ROYAL MARSDEN NHS FOUNDATION TRUST - HISTOPATHOLOGY REPORT
714203: [redacted] - NHS Number: 644 925 8292

Lab No	3825/20	**Reported**	22 May 2020	**Pathologist**	DR HALLIN/DR THWAY
Source	Internal Operation	**Sample Received**	20 Mar 2020	**Ward**	CRITICAL CARE UNIT (CHELSEA)
Sex	FEMALE	**Age**	18	**Branch**	FULHAM ROAD
Clinical Diagnosis		**Operation**	19 Mar 2020	**Consultant**	SMITH,MR M J F

SITE	DIAGNOSIS
A SOFT TISSUE AND OTHER CONNECTIVE TISSUE (T1X005)	NEOPLASM MALIGNANT (M80003)
B STOMACH (T63000)	NEOPLASM MALIGNANT (M80003)

18 YEAR OLD FEMALE WITH A LARGE TUMOR OF THE POSTERIOR GASTRIC WALL, CLINICALLY THOUGHT TO BE PAWS-GIST. THIS HAS PREVIOUSLY BEEN EMBOLIZED. NO PREVIOUS BIOPSY IS NOTED. THIS SPECIMEN: TOTAL GASTRECTOMY, ADRENALECTOMY, SPLENECTOMY AND DISTAL PANCREATECTOMY.

MACROSCOPY
Total gastrectomy: The specimen comprises stomach measuring 120 mm in length along the lesser curve and 240 mm in length along the greater curve. Attached is the omentum measuring 140 x 90 x 15 mm.The adrenal gland is identified and measures 25 x 5 x 5 mm. A portion if pancreas is included and measures 50 x 20 x 30 mm. The spleen is also present and measures 120 x 70 x 30 mm. A separate segment of small bowel is also received in the container and measures 120 x 30 mm. There is a large tumor with necrotic and haemorrhagic cut surface, measuring 90 x 90 x 10 mm. 1. Proximal resection margin 2. next to proximal resection margin 3. and 4. Distal resection margin 5. adrenal gland 6. adrenal gland 7 to 14. Tumor and adrenal gland (big blocks) 15 and 16. Tumor for tests 17 to 26. Greater curve lymph nodes 27 and 28. Omentum 29. separate segment of small bowel (resection margin) 30 opposite resection margin 31. Mesentery small bowel 32. mesentery small bowel 33. Small bowel sampling 34 and 35. Splenic lymph nodes 36 to 39. Spleen. 40-41 Tumor for test (MT). Tissue remains

HISTOLOGY
Sections from the maximally 90mm tumor show a large, necrotic and edematous, cellular neoplasm composed of spindle cells arranged in long or frequently intersecting fascicles. The tumor appears to arise from the muscularis propria, and extends to the submucosa with likely focal infiltration, with prominent ulceration here (slide 8). There is an infiltrative border, and the tumor appears to go penetrate the muscularis propria and to focally infiltrate the mesenteric adipose tissue, which is of mature type. The tumor comprises cells with ovoid to elongated nuclei and small nucleoli, with relatively abundant, darkly eosinophilic cytoplasm. The cells are plump, with occasional intranuclear inclusions. Cellular atypia ranges from minimal to focally mild. Occasional cells are slightly more polygonal, with abundant granular eosinophilic cytoplasm. No cross striations or rhabdomyoblasts are identified. Focally, the stroma is more myxoid (slide 8), with cells dispersed in strands and cords. No morphologic epithelial differentiation or heterologous elements are seen. Mitotic figures do not appear prominent, with an index of up to 2/25 hpf, without notable atypical forms. There is a moderate intermingled inflammatory infiltrate, of predominant small lymphocytes, with some mast cells. Plasma cells do not appear prominent. There is focal tumor necrosis (eg slide 7, 41), with surrounding mixed inflammation, likely amounting to microabscess formation.

The tumor is diffusely and strongly positive for CD10, and strongly positive for AE1/AE3 in most cells. There is very scant focal positivity for CAM5.2. Only scanty occasional cells show expression of MNF116, but the tumor is largely negative for this. There is weak to moderate focal cytoplasmic ALK expression. There is only scanty focal positivity for h-caldesmon, although this marker is often aberrantly overexpressed in this laboratory. CD68 is difficult to interpret, and shows strong expression in many cells, which may represent a histiocytic expression, with weaker expression in the background, and this is of uncertain significance. CD163 appears to stain background histiocytes only, but not tumor cells. The tumor is negative for EMA, desmin, SMA, myogenin, CD117, DOG1, S100 protein, SOX10, ERG, CD31 (positive in intervening histiocytic population), CD34, STAT6, MUC4, p16, CDK4, EBER, bcl-2, CD99, CEA, CK5/6, CK7, CK20, CK903, p63, GATA3, PAX8, TTF1, napsin-A, HepPar1, CD56, chromogranin, synaptophysin, CD45, PGM1, CD21/35, CD30, SALL4, OCT3/4, ER and PgR. INI1 is retained in nuclei. BRG1 appears essentially retained in tumor nuclei. The proliferation fraction by MIB1 is low to focally low-moderate. No mucin is identified with AB/DPAS stain. FISH shows features consistent with translocation involving ALK at 2p23. There was no evidence of translocations involving FUS, SS18 or EWSR1, or of amplification of MDM2. RT-PCR: No mutations were detected in the regions analysed within the BRAF, KIT or PDGFRA genes.

There is a malignant spindle cell neoplasm with keratin expression and ALK gene rearrangement. The features favor inflammatory myofibroblastic tumor with aberrant keratin expression. The overall features, including lack of

prominent mitotic activity, are not supportive of sarcomatoid carcinoma. Other keratin-positive neoplasms that might occur at this age, such as pseudomyogenic hemangioendothelioma, are not supported. However, the appearances are highly unusual, and expert opinion will be sought from Prof Cyril Fisher of UHB/ the ROH Birmingham, with a further report to follow.

The tumor has an edematous fibrous capsule and appears both macroscopically and histologically completely excised, with the circumferential margin at 1mm. The tumor is away from the adrenal gland in the tissue planes examined, although fibrosis is seen in the soft tissue separating the tumor from the adrenal gland. No significant pathology is seen within this gland. The sections from the distal resection margin show duodenal mucosa and wall including Brunner's glands. The section from the proximal resection margin shows fibroadipose tissue only. The esophageal lumen is not identified. The sections from the spleen show no metastatic disease. Eight lymph nodes identified in the gastrectomy specimen reveal no evidence of metastatic disease. Pancreatic tissue is not identified (case also seen by Dr A Wotherspoon (consultant hematolymphoid pathologist), who does not think this represents a hematolymphoid neoplasm), and by Dr S Hazell who agrees with the findings, and does not think this represents a germ cell tumor or any specific neoplasm arising from the genitourinary tract (including the kidney).

Dr Magnus Hallin/Dr Monica Terlizzo/Dr Khin Thway