diagnosis of carcinoma (either in situ or invasive) and proceeded to therapeutic surgery. Conclusion: In conclusion, all biopsies which were designated as B1 were discussed at an MDM, in keeping with the Royal College of Pathologists Guidelines. If there is any radiological discordance at an MDM in the setting of a B1 biopsy, further investigation should be undertaken to ensure all relevant pathological changes are identified and managed appropriately.

POSTER PRESENTATION #7

Molecular Testing for Microsatellite Instability (MSI)/ Rat Sarcoma (RAS) in patients with Colorectal Cancer in University Hospital Waterford between 2019 and 2021.

Waleed Mustafa

Background: Correct identification of MSI/RAS gene variants is a key for status identification and targeted treatment decisions in patients with metastatic colorectal cancer (CRC). Aim and objectives: To assess the rate of MSI/RAS testing in patients with CRC, in University Hospital Waterford between 1/1/2019 and 13/5/2021. Standards: While no official standards exist, many national guidelines recommend performing mismatch repair (MMR) immunohistochemistry (IHC) for MSI, and polymerase chain reaction (PCR) for RAS, on all new cases of CRC. Method: All CRC cases between January 2019 and May 2021 were searched in the laboratory information system and a list was obtained. The cases were added to a spreadsheet once the list was assessed. To see if MSI/RAS tests were performed, pathology reports were checked. Results: The total numbers of 553 cases of CRC were identified. For MSI, 476 tests were performed out of 553 (86.1 %), and for RAS, 115 tests were done out of 553 (20.8 %) Recommendations: 1. Template reporting of MSI/RAS will be introduced to include the email address of the family screening to ensure patients are appropriately referred for assessment. 2. Measures will be put in place in the laboratory to ensure that tests performed by external providers are followed upon. Re-audit: We will be repeating this audit on an annual basis to ensure that reflex testing is performed and algorithms are adhered to.

POSTER PRESENTATION #8

Retinoblastoma in Ireland; Next Generation Sequencing Molecular Profile with a Special Focus on Non-RB1 Mutations and a Comprehensive Review of the Retinoblastoma Caseload in Ireland over the Past 20 Years.

Jessica Maguire 1, Dr Michael Capra 2, Professor Susan Kennedy 1,3 1 St Vincent's University Hospital 2 Our Lady's Children's Hospital, Crumlin 3 Royal Victoria Eye and Ear Hospital

Background: Retinoblastoma is a rare aggressive tumour of childhood, attributable to a congenital or sporadic bi-allelic mutation in the RB1 tumour suppressor gene in 98% of cases. In the past decade, non-RB1 mutations in other tumour suppressor and oncogenes have been identified as contributors to the development of retinoblastoma, most commonly in BCOR, a BCL-6 co-repressor gene, located on chromosome X. Mutations in BCOR and other non-RB1 genes are shown to be associated with a higher pathological grade and more aggressive clinical course in retinoblastoma. Aim/Design: To assess the molecular profile of selected enucleation specimens from the Irish cohort of retinoblastoma cases and to provide a comprehensive 20 year retrospective review of retinoblastoma in the Irish population. Method: All enucleation cases for suspected retinoblastoma in the Irish population since 2001 were reviewed, using data from the Royal Victoria Eye and Ear Hospital, Dublin. Selected cases were sent for molecular analysis to Great Ormond Street Children's Hospital, London. Results: 61 enucleations were performed for 59 patients with retinoblastoma in the Irish population between 2001 and 2020. 59% male, 41% female. Average age at surgery 2.72 years (994 days). Laterality 61% right, 39% left. 56% had choroidal invasion at time of enucleation. 8% had neoadjuvant chemotherapy. 61% had optic nerve invasion, 5% had a positive optic nerve margin. Of the selected enucleation cases referred for molecular profiling, one patient did indeed have a non-RB1 mutated retinoblastoma. A 3 year old female with a high grade, poorly differentiated retinoblastoma of the left eye was found to have a mutation in BCOR on the paediatric NGS solid tumour panel. Conclusion: Our 20 year review shows the incidence of retinoblastoma in the Irish cohort is static, and highlights a case of an aggressive, high grade non-RB1 BCOR mutation. This supports the literature in showing the importance of molecular profiling to identify germline mutations and alternative pathways of retinoblastoma tumour development.

POSTER PRESENTATION #9

Primary Vitreoretinal Lymphoma

Dr H Fadlelseed1, Mr M Treacy2, Prof S Kennedy1,2 1Pathology Department, St Vincent's University Hospital, 2Royal Victoria Eye and Ear Hospital

Introduction:

Primary vitreoretinal lymphoma (PVRL) is a rare primary intraocular high- grade lymphoma that affect the retina and the vitreous in the absence of systemic involvement. The majority of PVRL are diffuse large B-cell lymphoma derived from activated B-cell (ABC) subtype. CNS involvement occurs in 15% of patients at diagnosis. Clinical features include blurring of vision, floaters and symptoms of CNS involvement. The true epidemiology of the PVRL is unknown but the underling risk factors are HIV and EBV. The morphology and ancillary studies play a major role in confirming the diagnosis. Other diagnostic tests include flow-cytometry which has 100% specificity and 82% sensitivity and this depends on the cellularity of the vitreous sample. Measurement of IL10 have 80-90% sensitivity while positivity for MYD88 has 60-80% sensitivity. Although, MYD88 has been found in 70% of PVRL cases and often requires fewer cells than flow-cytometry, it can also be found in lymphoplasmacytic lymphomas. Treatment of PVRL requires close collaboration between ophthalmologist, pathologist and oncologist but the prognosis is generally poor.

Discussion:

We reviewed 169 cases of vitreous samples from 2010 to 2021 and we found 6 cases diagnosed with vitreous lymphoma. Of these 6 cases we are presenting an example of PVRL; a 59-year-old gentleman with a known history of primary CNS non- Hodgkin's lymphoma (NHL) who presented with vitritis and deterioration of visual acuity for the last year. On examination he had vitreous chamber opacities and retinal infiltrate suspicious for lymphoma. Imaging and haematological investigations were performed to assess for causes of intraocular inflammation and they were non-diagnostic. Interleukins 10/6 ratio was >1 for few consecutive samples. A vitreous fluid was taken and the cytomorphology showed large pleomorphic lymphoid cells with vesicular nuclei. They were positive for CD20, Bcl2 and Bcl6 and negative for cyclin D1, MUM1, PAX5, and CD3. The features were c/w vitreous involvement by high grade NHL. MYD88 L265P mutation was detected by PCR supporting the diagnosis of PVRL. The patient received intravitreal chemotherapy treatment comprising Rituximab and methotrexate with close follow up by eye examination, photos and IL10/ 6 measurement. After 2 weeks of treatment his condition showed rapid subjective and objective improvement.

Conclusion:

PVRL is a rare aggressive lymphoma with frequent CNS involvement. Most PVRL are derived from ABC subtype. Cytokine profile analysis is considered an additional useful tool in suspected cases if IL10:IL6 > 1.0. MYD88 mutation is a valuable diagnostic tool; however, the molecular results should be interpreted within the clinical and cytological context.

POSTER PRESENTATION #10

Re-audit of compliance with renal biopsy request form requirements in Cork University Hospital.

Neil Fennelly, Sinead Dineen, Nick Mayer

Background: In 2011, an audit of the clinical details submitted with a renal biopsy request was performed in CUH. The criteria audited were established by consensus with the renal physicians. Results showed that the clinical details provided on the request form when a renal biopsy was submitted were often incomplete, omitting information often required for appropriate clinico-pathological correlation and diagnosis. This resulted in the introduction of a biopsy request form template to be submitted by clinical teams when requesting a biopsy. Aims: To re-audit compliance with the renal biopsy template request form. Methods: A computer generated list of medical renal biopsy specimens was obtained for the years 2018-2019. Information was gathered by reviewing pathology reports for clinical details provided, and audited against the consensus criteria. The percentage of renal biopsy forms complying with each criterion was calculated for the years 2018-2019 and directly compared with the data from 2011. Results: 88 renal biopsies were performed in 2011, comprising 75 native & 13 transplant biopsies. 143 biopsies were performed in 2018 - 2019, comprising 127 native & 16 transplant biopsies. For native biopsies, the percentage of biopsy forms containing the requested details rose upon re-audit for 2018 and was sustained for 2019. Several criteria were provided in >95% of cases (clinical scenario, medications, past medical history, the existence of a previous biopsy & serum creatinine). For transplant biopsies, several criteria that had not been provided at all in 2011 (presence of acute rejection, BK viraemia, haematuria & previous biopsy) now showed high rates of submission upon re-audit. Some criteria were still frequently omitted by clinicians, such as the cold ischemia time and episodes of acute rejection. Conclusions: The clinical details provided on the request forms for renal biopsy has improved. However, some criteria continue to be poorly provided, such as the clinical differential diagnosis in native biopsies, and the cold ischemia time and prior episodes of acute rejection in transplant biopsies. Recommendations: Clinicians will be informed of the results of the re-audit, and encouraged to continue a high level of compliance with the biopsy request form template, with emphasis on the deficient criteria identified.

POSTER PRESENTATION #11

Audit of the adequacy of renal biopsy specimens received in Cork University Hospital.

Neil Fennelly, Sinead Dineen, Nick Mayer

Background: Percutaneous renal biopsy is the gold standard in diagnosis of medical renal disease. Because glomerular diseases can be focal in nature, it is critical that a sufficient number of glomeruli are biopsied in order to reach an accurate diagnosis. Whilst generally safe, the procedure can be associated with serious bleeding. The need for repeat biopsy due to inadequate glomerular yield should ideally be minimal. Aims: To determine the adequacy of glomerular yield at biopsy over a three year period from 2018-2020, how often additional tissue was requested, how many additional glomeruli were received on average & how often it was required to reach diagnosis. Methods: Due to lack of an agreed international standard for the adequacy of renal biopsies, a consensus standard was defined based upon a review of studies published over the last 20 years. A computer generated list of biopsy specimens was obtained from the LIMS. Biopsy data were audited against the defined consensus adequacy criteria. Results: The mean number of cores per biopsy was similar overall (2.04-2.21). The number of glomeruli per biopsy varied significantly, with a mean of 27. 157/192 native biopsies (82%) met adequacy criteria. Of the 35 that did not, additional tissue was requested and a diagnosis was reached in 32. In all cases where additional tissue was requested, a diagnosis was subsequently reached. Further tissue was requested in 14 cases that were adequate & diagnostic upon receipt, & may not have been required in retrospect. 18/24 transplant biopsies (75%) met adequacy criteria. Of the 6 cases that did not, additional tissue was requested in 3 cases, & received in 1. In 23/24 cases a diagnosis was possible. Conclusions: 81% of the total biopsies met adequacy criteria. The overall diagnostic rate was 98%. Requesting additional tissue following real-time review of fresh tissue at the dissecting microscope increases the number of assessable glomeruli and diagnostic yield. Underestimation of the number of glomeruli present at the dissecting microscope occurs in a minority of cases (7%). Recommendations/action plan: Based on the audit, there will be prospective monitoring of the assessed number of glomeruli at real-time review, along with the final number of glomeruli per biopsy, to improve accuracy & reduce the incidence of unnecessary additional sampling

POSTER PRESENTATION #12

Review of surgically suspected appendicitis. Correlation with Histopathology. Impact of Covid-19 and early lockdown

Dr Sushrut Oomman, M.D., PgDip in Medical Education Dr J.K. Murphy MB BCh BAO, MRCPI, FRCPath, MA (Ethics of Healthcare)

Abstract Background The increasing incidence of Covid-19 cases in the UK led to the announcement of a National lockdown on 23rd March 2020. The effect on patient presentation of suspected appendicitis in Glangwili General Hospital in Wales was reviewed. It is noted that during the early lockdown patients were hesitant to come to hospital for a surgical review and treatment. Methods The 60 cases reviewed were from histopathology files recorded in the computer system. They included all the cases from the period of January 2020 to June 2020. We looked at the pre-Covid period (January to March 2020) and the early lockdown period (April to June 2020). The pathological reports were collected from the 'Pathology Laboratory Information Management System' (LIMS). The data was collected on Excel spreadsheet. Results There were 42 cases of appendicectomy during pre-lockdown from January to March, and 18 cases in early lockdown. The highest cases were in January with 17 cases, whereas 5 cases in June was the minimum during the early lockdown period. During the pre-lockdown period, the male/female ratio was 50%. However, in the early lockdown period the ratio was 61% males to 39% females. In pre-lockdown there were inflamed appendix as well as non-acute pathology presenting such as normal appendix, non-specific pathology, obstruction of appendiceal lumen by faecolith, enterobius vermicularis, and a fibrosed appendix. There was also one case of metastatic goblet cell carcinoid of the appendix (low grade goblet cell adenocarcinoma). On the other hand, there were only acute inflammation of appendix presenting during the early lockdown period. Preoperative imaging was performed in 40% of cases since they were either obese or were in other categories requiring imaging. Out of those who had imaging, 32%(19) had CT and 8%(5) had an US imaging. 18 cases who had a CT imaging which showed evidence of inflammation were also confirmed histopathologically as acute appendicitis. Conclusion The data shows that only acute surgical emergencies were presenting during the early lockdown period. This suggests that delay to access secondary care due to hesitancy contributed to delayed referral for a surgical review.

POSTER PRESENTATION #13

An audit of the completeness of histopathological reporting of appendiceal neuroendocrine tumours (NETs) in St Vincent's University Hospital (SVUH) from Jan 2012 to Apr 2021.

Ms Kara Swan, Dr Rhona Thuillier, Dr Niall Swan Histopathology Department, SVUH, Dublin

Introduction: The 2017 'ENETS Consensus Guidelines for Standards of Care in Neuroendocrine Tumours' document sets out minimum requirements for pathology reporting of gastroenteropancreatic neuroendocrine neoplasia including type of specimen, tumour site and size, histologic differentiation and grade, microscopic tumour extension, margin status, lymphovascular invasion (LVI), perineural invasion (PNI), and TNM stage. Aims: The aim of this audit was to examine: 1. the completeness of reporting of appendiceal NETs seen in SVUH from 2012 to 2021, and 2. whether this has improved over time with the introduction of a standardised reporting template Methods: 116 appendiceal NETs that were reported from 2012 to April 2021 were retrospectively examined to see whether the core data items as set out by the above guidelines were included in all reports. Results: 84% of cases had a complete report. Missing data items included location and size of tumour, excision status, grade, and a comment on PNI and LVI. A reduction was seen from 100% incomplete reports each year in 2012 and 2013 to less than 12% incomplete reports over a six year period (2015 to 2020). In 2020 all 18 reports were complete (100%). Discussion: 84% of cases of appendiceal NETs had complete reports between 2012 and April 2021. This highlights the generally high standard of reporting within the department. A large reduction in the proportion of incomplete reports was seen in 2014, following the introduction of a standardised reporting template for appendiceal NETs. Recommendations: Re-audit at the end of 2022 to ensure that the high standard of complete reporting is maintained.

POSTER PRESENTATION #14

Hepatic adenomas – classification dilemmas

Dr. Michaela Larkin, Dr. Peter De La Harpe Golden, Dr. Niamh Nolan

Hepatic adenoma classification has been updated in the current WHO book in 2019[1]. The hepatic adenoma subtype has significant implications on clinical and prognostic factors. Classifying hepatic adenomas requires a diverse panel of immunohistochemistry – CD34, Glutamine synthetase, beta -catenin, Liver fatty acid binding protein (LFABP) and serum amyloid A (SAA) / C-reactive protein (CRP), aberrant beta catenin expression being the most significant. The pattern of positivity of CD34 and Glutamine synthetase can also assist in the prediction of important mutation subtypes. A retrospective audit was carried out to review all hepatic adenoma resections in St. Vincent‘s University Hospital (SVUH) during a four year period (2017-2020). 11 cases were identified in which a pre-excision biopsy had been obtained. The provisional classification of these at the time of biopsy was reviewed. These were then re-classified using the current WHO guidelines. Immunostaining was carried out in SVUH, with the exception of LFABP, which was done in the University of Edinburgh. SAA/CRP was not available. On re-classification there were 4 ‘not otherwise specified’, 4 fatty, 1 inflammatory, 1 exon 3 S45 mutated, and 1 exon 7/8 mutated, hepatic adenomas. Full excision of the neoplasm is required for accurate classification.

References: [1] Digestive System Tumours. WHO Classification of Tumours, 5th Edition, Volume 1 (5th ed.). Lyon (France): International Agency for Research on Cancer. 2019. ISBN 978-92-832-4499-8.

POSTER PRESENTATION #15

Title: Mismatch repair protein status in ampullary carcinoma

Authors: Dr Corina Girleanu, Mr Ben Murray, Ms Nashwa Nadeem, Ms Jean Murphy, Dr Maura Cotter, Prof Niall Swan. Department of Histopathology, St Vincent's University Hospital, Elm Park, Dublin 4

Background: Mismatch repair protein (MMRP) deficiency is caused by high frequency DNA mutations in regions of repetitive DNA sequences, and creates a microsatellite instability (MSI) phenotype. The detection of MMRP deficiency by immunohistochemistry (IHC) has become standard practice for many tumour types as it is indicative of a favourable response to checkpoint inhibitor immunotherapy in addition to identification of potential underlying germline mutations. As a result of several studies [1] reporting a relatively frequent MSI phenotype in 2019 MMRP IHC was made routine for all ampullary carcinomas in the department. Aims: 1. To determine if MMRP IHC is being performed in all cases of ampullary carcinoma. 2. To evaluate the incidence of MMRP deficiency in our patient cohort. 3. To correlate pathological features to MMRP status. Methodology: All pathology reports of ampullary carcinoma resected at St. Vincent University Hospital between 2011 and 2021 were retrospectively reviewed. Pathological data were taken from the pancreatic tumor database created by extracting reports from the laboratory information system. The following variables were included: age, gender, histological type, grade, number of lymph nodes involved, MMRP IHC status (MLH1, PMS2, MSH2, MSH6), lymphovascular, and perineural invasion, and tumor budding. Results: Over the 10 year period 164 ampullary carcinomas were identified with MMRP IHC performed in 46% (76/164) of cases. From 2019 when routine testing was introduced MMRP IHC was performed in 86% (36/42) of cases. A total of 5 cases (6.5%) showed MMRP loss (2 for MSH6, 1 for PMS2, 1 for MLH1 and PMS2, and 1 for MSH2 and MSH6). Four of the 5 cases were intestinal type, and 1 case was pancreaticobiliary type (MSH6 loss). Conclusion: MMRP IHC is being performed in the vast majority of ampullary carcinomas with the rate of MMRP loss similar to published series. Ampullary carcinomas with intestinal differentiation are more likely to have MMRP loss.

References: 1. Narasimhan PA, Jinru S, Tang LH, et al. DNA Mismatch Repair Deficiency in Ampullary Carcinoma: A Morphologic and Immunohistochemical Study of 54 Cases. Am J Clin Pathol, 2010;133: 772–780.

POSTER PRESENTATION #16

Deeper Level sections on BowelScreen Polypectomies – how useful are they and do they impact patient follow-up?

D Martin1, C Ryan1 1 Department of Histopathology, St James's Hospital, Dublin

Background: Deeper level sections (DLS) may be performed on colorectal polypectomies when no lesion is identified on initial sections or to evaluate for higher grade lesions/invasion. While this represents an additional workload for laboratories, additional findings may impact clinical follow-up. This is a retrospective review of colorectal polypectomies from BowelScreen (BS) patients to ascertain the degree to which DLS were contributory. Methods: The audit population was BS specimens where endoscopically polyps were identified, reported by a single pathologist in a subspecialised pathology department from 2018 to 2020, upon which DLS were requested. Cases were extracted from the lab information system using SNOMED codes. Relevant slides were reviewed by the original reporting pathologist. DLS were deemed contributory if they yielded new diagnostic information. Results: 51 cases were included, totalling 64 polypectomy specimens. Of these, initial sections showed normal mucosa in 57 (89%), adenoma with high grade dysplasia in 5 (8%), a hyperplastic polyp and a sessile serrated lesion (SSL) in 1 (1.5%) each. DLS were contributory in 25 (49%) of cases. This group included: • Normal colonic mucosa changed to tubular adenomas with low grade dysplasia in 16 specimens (64%) • Normal colonic mucosa changed to hyperplastic polyp in 7 specimens (28%) • Normal colonic mucosa changed to SSL in 2 specimens (8%) No high grade dysplasia or invasive carcinoma was identified on DLS. The remaining 31 cases (51%) produced no diagnostic change on DLS. Follow-up (using BS guidelines) was changed in 3 patients based on findings following DLS as follows: 1 patients changed from colonoscopy at 3 years to colonoscopy at 1 year, 2 patients changed from routine recall to colonoscopy at 1 year. Conclusions: A change in diagnosis was made in approximately half (49%) of cases where DLS were performed. It translated into a change in follow-up in just 3 of 51 patients (6%). Perhaps the best strategy is to selectively perform DLS only in patients where a change in the number of adenomas/SSLs will alter follow-up. Weighing up the benefits of DLS versus laboratory resources and expanding this study to incorporate larger numbers will be essential in determining future practice changes.

POSTER PRESENTATION #17

The Impact of the COVID-19 Pandemic on Cytopathology Services in the West of Ireland

O'Connor, E., O'Connor, D., Murray, D., Quinn, A.M.

Introduction: Globally, cytopathology services have been greatly impacted by COVID-19, as each procedure leading to a cytology specimen needs a careful risk-benefit analysis incorporating the potential risk of COVID-19 to both the patient and healthcare providers. Aims: To investigate the impact of the COVID-19 pandemic on cytopathology services in the West of Ireland. Methods: We investigated trends in non-gynaecological (FNA and exfoliative) cytology caseloads at UHG for a continuous 24-month period, January 2019 through to December 2020. Results: There was a 25.5% (n=299) reduction in non-gynaecological cytology cases in 2020 compared to 2019. There was a statistically significant increase in the proportion of non-gynaecological cytology diagnosed as malignant in 2020 compared to 2019 (Pearson Chi square=6.56, p=0.012, OR 1.312, 95% CI 1.065-1.615), however the absolute volume of malignant cytology remained similar (n=242 in 2019, n=222 in 2020- a decrease of just 22 cases). There was a notable reduction of 41.1% (n=14) in the absolute volume of BAL cases positive for malignancy in 2020 (n=20) compared to 2019 (n=34), while overall BAL cytology cases fell by 55.6% (n=223). Discussion: There has been a clear reduction in the provision of non-gynaecological cytology services in 2020 compared to 2019. Despite this, the absolute number of malignant diagnoses remained similar, which means the most probable cause of the overall reduction in caseload was a decline in non-malignant cases. This likely reflects a rigorous process identification and testing of patients with a high-risk of malignancy. Certain procedures are more high risk than others in terms of aerosolisation/ COVID-19 risk and thus may have been impacted more than others. Signs of this can be seen by the notable reduction in BAL cytology specimens in 2020.

POSTER PRESENTATION #18

Coin-like lesion of the lung: Think sclerosing pneumocytoma

Sheena Heffernan1, Aoife Doyle1, Anne O'Mahony2, John Garvey2, David Murphy3, Aurelie Fabre1 1- Dept of Histopathology 2- Dept of Respiratory Medicine 3- Dept of Radiology St Vincent's University Hospital Dublin

Here we present a typical case of sclerosing pneumocytoma (SP), in a 29yo lady left lower lobe. This is a rare but important differential for a solitary lung tumour. This benign entity, common in middle-aged, non smoking women, has an excellent prognosis and can be cured with surgical resection alone. Recent reviews have highlighted that this diagnosis is often missed on frozen section and percutaneous biopsy and thus warrants attention. SP (previously named haemangioma, nomenclature regarded as obsolete in the new 2021 WHO classification of thoracic tumours) are histologically heterogenous which makes diagnosis challenging on a biopsy alone or where sampling has been inadequate. They have four morphologies; solid, papillary, sclerotic and haemangiomatous but typically display 2 or more of these 4. SP have two cell types which distinguish it from many of its differential diagnoses; cuboidal epithelial lining cells and polygonal pale stromal cells. Positive staining for Progesterone receptor (PR), epithelial membrane antigen (EMA), thyroid transcription facter-1 (TTF-1), vimentin and cytokeratins, negative staining for neuroendocrine markers, and low ki67 index can help outrule important differentials including primary adenocarcinoma, carcinoid tumour and papillary or alveolar adenoma. Here we summarize the typical clinical, radiological and histological and immunohistochemical findings of this tumour in relation to our case. We describe the important differentials to consider from a radiological and histopathological perspective. Continued emphasis of the key chracteristics of SP will improve knowledge and aid histopathological diagnosis on a small amount of tissue.

POSTER PRESENTATION #19

Olfactory neuroblastoma arising 13 years after a NK/T cell lymphoma and radiotherapy- a case report

Niall O'Neill

This presentation describes the case of a 56 year old woman with a history of NK/T cell lymphoma of her nasal cavity treated with radical radiotherapy in 2008. She presented 1 month ago with epistaxis and an area of thickening in the left nasal passage. CT scanning of neck and thorax, and MRI of head was performed. There was concern regarding recurrent disease in the nasal cavity and paranasal sinuses with abnormal lymph nodes in the neck, left supraclavicular fossa, maxilla and para aortic. Biopsy of the nasal lesion was performed. Histology shows nodular aggregates of tumour supported in a vascular fibrous stroma. There is focal gland formation and areas of cytoplasmic clearing are noted together with a hint of rosette formation. Within some of the basaloid areas, there are regions of neurofibrillary matrix. The cells are strongly positive for AE1/3 and Cam5.2 as well as for synaptophysin and CD56. CD20 and CD3 highlight lymphoid cells in the lamina propria but are negative in the lesional cells. The proliferative index as assessed by MIB-1 is brisk, approaching 80%. This is regarded as a high grade olfactory neuroblastoma. Fine needle aspiration of a cervical lymph node confirmed the presence of malignant cells. Olfactory neuroblastoma, also known as esthesioneuroblastoma, is rare with an annual incidence of 0.4 per million. They arise from sensory olfactory neuroepithelium, however the aetiology in unclear. This case is unusual as the patient had a history of NK/T cell lymphoma and radiotherapy to the region. Hyams grading and Kadish staging systems can be used to further categorise the lesion. The histological diagnosis can be challenging. This presentation discusses the clinical, radiological and pathological findings in this case and in olfactory neuroblastomas in general.

POSTER PRESENTATION #20

The Girl with the Eyeball Tattoo

Gavin Baker, Jena Ferguson, Joseph Houghton

Scleral (ocular) tattooing is a highly controversial cosmetic procedure and is illegal in a number of countries. There a number of recognised complications such as scleral laceration, corneal and anterior segment injury, chronic inflammation, infection and retinal detachment which can lead to chronic pain, blindness and, in some circumstances, exenteration. We herein report a case of a 31 year old female with ocular and cutaneous granulomatous inflammation in response to bilateral scleral tattooing. The patient underwent scleral tattooing of her right eye in July 2020 and her left eye in June 2020. She experienced intermittent paint and light sensitivity in both eyes from the date of both procedures then presented in July 2021 with intolerable pain. In the months prior to presentation she also developed irritation and swelling of multiple longstanding tattoos throughout her body. Clinical examination showed purple colouration of the right conjunctiva and green colouration of the left conjunctiva. Both were thickened and slightly chemotic with associated punctate corneal erosions. Fortunately, visual acuity was unaffected. The tattoos on her limbs and trunk showed raised and erythematous areas suspicious for a sarcoidal granulomatous reaction. Biopsies were taken of both conjunctiva, orbit and eyelid. A punch biopsy from her lower limb was also submitted. Histological examination of the conjunctival biopsies showed granulomatous inflammation composed of well-defined sarcoidal granulomas with numerous multinucleated giant cells containing tattoo pigment. Biopsies taken from the lower leg showed similar findings. Special stains for fungi and acid fast bacilli were negative. The patient has been treated with systemic and topical steroids with mild improvements in her symptoms. This case represents an unusual presentation of sarcoidal granulomatous reaction to tattoo pigmentation. Interestingly, the scleral tattooing procedure appears to have initiated a systemic granulomatous response to longstanding tattoos which requires further investigation.

POSTER PRESENTATION #21

Case Report – Large Cell Type Neuroendocrine Carcinoma of the Gallbladder.

Richard Liddy, Owen MacEneany, Louise Marie Lane, Jaipreet Singh Histopathology Department, Connolly Hospital.

A 52 year old lady presented with biliary sepsis after suffering from biliary colic for one year. She was managed conservatively with cholecystostomy placement and underwent cholecystectomy 3 months later. Intraoperatively, it was noted that the gallbladder was distended and thickened with empyema present, and there was an enlarged, reactive lymph node. Dense pericholecystic adhesions were present and a subtotal cholecystectomy was performed. Macroscopic examination revealed a ragged, dusky serosal surface, wall thickness of 7mm, and a 30mm necrotic fundic lesion. Microscopy showed an exophytic lesion comprising sheets of high grade malignant cells and geographic necrosis. The tumour cells were medium-to-large with minimal cytoplasm, vesicular nuclei, prominent mitoses and nuclear moulding. Immunohistochemistry showed the tumour cells to be positive for AE1/3, chromogranin, synaptophysin and CD56. TTF-1 showed focal positivity. The tumour cells were negative for CK7, CK20, CEA, CDX-2 and CD45. The tumour invaded through the muscle wall to penetrate the serosa. The lymph node was benign. A diagnosis was made of poorly differentiated neuroendocrine carcinoma (PDNEC), large cell type, of the gallbladder (pT3N0Rx). The patient has been referred to a tertiary centre for MDT discussion and further management. Neuroendocrine tumours (NETs) are rare neoplasms that account for just 2% of gallbladder cancers. Current WHO guidelines divide NETs into well-differentiated neuroendocrine tumours (WDNETs) and poorly differentiated neuroendocrine carcinomas (PDNECs) based on molecular differences, as well as mixed neuroendocrine-non-neuroendocrine neoplasms (MiNENs). Pure large cell neuroendocrine carcinoma (LCNEC), without an adenocarcinoma component, is an extremely rare form of PDNEC with less than 20 cases reported in the literature. LCNEC typically sees large polygonal cells grow in nests, trabeculae or rosettes. Tumour cells often have prominent nucleoli and abundant cytoplasm, and stain positive for neuroendocrine markers and pancytokeratin. Mitoses and necrosis are common. Localised disease is treated with extended resection. Treatment of metastatic disease with chemotherapy has shown minimal benefit and the role of radiotherapy is still unclear. The prognosis is poor.

POSTER PRESENTATION #22

Renal endometriosis mimicking a malignancy– a rare case of Reno-Mullerian fusion?

Dr. Diarmuid O'Connor, Mr. Kevin Gerard Byrnes, Mr. Kilian Walsh, Prof. Gerard O'Sullivan, Dr. Teresa McHale.

Endometriosis is a common gynaecological condition characterised by ectopic endometrial tissue growth beyond the uterine cavity. Urinary tract endometriosis represents only 1.2% of all cases, with renal endometriosis accounting for less than 1% of urinary tract involvement. Here, we report an exceptionally rare case of unilateral renal endometriosis which mimicked a neoplasm on imaging studies and explore its possible aetiology. On ultrasound imaging studies, an asymptomatic, 49-year-old, Irish female was found to have a 4.2cm incidental mass at the upper pole of the right kidney. Computed Tomography imaging characterised this lesion as a nodular, thick-walled, enhancing mass with possible central necrosis and perinephric fat stranding, with the key differential diagnoses being a renal malignancy or a haemorrhagic cyst. Histological analysis was recommended to exclude a neoplasm and an open radical nephrectomy was performed. However, histological analysis surprisingly revealed the presence of endometriosis and endosalpingiosis, focally accompanied by a histiocytic inflammatory reaction, prominent lymphoid aggregates and abundant smooth muscle stroma. Previous case reports have identified that endometriosis has the potential to mimic a neoplasm, as the disease presents with multiple components in varying quantities, such as smooth muscle. The fact that renal endometriosis is exceedingly rare, coupled with the prominent smooth muscle component, contributed to the diagnostic dilemma in our case. The right kidney was involved in our case, and in previous case reports where laterally is indicated (10 of 13), the majority of the lesions were also right-sided. The curious right-sided predilection and the frequent absence of endometriosis elsewhere suggest that renal endometriosis may develop from a residual Mullerian remnant in or adjacent to the kidney, rather than through retrograde menstruation or a metaplastic process. The proximity of the paramesonephric duct to the mesonephros during embryogenesis may account for this phenomenon. In conclusion, this was an exceptionally rare case of unilateral renal endometriosis which radiologically mimicked a malignancy, likely originating from ectopic endometrial tissue or possibly Reno-Mullerian fusion.

POSTER PRESENTATION #23

Large loop excision of the transformation zone (LLETZ) diagnoses pre and post the SARS-CoV-2 (COVID-19) pandemic.

Grace O. Crilly, Fergus MacSweeney.

University Hospital Waterford, Rep of Ireland.

Large loop excision of the transformation zone (LLETZ) is a procedure to treat high-risk squamous intraepithelial lesions (SIL) of the cervix. LLETZs are performed if there is abnormal cervical cytology (smear) results and/or the presence of high-risk human papilloma virus (HPV). Human papilloma virus (HPV) is the most common risk factor for the development of cervical squamous intraepithelial lesions (SIL) and invasive squamous cell cervical carcinoma. Thirteen high-risk HPV strains are associated with the development of high-grade SIL (HSIL) and invasive squamous cell carcinoma, with strains 16 and 18 accounting for approximately 70% of cervical neoplasia. In March 2020, the Irish National Cervical Check service introduced routine high-risk HPV testing on all smear tests. HPV screening, along with cytological examination, increases the sensitivity (and decreases the specificity) of detecting high-risk lesions. Our aims were 1) to examine the number of LLETZ carried out from March 2019 – March 2021, and 2) to compare LLETZ diagnoses before and after the introduction of HPV testing. We retrospectively searched the histopathology archives of University Hospital Waterford over 24 months from 01/03/2019 – 29/02/2020 (pre COVID-19 dataset) and 01/03/2020 – 28/02/2021 (post COVID-19 testing dataset). The incidence of SIL between the two years are comparable (LSIL; 36% vs 39% and HSIL; 49% vs 42%). Similarly, the incidence of squamous cell carcinoma is similar (<3% vs 2%) between the two years, as is the rate of benign diagnoses (13% vs 15%). Of note, 18% fewer LLETZ specimens were examined in 2020-2021 (n = 419) vs 2019-2020 (n = 509). It is possible that this is a consequence of the COVID-19 pandemic impact upon services. Overall, we found comparable incidences of LSIL, HSIL and squamous cell carcinoma between LLETZ specimens pre- and post- the COVID-19 pandemic, with fewer specimens examined during the 12 month period coinciding with the pandemic. Follow-up data over the coming years will be needed to monitor the trend in Ireland, and compare to international data.

POSTER PRESENTATION #24

Cervical biopsy diagnoses pre and post the introduction of high-risk human papilloma virus (HPV) testing in Irelands Cervical Check screening service

Grace O. Crilly, Fergus MacSweeney.

University Hospital Waterford, Rep of Ireland.

Human papilloma virus (HPV) is the most common risk factor for the development of cervical squamous intraepithelial lesions (SIL) and invasive squamous cell cervical carcinoma. SIL is categorized as low-grade (LSIL) or high-grade (HSIL). HSIL lesions have a higher risk of progression to invasive squamous cell carcinoma. Thirteen high-risk HPV strains are associated with the development of HSIL and invasive squamous cell carcinoma. HPV 16 and 18 account for approximately 70% of cervical neoplasia. In March 2020, the Irish National Cervical Check service introduced routine high-risk HPV testing on all smear tests. HPV screening, along with cytological examination, increases the sensitivity (and decreases the specificity) of detecting high-risk lesions. Our aims were 1) to examine the number of cervical biopsies carried out from March 2019 – March 2021, and 2) to compare cervical biopsy diagnoses before and after the introduction of HPV testing. We retrospectively searched the histopathology archives of University Hospital Waterford over 24 months from 01/03/2019 – 29/02/2020 (pre-HPV testing dataset) and 01/03/2020 – 28/02/2021 (post-HPV testing dataset). The incidence of SIL between the two years are comparable (LSIL; 53% vs 60% and HSIL; 42% vs 21%). Similarly, the incidence of squamous cell carcinoma is similar (<1% vs <1%) between the two years, as is the rate of benign diagnoses (23% vs 19%). Of note, 18% fewer cervical biopsy specimens were examined in 2020-2021 (n = 1963) vs 2019-2020 (n = 2387). It is possible that this is a consequence of the COVID-19 pandemic. Overall, we found comparable incidences of LSIL, HSIL and squamous cell carcinoma between cervical biopsy specimens pre- and post- routine HPV testing. As HPV testing with the Cervical Screening Service is quite a new diagnostic test, follow-up will be needed in the coming years to assess if there is a change in the incidence of high-risk SILs being identified.

Scientific Abstracts

POSTER PRESENTATION #25

Assessment of inverted maturation/proliferation in dysplastic lesions of the gastrointestinal tract. A diagnostic tool to differentiate dysplastic lesions from mimics.

Mary Mc Elroy BSc MSc (Hons) DEP FIBMS , Samara Fleville MRes MRCS , Iain Cameron FRCPath &; Osama Sharaf Eldin PhD FRCPath

Department of Histopathology, Western Health and Social Care Trust, Northern Ireland

Abstract

Dysplastic lesions of the gastrointestinal system include many categories from flat dysplasia to polyps, which are all known to progress into invasive malignancy. Such lesions can be too difficult to appreciate in cauterised and fragmented biopsies. It is crucial to differentiate such lesions from benign mimics. In dysplastic lesions compared to normal or benign lesions, there is a myriad of atypical changes and uncontrolled proliferation which are associated with phenotypic, cell cycle changes and molecular variations. The diagnostic clues in these dysplastic lesions include crowding of cells, cellular and architectural changes, in addition to, the loss of maturation of surface epithelium and the upward migration of proliferation centre from the basal crypts to superficial parts of the crypts and surface epithelium. The latter can be highlighted by MIB-1 (Ki67) proliferation marker which will give a unique staining pattern to dysplastic lesions in comparison with benign lesions/normal. With increased Ki67 intensity of staining of the superficial part of the crypts and surface epithelium, diagnosis of dysplasia can be made with confidence. This marker can even work in extremely cauterised and fragmented/poorly orientated specimens, which could prevent further intervention to seek another biopsy and hence decrease further patients' admissions and further procedures. We have examined the use of Ki67 in variable dysplastic and non-dysplastic lesions with promising results. The range of pathologies examined include prolapse polyps, tubular adenoma, tubulovillous adenoma, Barrett's oesophagus, hyperplastic polyps, traditional serrated polyps, juvenile polyps, fundic gland polyps, sessile serrated polyps and in dysplasia associated with inflammatory bowel disease and inflammatory polyps We quantitatively analysed 50 specimens from various sites along the gastrointestinal tract for the Ki67 proliferation index. The H&E and their respective Ki67 immunohistochemical stained slides were scanned using the Sectra Pacs digital pathology system. The Ki67 proliferation index was independently scored by the consultant pathologist and the medical scientist trainee GI reporter. We concluded that immunohistochemical staining of Ki67 is a useful aid to highlight the inverted proliferation in dysplastic conditions and is most useful in difficult cases particularly in inflammatory bowel disease cases where reactive atypia is a prominent feature.

POSTER PRESENTATION #26

Development of a semi-automated method for tumour budding assessment in colorectal cancer and comparison with manual methods

Natalie C Fisher, Maurice B Loughrey, Helen G Coleman, Melvin D Gelbard, Peter Bankhead and Philip D Dunne

Tumour budding (TB) is the histological manifestation of local tumour cell dissemination, usually most evident at the invasive front region of a tumour mass. Despite TB being an established prognostic feature in multiple cancers, inconsistent qualitative criteria, definitions and non-standardised reporting have proven an obstacle to routine implementation in pathology practice. Efforts to standardise and automate assessment have shifted from haematoxylin and eosin (H&E)-stained images towards cytokeratin (CK) immunohistochemistry. In this study, we compare manual H&E and CK assessment methods with a new, semi-automated approach built within QuPath open-source software. The semi-automated workflow is entirely transparent and informed by manual budding assessment. Budding was assessed in cores from the advancing tumour edge in a cohort of stage II/III colon cancers (n=186). The total numbers of buds detected by each method were as follows; manual H&E (n=503), manual CK (n=2290) and semi-automated (n=5138). More than four times the number of buds were detected manually using CK compared to H&E. 1734 individual buds were identified on both manual and semi-automated assessments applied to CK images, representing 75.7% of the buds identified manually (n=2290) and 33.7% of the buds detected using the semi-automated method (n=5138). Higher semi-automated bud scores were due to any discrete area of CK immunopositivity within an accepted area range being identified as a bud, regardless of shape or crispness of definition, and to inclusion of tumour cell clusters within glandular lumina (“luminal pseudobuds”). Although absolute numbers differed, semi-automated and manual bud counts were strongly correlated across cores ($\rho=0.81$, $p<0.0001$). All methods of budding assessment demonstrated poorer survival associated with higher budding scores. We present a new QuPath-based approach to tumour budding assessment, which compares favorably to established methods. More importantly, it offers a freely-available, rapid and transparent tool for TB assessment, applicable to whole slide images, which can be used in translational research as a standalone method or as an aid in developing future approaches suitable for clinical implementation.

Undergraduate Abstracts

POSTER PRESENTATION #U1

Identification of treatment effect in negative axillary lymph nodes from patients who received neoadjuvant chemotherapy for primary invasive breast cancer diagnosed as lymph node positive on cytology prior to treatment.

Shauna Galligan (1), Cecily Quinn (1, 2), Aoife Maguire (2) 1. UCD School of Medicine 2. Dept. of Histopathology, St. Vincent's University Hospital & BreastCheck, Merrion Screening Unit

Background: Neoadjuvant chemotherapy (NACT) is increasingly used in the treatment of patients with breast cancer due to its downstaging effect on the primary tumour and axillary lymph node (LN) metastases. Chemotherapy (CT) induces characteristic histologic changes in the regional LNs that enable the pathologist to confirm that the pre-NACT cytologically-proven positive LN has been surgically removed. However, post-NACT LN status and presence of CT effect can be difficult to evaluate because metastases occasionally resolve without fibrosis or other evidence suggestive of CT effect. Our study aims to audit the frequency at which this occurs, and to identify any tumour biological parameters that might predict the absence of CT effect. Methods: Patients with cytologically-proven LN positive disease at presentation, who received NACT at St. Vincent's University Hospital between 2014 and 2017, were identified. H&E slides relating to patients with nodal pathological complete response (pCR) following axillary LN dissection or sentinel LN biopsy were reviewed for CT effect in the LNs, classified as 'classic', 'subtle' or absent. Results: From 2014 to 2017, 126 LN positive patients received NACT, of whom 45 had a nodal pCR. In 38 of 45 (84.5%) CT effect was present in one or more LNs, classified as 'classic' in 35 and subtle in 3. CT effect was not identified in LNs from 7 of 45 (15.5%) patients. 3 of the 7 patients (42%) had breast pCR while 18 of 35 (51%) patients with histologic evidence of LN treatment effect had breast pCR. Of the 7 patients without histologic features of LN treatment effect, the tumour biomarker profile was hormone receptor (HR) +/HER2+ (3); HR +/HER2- (2); HR-/HER2+ (1) and triple negative (1). Conclusions: Following NACT, LN CT effect was identified in 84.5% of patients in our cohort. It is difficult to identify associations or correlations between absence of CT effect and biological characteristics of tumours in this small series. Our findings confirm that nodal pCR is not always accompanied by histological evidence of CT effect.

POSTER PRESENTATION #U2

Sentinel Lymph Node Biopsy In Melanoma: A Retrospective Audit In An Academic Hospital 2019-2020 Compared To 2017-2019

Authors: T Meade 1, K Beauchamp 2, A Lally 3, A Fabre 1,2. 1- University College Dublin School of medicine, 2- Department of Histopathology, St Vincent's University Hospital, Dublin, Ireland. 3- Department of Dermatology, St Vincent's University Hospital, Dublin, Ireland.

Background: The purpose of our study was to assess the rate of positive SLNB and explore any impact of COVID-19 restrictions on referrals to SLNB. Patients with intermediate cutaneous melanoma (1mm- 4mm Breslow thickness) are recommended to undergo sentinel lymph node biopsy (SLNB) for staging.

Methods: Cutaneous melanoma patients who underwent SLNB in our institution between August 2019 and December 2020 were identified using the pathology laboratory system and compared to January 2017 to July 2019.

Results: There were 35 patients during this period, compared 111 in 2017-19. 63% were male, 49% less than 60 yo. 37% of cases involved the lower extremities, 26% upper extremities, 14% head&neck, 23% trunk. 57% were superficial spreading, 35% nodular, 5% lentigo maligna melanoma. 32% were staged pT2, 30% pT3 , 11% pT4. In 2017-2019, 72% of patients were either pT1 or pT2. As capacity for SLNB was significantly reduced following COVID surgery guidelines issued by Melanoma Focus and the British Association of Plastic, Reconstructive and Aesthetic Surgeons (BAPRAS), the procedure was offered to patients with stage pT2 and pT3. Year No. SLNB ≤1mm 1-4mm >4mm 2017 35 11 (32%) 19 (54%) 5 (14%) 2018 30 11 (37%) 18 (60%) 1 (3%) 2019 35 17 (49%) 16 (46%) 2 (5%) 2020 25 4 (16%) 17 (68%) 4 (16%) Positive SLNB were reported in 6 patients (17%), a slight increase from 14% in 2017-19. None of the the minority with thin melanoma (<1mm) had positive SLNB, a decrease from the previous rate of positive SLNB in 11%.

Conclusions: Patients with thin melanoma did not undergo SLNB due to COVID-19 restrictions. The number of patients who underwent SLNB in our institution had more advanced stage, and overall was greatly reduced between August 2019 and December 2020, due to reduced capacity for SLNB during COVID-19.

POSTER PRESENTATION #U3

Audit of Common Bile Duct Brushing Outcomes in a National Hepatobiliary Unit

L Timon 1, N Swan 1,2, D. Gibbons 1,2. 1. School of Medicine and Medical Sciences, University College Dublin, Dublin 4. 2. Department of Pathology, St. Vincent's University Hospital, Elm Park, Dublin 4, Ireland.

Aims To examine the correlation between Common Bile Duct (CBD) brushings and subsequent diagnoses as determined by histological analysis of resection specimens. Materials and Methods 174 patients with at least one biliary brushing were identified between 01-Jan-2019 to 31-Dec-2019. 65 relevant surgical specimens that met inclusion criteria were identified. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. These values were calculated twice, once for malignant cytology alone and the other with malignant and suspicious cytology (C4), counted together as malignant for analysis. Results None of these 65 cases were identified as false positives. When suspicious cytology was considered malignant, there were 12 false negative cases. When suspicious cytology was considered benign, there were 13 false negative cases. Specificity was 100% for both sets of results. For C4 cytology considered benign the sensitivity was 70% and for C4 considered malignant the sensitivity was 78%. PPV was 100% for both sets of results and NPV was 62% and 60% respectively. Conclusion CBD brushing is an accurate and clinically useful diagnostic modality as demonstrated by this analysis. Specificity at 100% is in keeping with internationally published figures. Sensitivity at 78% is higher than many published series.