Recently described and recently re-evaluated soft tissue tumours

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Abstract

Several soft tissue lesions have been recently highlighted in the medical literature. Some are recently recognized, hence often underdiagnosed because of limited knowledge whereas others have been recognized for sometime but can be viewed afresh in light of emerging molecular data. The aim of this review is to be more familiar with these entities and pathologists should consider these differential diagnosis. We discuss anastomosing haemangioma, soft tissue myoepithelial lesions, and the evolving story of myxoinflammatory fibroblastic sarcoma and other lesions that may or may not be related, namely pleomorphic hyalinizing angiectatic tumour and haemosiderotic fibrohistiocytic inflammatory lesion.

Keywords anastomosing haemangioma; myoepithelial lesions; myxoinflammatory fibroblastic sarcoma; namely pleomorphic hyalinizing angiectatic tumour and haemosiderotic fibrohistiocytic lipomatous lesion (haemosiderotic fibrolipomatous tumour)

Anastomosing haemangioma

Anastomosing haemangioma (AH) is a recently described, rare type of haemangioma that most often arises in the genitourinary system, where it was initially described.[1] About 30 cases have been reported.[1–7] Haemangiomas in general tend to arise in the skin and subcutaneous soft tissues. When they are visceral, the liver is a favoured site. AH most commonly arise in the genitourinary system, with a predilection for the kidneys[5] but it is also reported at other sites including testes, adrenal gland, ovaries, thigh, abdominal wall, liver and the gastrointestinal tract.[1,3,4]

The clinical presentation of the tumour is generally non-specific but the patient may present with flank pain, haematuria and lower urinary tract symptoms. Most of the lesions are, however, discovered incidentally. Tumours usually present in the fifth decade of life with a slight male predominance and are typically unilateral.[5] The mean size is 1.5 cm, but a 7 cm tumour has been reported.[5] AH has also been reported in association with polycythaemia due to extramedullary haematopoiesis which resolved after the removal of AH by a nephrectomy.[3] There is some association of AH with end stage renal disease (ESRD). The exact pathogenesis of ESRD secondary to AH is unknown.[5] Whereas bladder haemangioma is sometimes seen with Sturge–Weber syndrome, Klippel–Trenaunay syndrome and tuberous sclerosis, renal AH has not been associated with any systemic or syndromic condition. Although AH is seen in patients with ESRD, but it has also been reported with normal functioning kidneys. The radiographic appearance of AH is relatively non-specific and most are detected incidentally.

Macroscopically, AH has typically been described as mahogany brown with a spongy consistency and well-demarcated borders without a capsule. No gross necrosis or invasion has been reported. Most examples are solitary, but multifocal lesions have been described.

Histologically, on low magnification, AH are well-demarcated, vaguely nodular and display minimal surrounding tissue reaction (Figure 1). Some are focally infiltrative with areas of intravascular extension. There are alternating paucicellular and hypercellular areas. The cellular areas are actually the proliferations of capillary sized vessels in an anastomosing pattern, while loose stroma tissue with elastic thin-walled blood vessels form the hypocellular areas. At high power, AH is composed of tightly packed vessels lined by hobnail endothelial cells and a flat endothelium focally (Figure 2); an anastomosing sinusoidal pattern. The endothelial cells are plump with eosinophilic cytoplasm. The stroma may demonstrate zones of sclerosis or hyalinization or necrosis. Many examples display zones of extramedullary haematopoiesis and hyaline globules (Figure 3) that are reminiscent of those seen in Kaposi sarcoma. There is no apoptosis or mitosis or multilayering of endothelial cells although mitoses may be encountered in supporting cells surrounding the vessels.

Endothelial cells in these tumours express CD31, CD34 and factor VIII-related protein. These tumours are negative for CD8, GLUT-1, D2-40, cytokeratin, HMB-45, epithelial membrane antigen and HHV-8, readily differentiating this tumour from

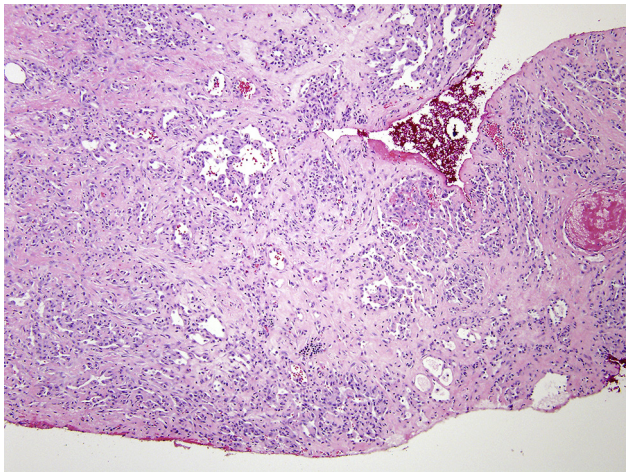

Figure 1 Anastomosing haemangioma. This lesion arose in the breast. There is a vaguely lobulated pattern at low magnification. The endothelial cells have a hobnail pattern but are not multilayered.

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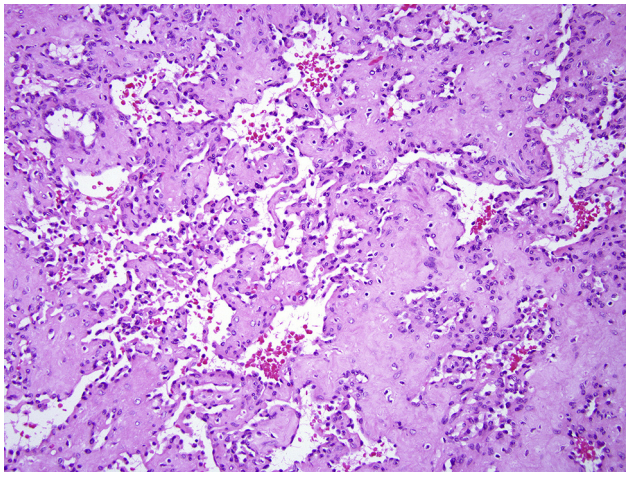

Figure 2 Anastomosing haemangioma. This was a renal example. Note the sclerotic stroma and anastomosing pattern.

juvenile haemangioma, splenic sinusoids, and PEComa/angiomyolipoma, and Kaposi sarcoma. The eosinophilic globules are seen to be strongly positive for PAS. Some cases have reported the presence of mast cells; and have also shown increase positivity with KIT, possibly representing the degranulated mast cells-9. Ki-67 demonstrates a low proliferative index-2.

AH may easily be misdiagnosed as angiosarcoma as the clinical presentation for both may include haematuria and flank pain. These tumours share some histological features, including the presence of hyaline globules and positive immunohistochemistry for the endothelial markers. However, angiosarcoma lacks a lobulated architecture and often displays dense cellularity and cytologic atypia and the individual vascular channels are typically not surrounded by supporting elements. Furthermore, angiosarcoma often presents as a large mass that has metastasized at the time of diagnosis. Kaposi sarcoma can sometime be a diagnostic challenge because of the presence of hyaline globules; however, Kaposi sarcoma is immunoreactive to HHV-8 while AH is negative. Angiomyolipoma may also be included in the differential diagnosis. These tumour are composed of an adipose tissue component and eosinophilic spindle cells that are immunoreactive to smooth muscle actin and HMB-45.

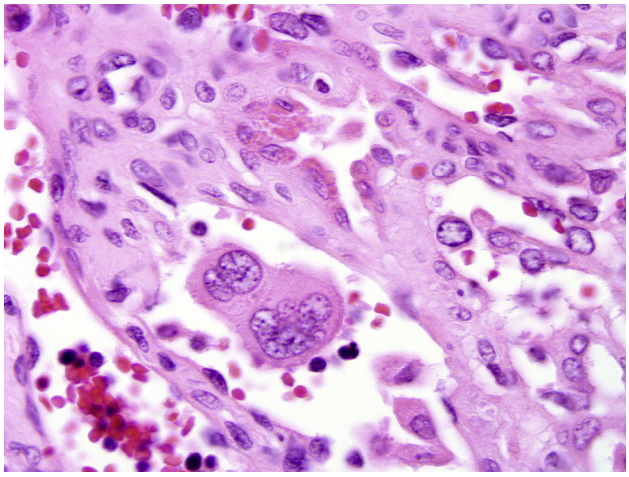

Figure 3 Anastomosing haemangioma. This oil immersion image shows extramedullary haematopoiesis with a megakaryocyte in the centre. There are a few hyaline globules above the megakaryocyte.

Myoepithelioma

The myoepithelial tumours of soft tissue are rare and recently have been shown to have characteristic gene rearrangements. These tumours are well recognized as salivary gland tumours, and recently they have been increasingly reported in various anatomic sites, most commonly as subcutaneous nodules in the proximal limb girdles and extremities.[8] They are classified as mixed tumour/chondroid syringoma, myoepithelioma, and myoepithelial carcinoma; but there is considerable morphologic and immunohistochemical overlap between these, which makes the classification difficult. Tumours formerly classified as parachordoma of soft tissues are a subset. They not only arise in skin, lung, larynx and breast, the areas where the normal myoepithelial cells are found but also seen in deep soft tissue and bone, which are believed to lack myoepithelial cells. Several genetics subsets have been identified, though initially these tumours were believed to be morphologic variants of single type of tumour.[9,10]

Myoepithelial tumours generally arise in patients between the second and fourth decades; however they have been reported in infants and in patients in the ninth decade.[8] They commonly manifest in children, comprising up to 20% of cases, and those in children are frequently malignant.[8,10] There does not seem to be a sex predilection. Myoepitheliomas and mixed tumours are usually benign; however approximately 20% recur, especially if the resection is incomplete.[11] They are usually subcutaneous but deep examples (including retroperitoneum) are known. The extremities and proximal limb girdle are the most common locations. The usual presentation of a myoepithelioma is a painless, slow growing cutaneous or subcutaneous mass. Malignant examples may present as large painful masses and are likely to recur. A recently described morphological variant termed cutaneous syncytial myoepithelioma is usually intradermal with a male predominance and a wide age range.[12] These tumours tend to arise on the extremities. They have a low risk of recurrence and no metastases have been reported. A rhabdoid variant has also been identified.[9] Myoepithelial tumours of soft tissue resemble their salivary gland counterpart in multiple aspects, however they may be distinguished on the basis of cytological atypia (for salivary gland tumours malignancy is based on invasive growth), and the presence of *EWSR1* rearrangements.[13]

Myoepithelial tumours are usually well circumscribed, multinodular to lobulated but non-encapsulated and they may have infiltrative margins. Benign examples are usually small, on the order of 1 cm whereas malignant examples are larger. The cut surface is tan-white to yellow and the consistency may be firm, solid, and fleshy to smooth myxoid, glistening, and gritty, or even calcified. Although necrosis and haemorrhage are not usually seen, they may be present in malignant examples.

Microscopically, most have a lobular pattern at low magnification (Figure 4) and with a wide variety of cell types as a combination of spindle, epithelioid, or even plasmacytoid and clear cells. The architectural pattern may be nested, trabecular, reticular or even solid (Figure 5) in a chondromyxoid or hyalinized stroma. The individual cells usually have an eosinophilic to vacuolated

