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Rare case of spindle cell/ sclerosing rhabdomyosarcoma in adult liver

Sir,

Rhabdomyosarcoma (RMS) is a common soft tissue sarcoma in children that can infrequently present in adulthood.[1] Although alveolar and embryonal RMS are the most common (>80%) of all histological subtypes encountered, rare variants can occur. Seldom, RMS can involve solid organs. Herein, we present a case of spindle cell/sclerosing variant of RMS in an adult liver, first diagnosed on a partial hepatectomy specimen for suspected cholangiocarcinoma.

A 57-year-old Caucasian female with no significant past medical history presented with a 6-week history of shortness of breath, epigastric discomfort and fatigue. Magnetic resonance imaging with intravenous contrast identified a large (>18.0 cm) exophytic left hepatic lobe mass (Fig. 1A) elevating the left hemi-diaphragm and impinging on the heart, together with multiple omental nodules. Imaging findings were interpreted as concerning for intrahepatic cholangiocarcinoma with peritoneal carcinomatosis. The patient's blood work-up revealed mild anaemia (Hb 11.2 g/dL; range 12−15 g/dL) but clinical biochemistry results were within normal limits including serum tumour markers CA125, CA19.9 and CEA. The patient underwent partial hepatectomy, left hemi-diaphragm resection and omentectomy. Surgical specimen showed an 18.5 cm white-yellow, fleshy liver mass (Fig. 1B) adherent to the diaphragm. Histological examination demonstrated a spindle cell lesion composed of fascicles of cells with eosinophilic cytoplasm and elongated nuclei (Fig. 2A). Frequent strap cells with cross striations (Fig. 2B) and multiple areas of stromal hyalinisation/sclerosis with pseudovascular arrangement of tumour cells (Fig. 2C) were also noted. Omental nodules showed similar tumor histology.

On immunohistochemical studies, the neoplastic cells showed expression of Myo-D1 (strong and diffuse; Fig. 2D), desmin and myogenin (patchy) with no expression of cytokeratins, SOX-10, HMB-45 and Melan-A. Interphase fluorescent *in situ* hybridisation was negative for *FOXO1* gene rearrangement. The morphology and immunophenotypic features of this liver mass were diagnostic of RMS, with further categorisation into a spindle cell/sclerosing variant of rhabdomyosarcoma (SRMS), per the current World Health Organization (WHO) classification of soft tissue tumours.[2]

Four broad categories of RMS are recognised by the 2013 WHO classification, namely alveolar, embryonal, pleomorphic and spindle cell/sclerosing.[3] The 'spindle cell' and 'sclerosing' variants were separate entities individually described first by Cavazzana *et al*.[4] and Mentzel and Katenkamp,[5] respectively. SRMS is classified as a standalone variant in the current (2013) edition of the WHO classification system[3] after studies showed that both the spindle cell and sclerosing variants share similar clinical, histopathological, and molecular characteristics. SRMS comprises 5−10% of all RMS cases, with a predilection for the head and neck region, and rarely presents in adulthood.[2] At the time of diagnosis of our case (May 2018), SRMS had not been reported in the liver; however, recently Agaram *et al.*, described one case of RMS with pure spindle cell morphology within the liver.[6] In contrast, our case demonstrated both spindle cell and sclerosing morphologies that were intermixed. Embryonal and alveolar RMS are more common, and both variants have been previously reported in adult liver, albeit in rare case reports.

Histomorphology of SRMS can be characteristic as described above and as depicted in Fig. 2A−C, facilitating a histological diagnosis. Immunohistochemical studies that are particularly helpful in the diagnosis of SRMS include myogenin, Myo-D1, desmin and vimentin, all of which can show variable staining. Studies on SRMS have previously demonstrated that the neoplastic cells in all cases tend to express Myo-D1.[6,7] Diffuse and strong positivity for Myo-D1

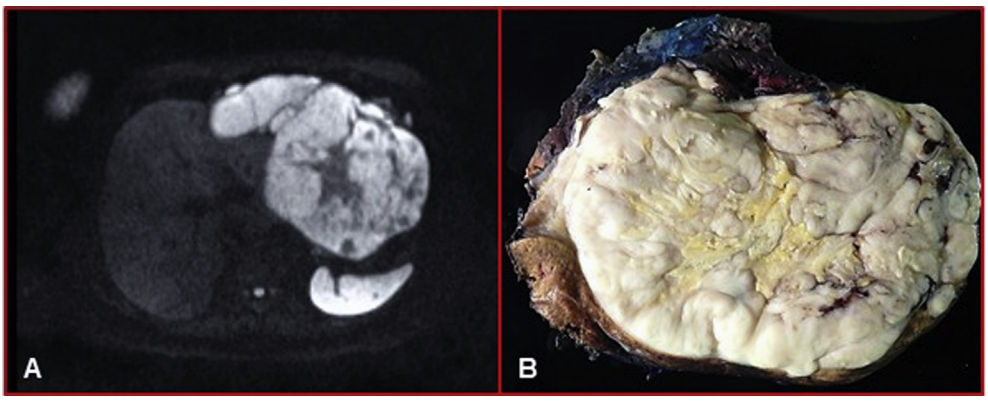

Fig. 1 (A) Abdominal magnetic resonance imaging with IV contrast showing a large mass in the left hepatic lobe. (B) Surgical specimen showing a well-defined fleshy mass with a thin rim of surrounding liver parenchyma.

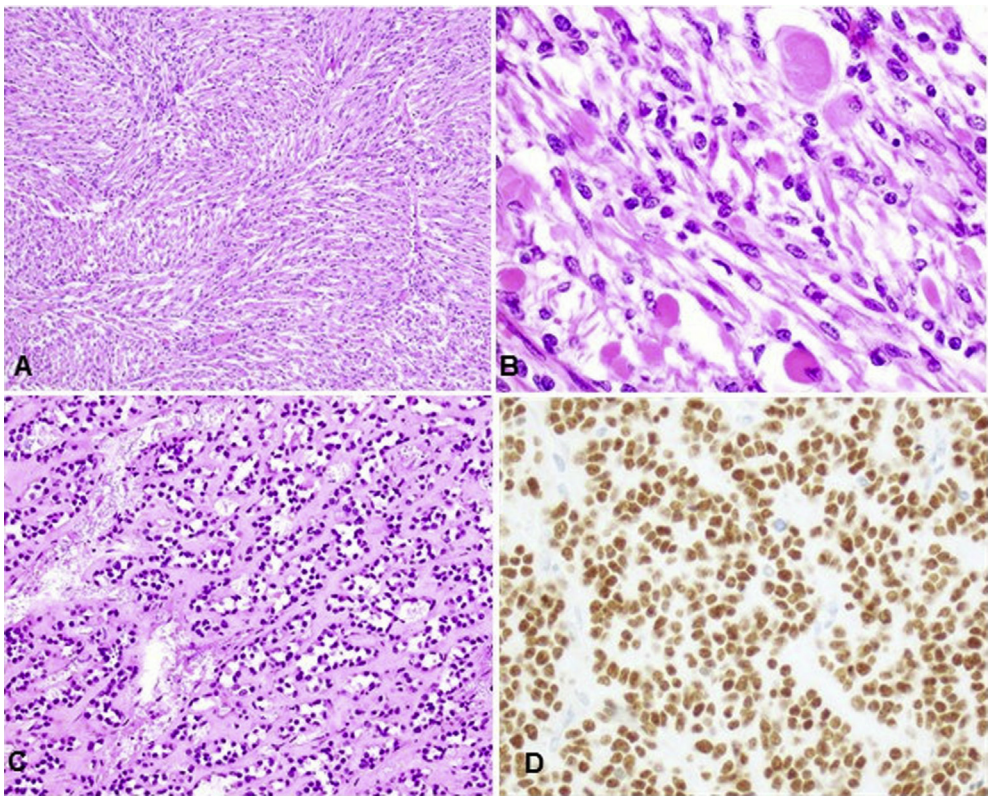

Fig. 2 Histology of the mass revealed (A) fascicles of spindle cells (H&E) and (B) frequent strap cells with striated cytoplasm (H&E). (C) Foci of sclerosis/stromal hyalinisation with pseudovascular arrangement of tumour cells (H&E). (D) Strong nuclear expression of Myo-D1 within tumour cells.

in our case further supports our diagnosis, as Myo-D1 has been shown to be a more sensitive marker for the sclerosing variant of RMS in comparison to myogenin.[8]

Key differential diagnoses for SRMS include synovial sarcoma, leiomyosarcoma, spindle cell carcinoma, spindle cell melanoma, and malignant peripheral nerve sheath tumour (MPNST), among others. Immunohistochemistry is most helpful in differentiating RMS from these other malignancies since most do not demonstrate myogenin, Myo-D1, or desmin positivity. Leiomyosarcoma may demonstrate desmin positivity but will not demonstrate Myo-D1 and myogenin or contain strap cells. MPNST with rhabdomyoblastic differentiation (Triton tumour) may be differentiated from SRMS by histology and immunohistochemistry. Classic descriptions of MPNST include a malignant spindle cell neoplasm with alternating hypo/hypercellularity, geographic necrosis and variable S-100 or SOX-10 positivity. Heterologous rhabdomyoblastic differentiation is mostly focal/patchy; however, two cases with complete heterologous rhabdomyoblastic differentiation with diffuse positivity for desmin and myogenin have recently been reported.[9] Although the immunophenotypic profile of these two cases is largely similar to our findings, both cases lacked strap cells that were diffusely present in our case. Our case had foci with sclerosing RMS morphology that further assists in morphological distinction. Additionally, our patient lacks clinical stigmata and family history of neurofibromatosis.

Recently, *MYOD1* (L122R) mutations have been reported in a subset of SRMS (some with accompanying *PIK3CA* mutations) associated with aggressive clinical courses[10] and higher mortality rates unrelated to the age of the patient.[6] A next-generation sequencing based panel designed for detection of substitutions, insertion/deletion alterations, and copy number alterations in 324 genes and select gene rearrangements identified *PIK3CA* (E542K), *NRAS* (G12D) and *ARID1A* (R1722*) mutations in our case, while confirming the tumour as microsatellite stable. *MYOD1* gene was not included in this panel. However, current treatment strategies based on experience with paediatric RMS only incorporate results of *FOXO1* translocation testing.[1] As seen in our case, *FOXO1* gene rearrangements are usually absent in SRMS. *PIK3CA* (E542K) mutations similar to our case have been documented in SRMS, especially in a subset of cases that have *MYOD1* mutations.[6] In contrast, infantile SRMS have been associated with *VGLL2* rearrangements (a subset harbouring *NCOA2* rearrangements),[11] with both types showing favourable prognosis compared to SRMS occurring in older patients and *MYOD1*-mutant tumours showing sclerosing morphology. More recently, aggressive SRMS occurring in bone and soft tissue harbouring novel translocations *FUS-TFCP2* or *EWSR1-TFCP2* have been described.[12]

Our patient was disease-free 12 months following adjuvant chemotherapy with alternating cycles of vincristine, cyclophosphamide, doxorubicin, and ifosfamide with etoposide.

In summary, we describe a rare case of SRMS in adult liver masquerading as cholangiocarcinoma on imaging studies. Although rare, RMS should be considered in the differential diagnosis of an exophytic liver tumour exerting mass effect.

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Intra-abdominal pulmonary sequestration: a rare diagnostic pitfall on EUS-FNA

Sir,

Pulmonary sequestration (PS) is a rare congenital malformation characterised by a segment of pulmonary tissue that does not communicate with the tracheobronchial tree, and that draws its blood supply directly from the systemic arterial tree. PS is most frequently diagnosed antenatally and during childhood, with imaging classically showing a variably cystic lesion with a systemic feeding vessel. Intralobar sequestration (ILS), being the more common type, is localised within the normal pulmonary parenchyma. Extralobar sequestration (ELS) is relatively uncommon, and features lung tissue that is found external to the visceral pleura.[1] ELS can occur in the thorax (90%), mediastinum, pericardium, and within or below the diaphragm.[2] Thus, ELS poses a significant diagnostic challenge, particularly in adults.

We document an unusual case of intra-abdominal ELS in an adult, presenting the findings on endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA), together with a literature review of this rare entity.

A 67-year-old Chinese female was incidentally found on computed tomography (CT) scan to have a well-defined, low-density retroperitoneal mass measuring 4.9 × 2.0 × 2.9 cm with small mildly enhancing areas and a speck of calcification. It was medial to the spleen and above the left adrenal gland. The possibility of a retroperitoneal haemangioma or lymphangioma was raised.

EUS revealed a 3.5 × 2.7 cm solid-cystic lesion adjacent to the pancreatic tail and spleen. Transgastric EUS-guided FNA was performed. The smears were hypocellular, showing scattered clusters of bland columnar epithelial cells, some with discernible terminal bars and cilia (Fig. 1), on a background of mucoid material. Occasional macrophages were also present. No significant nuclear atypia, necrosis or mitotic activity were seen. The cytological diagnosis was 'cyst contents; mucinous cystic neoplasm not fully excluded'.

Laparoscopic excision was performed, and an encapsulated, retroperitoneal parasplenic, partially cystic mass measuring approximately 4 × 3 × 2 cm was removed. The specimen comprised three friable fragments of spongy red to tan coloured tissue admixed with mucinous material, altogether measuring 6 × 3 × 2 cm. Microscopy revealed a solid-cystic lesion with a thin fibrous rim composed of variably sized, mucin-filled cystic spaces lined by ciliated respiratory type epithelium with occasional goblet cells (Fig. 2). An island of cartilage was noted adjacent to a cystic space, reminiscent of a bronchial structure. Serous and mucous peribronchial-like glands were also identified. The intervening stroma was composed of bundles of smooth muscle and muscular arteries. Patchy chronic inflammation was present. Other areas showed partially collapsed alveolar spaces with scattered intra-alveolar macrophages. No significant nuclear atypia, mitotic activity or necrosis were identified. The morphological features were compatible with those of pulmonary sequestration.

Post-operative recovery was uneventful. Follow-up CT scan revealed a residual lesion measuring 3.2 × 1.5 cm, which remained stable over the next 2 years.

Intra-abdominal pulmonary sequestration (IAPS) is extremely uncommon, comprising 10–15% of ELS cases and 2–5% of cases of PS.[3] In adults, IAPS is usually discovered incidentally at autopsy or during other surgical or radiological procedures.[1] ELS is believed to arise from an outpouching of the foregut that is structurally separate from the normally developing lung, with a systemic arterial supply draining into the azygos system.[1] It is usually single but can sometimes occur as multiple lesions. Association with the gastrointestinal tract occurs frequently at the region of the lower oesophagus and stomach. ELS may be associated with other congenital abnormalities such as diaphragmatic hernia. Superimposed infection is rare, as ELS is anatomically