BLPG Spring/Summer Meeting 2016
at
Nottingham Pathology 2016
9th Joint Meeting of the British Division of the IAP and the Pathological Society
East Midlands Conference Centre, Nottingham
30 June – 1 July 2016

Organiser: Dr Vishakha Sovani, Nottingham University Hospital

Programme

Thursday 30th June 2016

09.00-09.30 Registration & Coffee

09.30-10.30 Business Meeting

10.30-11.05 Introduction to histiocytic, dendritic and other accessory cells - classification and immunophenotype
Dr Elizabeth Soilleux, John Radcliffe Hospital, Oxford

11.05-12.05 **Keynote lecture** - Classification and diagnosis of histiocytic and dendritic cell tumours
Professor Fabio Facchetti, University of Brescia

12.05-12.40 Clinical spectrum of histiocytoses
Dr Mark Bishton, Nottingham University Hospitals

12.40-13.40 Lunch

13.40-14.15 HLH - the clinical syndrome
Dr Chris Fox, Nottingham University Hospitals

14.15-14.50 Histiocytic sarcomas - Pathology and molecular markers including BRAF
Prof Mathew Collin, Nottingham University Hospital

14.50-15.20 Tea break

15.20-16.25 Workshop – Histiocytic lesions

16.25-17.00 Applying Lean to integrated haematological diagnostic pathways
Dr David Clark, Nottingham University Hospitals

Friday 1st July 2016

09.00-10.00 **Keynote lecture** - WHO classification of lymphoid neoplasms 2016
Professor Elaine Jaffe, NCI, Bethesda

10.00 – 11.15 EQA, Presented by Marie Calaminici

11.15-11.30 Coffee break

11.30-12.50 Workshop – Dendritic cell tumours

12:50-13:45 Lunch

13.45-14.45 **Keynote lecture** - WHO classification of tumours of non-lymphoid haematopoietic tissue 2016
Dr Robert Hasserjian, Massachusetts General Hospital, Boston

WORKSHOP VIRTUAL SLIDES LINK

SCHEDULE OF WORKSHOP PRESENTATION

SPEAKERS ARE KINDLY REQUESTED TO PRESENT THEIR CASES IN 7 MINUTES AND ALLOW 3 MINUTES AFTER EACH PRESENTATION FORE DISCUSSION

Thursday 30th June 2016
15.20-16.25

15.20-15.30	WS1 Fabio Facchetti
15.30-15.40	WS2 Ye Lin Hock
15.40-15.50	WS3 Stefan Dojcinov
15.50-16.00	WS4 Ye Lin Hock
16.00-16.10	WS5 Meg Ashton Key
16.10-16.20	WS8 Kikkeri Naresh
16.20-16.25	Discussion

Friday 1st July 2016
11.30-12.50

11.30-11.40	WS6 Jacob Joseph
11.40-11.50	WS19 Matthew Pugh
11.50-12.00	WS9 Paul Matthews
12.00-12.10	WS10 Anurag Joshi
12.10-12.20	WS11 Bridget Wilkins
12.20-12.30	WS20 Emily Shaw
12.30-12.40	WS13 Reza Abdollahi
12.40-12.50	Summary cases WS7, WS14, WS15, WS16, WS17, WS18, WS21

WORKSHOP CASE SUMMARIES

Case WS1

Case submitter and presenter:	Fabio Facchetti
Institution:	Pathology Unit, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy
Case number:	Case 2_B2014-036375
Materials submitted:	H&E, CD11c, CD14, CD163 (virtual slides)
Patient demographics: (gender, age)	Female, 48.
History:	Patient in good general conditions, with abdominal pain since 4 months. In 6/2014 a CT scan reveals intraabdominal lymphadenopathy, which extended to supradiaphragmatic and laterocervical and supraclavicular lymph nodes after four months; no hepato-or splenomegaly. A needle biopsy of an abdominal lymph node was inconclusive, then a supraclavicular lymph node was surgically removed. Blood tests were normal. A bone marrow aspirate showed normal cellularity and maturations.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	Bone marrow aspirate and flow cytometry showed a normal cell morphology and a 0.3% percentage of myeloid blasts (CD34+/CD117+/CD33+). Tumour cells showed a diffuse and intrasinusoidal growth, with occasional hemophagocytosis. Their phenotype was CD4+, CD1a-, CD3-, CD11c+, CD14+, CD20-, CD21-, CD23-, CD30-, CD34-, CD68+, CD117-, CD163+, lysozyme+, myeloperoxidase-, cyokeratins-. Stain for S100 showed focal positive areas; PDL1 was positive; anti BRAF ^{V600E} was negative. PCR analysis for BRAF and other gene mutations pending.
Diagnosis:	**Histiocytic sarcoma (HS)**
Interesting points and references:	Differential from HS and other myeloid leukaemia (myeloid sarcoma (MS)) can be challenging and BM analysis is mandatory. Intrasinusoidal growth is unusual in MS. Expression of PDL1 has been recently reported in 7/14 (50%) HS cases, opening new potential avenues for treatment (Xu J, et al. Am J Surg Pathol. 2016 Apr;40(4):443-53). Data on *BRAF* ^{V600E} mutation on HS are controversial (5 positive cases from 16, in 3 distinct studies)(Haroche J, et al. Blood 2012; 120:2700-2703; Go H, et al. Histopathology 2014; 65:261-272; Liu Q, et al. Virchows Arch. 2016 Jun 3); recently, using NGS mutations others than *BRAF* ^{V600E} have been identified in 3/5 cases of HS, some of them with potential activation of *BRAF* (Liu Q, et al. Virchows Arch. 2016 Jun 3. [Epub ahead of print]).

Case WS2

Case submitter and presenter:	Ye Lin Hock, Daniel Gey van Pittius[1]
Institution:	Walsall Healthcare NHS Trust, University Hospitals of North Midlands NHS Trust[1]
Case number:	L14-22005
Materials submitted:	H&E, CD163, Muramidase, Ki67, CD23
Patient demographics: (gender, age)	Male, 47.
History:	48 year fit man, a welder; non-smoker, minimal alcohol intake with no long term medication, no significant PMH, no allergies; first presented Jan 2012 with swelling in the left neck. Examination showed a 6 cm level 2 neck mass which was smooth, non-tender and non-mobile. Described as 'rapidly growing'. There were no systemic symptoms and no other adenopathy. Excisional biopsy of left neck node (February 2012) showed an inflammatory spindle cell tumour regarded as 'nodal inflammatory pseudotumour'. He was treated with steroids with a 'dramatic response'. The swelling reappeared in mid-2013 and a second left neck node biopsy (July 2013) showed a recurrent disease favouring low grade malignant lymph node stromal tumour. Treated with steroids with good response. Some residual neck disease so left neck dissection performed (September 2014), and this showed 4/31 involved nodes (the submitted sample). Treated with steroid with PET follow-up in 3 months. PET in February 2015 showed a lesion in the liver. Liver core biopsy followed by resection of liver deposit performed in August 2015. Disease recurrence in left neck also confirmed on core biopsy of left neck node. Haematology review May 2016: growing left neck mass, 54 x 55mm; dramatic response to steroids (prednisolone 40mg od) with the mass reducing to less than half the original size. Patient remained well with no night sweats, no pain, no weight loss, working full time, good energy levels. ICE chemotherapy considered but current plan is resection and steroid treatment and withhold more aggressive treatment in view of slow/indolent disease course.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	Negative for cytokeratins, myeloperoxidase, Pax 5, ALK1, CD3, CD10, CD20, CD21, CD23, CD35, CD30, CD79a, CD117, S100, CD1a, CD123, desmin, H-caldesmon, EBER-ISH and ZN. Positive for CD68 (PGM1), CD4 & CD43 with focal CD15 and CD45Ro positivity, CD33 weak+, CD13 weak+. No mutation within codon 600 of BRAF on RT-PCR.
Diagnosis:	**Histiocytic sarcoma**
Interesting points and references:	Difficult to subclassify histiocytic, dendritic & accessory cells tumour. Morphologically, it shows a predominantly spindle cell component, and appeared relatively low grade. Clinically, it has behaved in a relatively low grade / indolent fashion with repeated recurrences, but with a liver metastasis later. Although histiocytic sarcoma is regarded as an aggressive neoplasm with a poor response to therapy, exceptions have been reported, and a histiocytic sarcoma with a predominant spindle cell component has also been described.

Alexiev BA et al. Primary histiocytic sarcoma arising in the head and neck with predominant spindle cell component. Diagnostic Pathology 2007,2:7 doi10. 1186/1746-1596-2-7.
Chen X et al. Complete response after chemotherapy and radiotherapy of a tonsillar histiocytic sarcoma with regional lymph node involvement. Int J Clin Exp Med. 2015; 8(9):16808-16812.

Case WS3

Case submitter and presenter:	Stefan Dojcinov
Institution:	All Wales Lymphoma Panel, University Hospital of Wales, Cardiff
Case number:	L690/07
Materials submitted:	HE, CD4, CD45, CD68, CD21, CD35
Patient demographics: (gender, age)	Female, 33.
History:	This young lady presented with a lump in her left breast. She had a strong family history of BRCA1 positive breast cancer. This was surgically and radiologically suspicious of a neoplasm and she underwent a trucut needle biopsy. This was initially reported as an inflammatory process and she was followed up. Six months later, the lesion had significantly increased in size to approximately 5.5 cm. Ipsilateral palpable lymphadenopathy had developed. The tumour was resected.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	Microscopically, this was a well circumscribed lesion within the breast parenchyma displaying a rich lymphocytic and histiocytic infiltrate with scattered variably sized pleomorphic stellate, fusiform and epithelioid cells. Some of the cells displayed Reed-Sternberg/Hodgkin-like morphology. There was prominent emperipolesis. Patchy fibrosis was noted. There were occasional mitotic figures. A wide differential diagnosis was proffered before referral. IHC: There was no expression of EMA, AE1/AE3, CAM5.2, CK14, CK5/6, TTF1, SM actin, desmin, CD34, S100, HMB45, CD117, AFP, PLAP, CD1a, CD45, CD15, ALK1, CD3, CD5, CD4, CD8,, CD30, CD43, CD138, granzyme or TIA1. ISH for EBER was negative. The large tumour cells showed diffuse expression of vimentin together with patchy and variable positivity for CD21, CD23, CD35 and podoplanin. No cytogenetic or molecular investigations were performed.
Diagnosis:	**Follicular dendritic cell sarcoma**
Interesting points and references:	The patient was managed by wide local excision and local radiotherapy (50Gy). 5 years after initial presentation she developed contralateral ductal carcinoma and underwent bilateral mastectomy followed by chemotherapy and radiotherapy. She is currently alive with no evidence of either follicular dendritic cell sarcoma or breast cancer (8 years after initial presentation). This is a rare breast presentation of follicular dendritic cell sarcoma. Diagnosis may be difficult if a small range of specific follicular dendritic cell markers are not included in the diagnostic panel. While most cases display spindle cell morphology, this case was characterised by a variety of patterns with stellate and epithelioid cells in a rich lymphoid background with very marked emperipolesis. These inflammatory pseudotumour-like morphological features are more often seen with the EBV positive intraabdominal variant of follicular dendritic cell tumours, however, this case showed no EBV expression.

Perez-Ordonez et al. Semin Diagn Pathol 1996, 15:144-154
Chan et al. Cancer 1997, 79:294-313
Cheuk et al. Am J Surg Pathol 2001, 25(6): 721–731
Grogg et al. Am J Surg Pathol 2004, 28: 988-998
Shia et al. Virchows Arch. 2006, 449(2):148-158
Li et al. Am J Surg Pathol 2014;38:646–653
Facchetti et al. Semin Diagn Pathol. 2016 May 13

Case WS4

Case submitter and presenter:	Ye Lin Hock, Jane Walker, Sara dyer[1], VP Sumathi[2]
Institution:	Walsall Healthcare NHS Trust, West Midlands Regional Genetics Laboratory (Birmingham Women's NHS Foundation Trust)[1], Royal Orthopaedic Hospital Birmingham NHS Foundation Trust[2]
Case number:	13-3092
Materials submitted:	HE, S100, CD34, CD30. CD45 (LCA), CD43 on needle bx 13-2816
Patient demographics: (gender, age)	Male, 6.
History:	Presented with 4 weeks history of rapidly growing groin lump (4 cm mass on medial aspect of right thigh). Following the diagnosis on needle biopsy (13-2816), complete excision with a wide margin was performed (the submitted H&E). Macroscopically, the mass was a 55 x 45 x 40 mm well-circumscribed, lobulated, firm white mass. The patient did not receive any chemotherapy or radiotherapy. No other disease was identified on staging CT & MRI. Regular follow up (3 years now) showed no evidence of any tumour recurrence (local or metastatic), and patient is clinically very well (fastest in his rugby team!!).
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	**IHC**: Negative for CD15, cytokeratins, MyoD1, Stat6, CD99, CD21, CD23, CD35, CD1a, CD3, CD20, CD79a, Pax5, CD45Ro, CD56, CD117, myeloperoxidase, melan A, EBER-ISH, FXIIIa. Only weak focal positivity for CD68 (PGM1), CD33, CD4. **Cytogenetics** (unstimulated cultures examined by G-band chromosome analysis): deletion of most of 17p - 46,XY, add(9)(p1),del(17)(p1)[4]; 46,XY[8] **SNP array**: Confirmed 'add (9p) & del (17p)'. Loss of a ~45Okb region within 9q21.13 including CDKN2A; Loss of a ~8.9 Mb region of 9p21.1 to p21.3; Loss of a ~1.4 Mb region within 17p11.2. Additional cytogenetically cryptic abnormalities detected: Duplication of 17q and further deletions within 1q & 3q [Loss of one copy of ~60Okb region of 1q22q23.1 including PRCC & NTRK1; Loss of the majority of 3q; including loss of SPECC1; Gain of 17q (~25.7 Mb)] **RT-PCR** (on needle bx 13-2816) has ruled out infantile fibrosarcoma & mesenchymal chondrosarcoma.
Diagnosis:	**Interdigitating dendritic cell sarcoma (IDCS) (by WHO 2008)**
Interesting points and references:	Difficult to subclassify histiocytic, dendritic & accessory cells tumour. Morphologically, it closely resembles follicular dendritic sarcoma, but is negative for FDC markers. Only one published case series of paediatric IDCS can be identified and only 2 are soft tissue tumour in that series. Although chromosome 17 abnormalities are the most common abnormality observed by FISH in clonally related histiocytic/dendritic cell sarcoma associated with CLL/SLL, to our knowledge, this is the first paediatric (de novo) IDCS with a confirmed 17p deletion and the first detailed description of SNP array findings. CD34+ is unusual in stromal derived dendritic cells (follicular dendritic cells & fibroblastic reticular cells) or in Langerhans cells and interdigitating dendritic cells of myeloid derived dendritic cells, but is well-described in a subtype of myeloid derived dendritic cells, known as dermal / interstitial dendritic cells, which are found in soft tissue and dermis. CD34+ and clinical behaviour (a low grade fashion with no recurrence after complete excision and no metastasis) of our case, in our opinion raise the possibility that it shows a degree of interstitial dendritic cell differentiation,

even though this is FVIIIa negative. As IDC are present in T-cell areas of lymphoid organs only, extra-nodal IDCS, especially of soft tissue origin may be derived from interstitial dendritic cells / show interstitial dendritic cell differentiation.

1. Pillay K et al. Interdigitating dendritic cell sarcoma : a report of four paediatric cases and review of the literature. Histopathology 2004, 44;283-291.
2. Shao H et al. Clonally related histiocytic/dendritic cell sarcoma and chronic lymphocyti leukemia/small lymphocytic lymphoma: a study of 7 cases. Modern Pathology (2011) 24,1421-1432.

Case WS5

Case submitter and presenter:	Meg Ashton-Key
Institution:	University Hospital Southampton
Case number:	11HS33018H (H&E also 11S00015650)
Materials submitted:	H&E CD56, TDT, LCA, CD4, CD7, Ki67
Patient demographics: (gender, age)	Male, 80.
History:	Multiple skin nodules on chest, ?metastases.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	Bone marrow flow contained abnormal cells are positive for CD56+ and CD45(weak) and comprised ~1% of total nucleated cells.
Diagnosis:	**Blastic plasmacytoid dendritic cell neoplasm**
Interesting points and references:	This patient did not respond to treatment and died a few months after diagnosis.

Case WS6

Case submitter and presenter:	Jacob Joseph
Institution:	Royal Preston Hospital
Case number:	N14-300
Materials submitted:	H&E, CD68
Patient demographics: (gender, age)	Male, 51.
History:	History of post chiasmatic suprasellar SOL, previous biopsy inconclusive, complains of visual problems, lesion growing in right side, brain biopsy, frontal right
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	These are fragments of tissue containing n infiltrate mainly of histiocytes with a diffuse scattering of lymphocytes intervened by collagen fibres. Some fragments appear to show condensation of fibrous tissue at the surface. There are small focal collections of neutrophils. Eosinophils and plasma cells are seen rarely. The histiocytes have abundant foamy cytoplasm and are PAS negative. No typical emperipolesis is present. The nuclei are rounded and uniform and there are occasional multinucleate histiocytes. No Touton giant cells are present. There is no evidence of a glioma or a pituitary granular cell tumour. Immunohistochemistry: CD68 shows strong positivity in the histiocytes. Some of the cells show S100 positivity but this is very weak. CD1a is negative. The lymphoid infiltrate is mainly composed of T cells. Neurofilament and synaptophysin reveal a few nerve twigs near the surface of the lesion. EMA labels the surface leptomeningeal cells. GFAP and IDH1 are negative in the cells. Ki67 shows a few scattered positive cells.
Diagnosis:	**Erdheim-Chester disease**
Interesting points and references:	This is a histiocytic lesion the differential diagnosis of which includes Langerhans cell histiocytosis, Rosai-Dorfman disease (RDD) and “non-Langerhans” histocytosis. Diagnosis relies on pathological features but also on typical clinical/radiological presentation. The lack of CD1a and S100 are somewhat against LCH and RDD respectively. The overall morphology and immunohistochemical results together with the clinical presentation tend to favour Erdheim-Chester disease (ECD). Most recent classification puts ECD in the same group with LCH, abandoning the approach of dichotomous classification of non-LCH and LCH types. This is justified by the fact that 20% of patients with ECD have LCH, both have clonal mutations involving genes of the MAPK pathway and in 80% of cases of either blood monocytes harbour the same mutations. BRAF mutational analysis represents a diagnostic requirement and facilitates novel targeted therapy. 1. Non-Langherhans cell histiocytosis with isolated CNS involvement – an unusual variant of Erdheim Chester disease . Alexandria Conley et al, Neuropathology 2010, 30, 634-647 2. Consensus guidelines for the diagnosis and management of Erdheim Chester disease. Diamond et al. Blood 2014, 124(4): 483–492. 3. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Emile et al. Blood. 2016;127(22): 2672-2681

Case WS7

Case submitter and presenter:	Matthew Pugh, Stefan Dojcinov
Institution:	All Wales Lymphoma Panel, University Hospital of Wales, Cardiff
Case number:	L981/10
Materials submitted:	HE, CD33, CD34, CD45, MPO
Patient demographics: (gender, age)	Female, 72.
History:	The patient initially presented in 2009 with bruising and mild pancytopenia. Her bone marrow aspirate and trephine biopsy showed features in keeping with myelodysplastic syndrome (RAEB-1). Her bone marrow shoed features of RAEB-1 with 10% myeloblasts IPSS 1. She was managed conservatively with good clinical response. In 2010 she presented with a 2 cm nodule on left scalp, appeared following trauma. Clinically suspicious of infected haemangioma or an abscess. "Leukaemia cutis" was diagnosed. The patient was treated with Azacitidine but acquired hospital pneumonia and died 11 months after presentation.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	Skin biopsy showed ulcerated lesion with a diffuse infiltrate of primitive looking medium size and large blasts with regular round nuclei and amphophilic and acidophilic cytoplasm. IHC: CD45+, MPO+, CD13+, CD15+, CD33+, CD34+/-, CD117+/-, CD43+, CD68+ 2009 BM flow cytometry: 10% blasts CD34+/CD117+/CD13+/CD33var/HLA-DR+; Mature monocytes (CD64+++/CD14+) comprise 4% of total nucleated cells. Bone marrow karyotype 46 XX, no clonal abnormalities RTPCR: INV16, t(8;22), FLT3 all negative. 2011 BM flow cytometry: 43% myeloid blasts, with a CD13+/CD33 variable/CD34+/CD117+/DR+/TdT-+/MPO-+ phenotype. The rest of the cells are mostly CD15+, with low side scatter (probably dysplastic granulocytes). RTPCR: RUNX1-RUNX1T1: neg, CBFB-MYH11:neg, FLT3 ITD, TKD and NPM1:WT. Bone marrow karyotype: 47,XX,+8[3]/46,XX[7]
Diagnosis:	**Myeloid sarcoma (Extramedullary myeloid tumour) evolving from MDS**
Interesting points and references:	Myeloid sarcoma represents a tumour masses, consisting of myeloid blasts presenting at an extra-medullary site. It may follow known MPN or MDS or develop in the course of de novo AML, simultaneously, preceding it or as a relapse. Diagnosis could be problematic and poses a differential diagnosis with non-haematological malignancies, blastic plasmacytoid dendritic cell tumour and histiocytic sarcoma when presentation is unaccompanied by clinical features of leukaemia.

Case WS8

Case submitter and presenter:	Kikkeri Naresh
Institution:	Hammersmith Hospital, Imperial College Healthcare NHS Trust
Case number:	KN1
Materials submitted:	HE, CD45, CD1a, CD4, CD68, HLADR, lysozyme, S100, Ki67
Patient demographics: (gender, age)	Male, 21.
History:	Skin / soft tissue lesion on back
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	Lesional cells were positive for CD45, CD1a, HLADR, CD4, CD68R, and lysozyme. There was only focal positivity for S100. The cells were negative for langerin, CD163, CD3, CD20, CD21, CD23, CD35 (most cells), CD30, ALK1 and Melan-A. The Ki-67 proliferation index was estimated at about 40-50%. There was no significant increase in p53 staining. Occasional cells were positive for cyclin D1.
Diagnosis:	**Indeterminate cell histiocytosis**
Interesting points and references:	This diagnosis would best be supported by demonstration of lack of Birbeck granules on electron microscopy.

Case WS9

Case submitter and presenter:	P Matthews
Institution:	University Hospitals Coventry and Warwickshire
Case number:	H16-11378
Materials submitted:	HE, S100, CD1a, CD68
Patient demographics: (gender, age)	Male, 32
History:	
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	
Diagnosis:	**Langerhan's cell histiocytosis**
Interesting points and references:	

Case WS10

Case submitter and presenter:	Anurag Joshi, Stefan Dojcinov Acknowledgement: Jason Hornick, Boston
Institution:	All Wales Lymphoma Panel University Hospital of Wales Cardiff
Case number:	L,933/14
Materials submitted:	H&E, CD68, CD4, CD123, CD56, CD11c
Patient demographics: (gender, age)	Female, 61.
History:	2x3cm right nasal vestibule lesion- clinically ?pyogenic granuloma ?squamous cell carcinoma ?lymphoma ?basal cell carcinoma. Previous biopsy- atypical histiocytoid infiltrate- excision recommended.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	Negative for cytokeratins, myeloperoxidase, CD20, CD21, CD23, CD35, CD3, desmin, CD1a, langerin, CD15, CD43, CD56, CD117, CD34, HHF35. Positive for CD68 (PGM1), CD4, CD11c, CD163, PU1. CD123 +/-, Focal S100+
Diagnosis:	**Xanthogranuloma**
Interesting points and references:	1/3 of xanthogranulomas show some expression of S100 protein. Although xanthogranulomas are most often seen in the skin of young children, occasional examples may be encountered in adults. The proportion of Touton Giant cells is quite variable; in some cases they are scarce or even entirely absent. Xanthogranulomas are benign, although some patients may develop multiple lesions. Adult Xanthogranuloma is usually solitary and persistent. Mature lesions contain foamy cells, foreign body giant cells and Touton type Giant cells as well as macrophages, lymphocytes and eosinophils. Older, regressing lesions show proliferation of fibroblasts and fibrosis that replace part of the infiltrate. Of interest is the CD123 staining pattern in this case which in small biopsies may lead one to consider a differential diagnosis of blastic plasmacytoid dendritic cell neoplasm (BPDCN)/ Leukaemia cutis (LC)- rare cases of BPDCN have been described with marker loss for CD56 (especially in relapses) and CD123 is positive in many cases of LC.

Ref:

1. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages
2. Jean-Francois Emile et al; Blood, 2 June 2016.Volume 127, Number 22.
3. Haematopathology. Jaffe et al. 2011 Elsevier Saunders
4. Immunophenotypic analysis of myeloperoxidase-negative leukemia cutis and blastic plasmacytoid dendritic cell neoplasm. Am J Clin Pathol 2012 Mar;137(3):367-76.
5. Cronin DM et al

Case WS11

Case submitter and presenter:	Bridget Wilkins
Institution:	St Thomas' Hospital
Case number:	OC-12-18189
Materials submitted:	HE, PGMI (CD68R), CD3, MUM1, CD20, PAS
Patient demographics: (gender, age)	Male, 25.
History:	HIV positive, night sweats, rigors and poor appetite. Bilateral cervical lymphadenopathy for several months, 30mm in maximum dimension. Also smaller axillary and inguinal LNs.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	
Diagnosis:	**Mycobacterial tumour (MA1) mimicry histiocytic neoplasm / inflammatory pseudo tumour**
Interesting points and references:	

Case WS12

Withdrawn from Workshop

Case WS13

Case submitter and presenter:	Reza Abdollahi, Meg Ashton-Key
Institution:	University Hospital Southampton
Case number:	
Materials submitted:	BM aspirate 6081255T BM trephine 06HS17991Q H&E, giemsa, retic, PAS
Patient demographics: (gender, age)	Male, 3.
History:	Incidentally found to have splenomegaly and on investigation had thrombocytopenia. White cell count and haemoglobin normal.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	Well child with normal growth and development.
Diagnosis:	**Gaucher's disease**
Interesting points and references:	Now 13 years old and currently well on enzyme replacement therapy.

Case WS14

Case submitter and presenter:	Areeg Abbas, Vishakha Sovani
Institution:	Nottingham university Hospitals
Case number:	15D54066
Materials submitted:	HE, LCA, CD4, CD68, CD34, TDT
Patient demographics: (gender, age)	Male, 7.
History:	Diagnosed with T-ALL 18 months prior was on maintenance chemotherapy and in complete bone marrow remission. He presented with spiking temperature and pain and swelling of right leg, clinically thought to be osteomyelitis. Tissue obtained at debridement surgery for suspected osteomyelitis.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	No evidence of recurrent ALL
Diagnosis:	**Histiocytic sarcoma in a patient with T-ALL**
Interesting points and references:	Interesting points and references: PCR analysis showed BRAF mutation and clonal TCR gene rearrangement. Patient did not have evidence of recurrent ALL. References: Histiocytic sarcoma and Acute Lymphoblastic leukaemia, a rare association, Indian J Hematol Blood transfu: Sept 2014, 30(supple); S305-S308

Case WS15

Case submitter and presenter:	Areeg Abbas, Vishakha Sovani
Institution:	Nottingham university Hospitals
Case number:	15D50941
Materials submitted:	H&E, LCA, CD4, CD68, CD34, TDT
Patient demographics: (gender, age)	Male, 75.
History:	Known hairy cell leukaemia with multiple relapses and remissions, presented with fever and a large mass over right iliac bone
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	Bone marrow showed hairy cell leukaemia
Diagnosis:	**Histiocytic sarcoma in a patient with hairy cell leukaemia**
Interesting points and references:	Interesting points and references: PCR analysis showed BRAF mutation and clonal IgH gene rearrangement. References: BRAF mutation in a patient with Histiocytic sarcoma arising from hairy Cell Leukaemia, Journal of Clin Oncol; Vol 32, No35; Dec 2014

Case WS16

Case submitter and presenter:	Kikkeri Naresh
Institution:	Hammersmith Hospital, Imperial College Healthcare NHS Trust
Case number:	KN2
Materials submitted:	HE, fascin, S100, P53, Ki67
Patient demographics: (gender, age)	Male, 88.
History:	Right neck lump CT scan revealed a necrotic lymph node at the upper border of parotid with two associated pathological nodes at level 2.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	
Diagnosis:	**Spindle cell malignant tumour; features are compatible with interdigitating dendritic cell sarcoma.**
Interesting points and references:	Tumour cells expressed vimentin, S100 (strong), fascin (weak) and P53. They were negative for CD20, PAX5, CD3, CD4, CD8, CD30, ALK, EBER, CD21, CD23, CD68R, CD163, Factor XIIIa, CD1a, Langerin, myeloperoxidase, Keratins (CK5, MNF116 and AE1/AE3), 34betaE12, PGP9.6, CD56, NFP, Melan A, HMB45, SMA, desmin and TTF1. Ki-67 expression was ~60%.

Case WS17

Case submitter and presenter:	Kikkeri Naresh
Institution:	Hammersmith Hospital, Imperial College Healthcare NHS Trust
Case number:	KN3
Materials submitted:	HE, S100, CD30, CD68, CD168, Ki67
Patient demographics: (gender, age)	Male, 65.
History:	Cervical lymph node enlargement
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	
Diagnosis:	**Features are suggestive of Histiocytic sarcoma**
Interesting points and references:	Lesional cells were positive for CD45, CD68, CD68R and CD163, and focally positive for CD30 and S100. They were negative for CD1a, ALK, CD2, CD3, CD5, CD7, CD20, Desmin, MNF116, Cam5.2 and EBER. The Ki67 proliferation index was up to 30%. The small lymphocytes within the infiltrate were largely CD8+ T cells and CD20+ B cells

Case WS18

Case submitter and presenter:	Bridget Wilkins
Institution:	Guy's and St Thomas', London
Case number:	SP-16-2242
Materials submitted:	HE, CD79a, CD3, CD4, CD56, TdT
Patient demographics: (gender, age)	Male, 82.
History:	Purplish indurated plaque on right side of chest wall. Clinical differential diagnosis of Merkel tumour or cutaneous lymphoma
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	
Diagnosis:	**Blastic plasmacytoid dendritic cell neoplasm**
Interesting points and references:	Superficial mimicry of a low grade B-NHL in skin but IHC atypical initially leading to wider staining + correct diagnosis. Also, BM is packed, which would never happen with cutaneous B-NHL

Case WS19

Case submitter and presenter:	Matthew Pugh, Stefan Dojcinov
Institution:	All Wales Lymphoma Panel, University Hospital of Wales, Cardiff
Case number:	L513/16
Materials submitted:	HE (lymph node), HE (skin), HE (bone marrow), CD4, CD68, CD123, CD56
Patient demographics: (gender, age)	Male, 54.
History:	This patient presented with a 6 week history of rapidly developing erythematous nodular rash over back, lateral trunk, groin folds, scalp and chin. Clinically a differential diagnosis including drug eruption, atypical infection, Kaposi sarcoma or paraneoplastic change was considered. This was followed by abdominal pain and right leg swelling. He was treated with Flucloxacillin for possible cellulitis of right leg and managed conservatively for possible pancreatitis. His laboratory investigations showed mild pancytopenia, LDH 560 and derange liver function tests which improved gradually. CT revealed mediastinal, retroperitoneal and intraabdominal lymphadenopathy together with diffuse cutaneous changes, which could be in keeping with lymphoma. There were also diffuse pulmonary changes which might represent pulmonary involvement. The clinical impression was of probable lymphoma. Skin biopsy, lymph node biopsy and bone marrow trephine biopsy with an aspirate were taken.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	The lymph node core showed a diffuse infiltrate of cells similar to those seen in the skin. These were medium-size blasts with amphophilic cytoplasm and primitive looking stippled chromatin. The tumour shows strong expression of CD4, CD56, lysozyme and CD68, with patchy weak expression of CD123 and no expression of MPO. CD45 and CD2 were also positive with patchy expression of CD15. A range of other T-cell, NK and cytotoxic and acute leukaemia markers were negative. Flow cytometry from the biopsy material showed the following phenotype: CD3-, CD4+, CD16-, CD56+, CD123-/+, CD68+. From bone marrow aspirate, the same phenotype was noted, also CD13+, CD14+, CD15+, CD117-, CD34-, CD33+, CD36+, CD64+, CD85k+, CD303-. Monoblasts were identified morphologically. No MLL gene abnormality; Karyotype : 49, XY, add 3(p22), +8, +8 +mar.
Diagnosis:	**Acute monoblastic leukaemia**
Interesting points and references:	In the differential diagnosis includes blastic plasmacytoid dendritic cell neoplasm (BPDCN), acute leukaemia of ambiguous lineage (ALAL) and acute monoblastic leukaemia. BPDCN is mostly interrogated with CD4, CD56 and CD123 and is characterised by core expression of these markers in the absence of other T-cell and NK lineage markers and importantly also lacking expression of myeloid markers, specifically CD11c, CD14 and CD163. In addition to CD123, other specific markers associated with this tumour are CD303, TCL1, CD2AP, BCL11a and SPIB. Other markers which could be seen in the neoplasms could occasionally be seen including CD2, CD7 CD 33, TdT, CD38, CD117 and CD68, importantly, CD68 is usually weakly expressed and in a fashion of Golgi dot staining. However, markers usually associated with BPDCN such as CD56 and CD123 could be seen in other leukaemias. In circumstances where tumours are found to share some phenotypic features but not all of those associated with BPDCN, it is advised that a diagnosis of acute leukaemia of ambiguous lineage is considered. A set of features which have recently been described may complicate diagnosis. As plasmacytoid dendritic cells are transformed, it has been shown that they tend to lose

the markers of specific differentiation, which includes those which have been considered highly specific and diagnostic such as CD123 and TCL1. Moreover, in a small proportion of cases, marker losses are multiple. CD303 has recently been shown to be particularly useful for use in flow cytometry probably representing the highest specificity and very high sensitivity in comparison to other markers of this tumour. Acute leukaemia of ambiguous lineage comprises cases were no particular differentiation could be verified or those which display mixed phenotypes. Our case expressed a number of monocytic differentiation markers and T-cell markers, however, importantly, in this context an essential requirement for T-cell differentiation is expression of CD3, which is here lacking. Acute monoblastic leukaemia requires monocytic morphology or phenotype in 80% of the lesional cells. Phenotypically the constant markers are HLADR, CD13, CD33, CD15 and CD65. It is required that at least two markers of monocytic differentiation including CD4, CD14, CD11b, CD11c, CD64, CD68, CD36, CD136 and CD85k are represented. In summary, monoblastic leukaemia may represent that close differential diagnosis with BPDCN. In this context multidisciplinary laboratory approach is required. Flow cytometry plays a significant interrogated modality providing application of a number of antibodies including those most specific such as CD303. It is also worth keeping in mind that a number of markers associated with BPDCN could be seen in other leukaemias, however, on the other hand, BPDCN could be characterised by a significant loss of expression of specific markers.

Montes-Moreno et al. Blood. 2013;121(4):643-647
Cota et al. Am J Surg Pathol 2010;34:75–87
Boiocchi et al. Blood 2013; 122(2):296-297
Arber et al. Blood. 2016; 127(20):2391-2405

Case WS20

Case submitter and presenter:	Emily Shaw, Meg Ashton-Key
Institution:	University Hospital Southampton
Case number:	15HS34818L
Materials submitted:	HE
Patient demographics: (gender, age)	Male, 13.
History:	Enlarged submandibular lymph node, otherwise well. Previous B-ALL age 1.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	
Diagnosis:	**Rosai-Dorfman disease**
Interesting points and references:	Rosai-Dorfman disease has been reported in occasional patients with ALL but it is uncommon.

Allen MR, Ninfo V, Viglio A, et al. Sinus histiocytosis with massive lymphadenopathy (Rosai–Dorfman disease) in a girl previously affected by acute lymphoblastic leukemia. Med Pediatr Oncol 2001;37:150–152.

Case WS21

Case submitter and presenter:	Jessie Wu, Vishakha Sovani
Institution:	Nottingham university Hospitals
Case number:	16D12200
Materials submitted:	HE, ZN and bone marrow aspirate
Patient demographics: (gender, age)	Male, 54.
History:	One week history of malaise, weight loss and pyrexia. Known hypertensive with haemodialysis dependent end stage renal failure.
Other relevant results: (e.g. PCR, FISH, Flow cytometry, etc.)	Pancytopenia, hypoalbuminaemia, markedly elevated levels of C-reactive protein, alkaline phosphatase, ferritin, and lactate dehydrogenase. Coagulopathy with prolonged prothrombin time and activated partial thromboplastin time was noted. D-dimer level was also markedly elevated and fibrinogen level was within normal range. Chest X-ray revealed clear lung fields with bilateral small pleural effusion.
Diagnosis:	**Hemophagocytic lymphohistiocytosis secondary to mycobacterial infection**
Interesting points and references:	TB is a recognised cause of secondary HLH. The diagnosis of TB was made on the bone marrow trephine along with HLH References: Tuberculosis -associated hemophagocytic syndrome; Lancet Infect dis 2006, Jul; 6(7): 477-84 HLH associated with myocobacterial tuberculosis, BMJ 2015 April 13