Anastomosing haemangioma of the colon

To the Editor,

Anastomosing haemangioma (AH) is a rare variant of capillary haemangioma usually occurring in the genitourinary system. AH is benign but is easily confused with low-grade angiosarcoma due to its rarity and unusual morphology. Since AH was first described in a 2009 case series as involving the kidney, perinephric adipose tissue, and testis, approximately 130 cases have now been described in an array of organs and soft tissues. We present a case of this rare tumour occurring in the colon, of which only one other case has been reported to our knowledge.

A 55-year-old male underwent an upper gastrointestinal endoscopy to exclude autoimmunity gastritis and colonoctopy to exclude microscopic colitis. The patient had a history of positive anti-parietal antibodies and rectal hyperplastic polyps, but no history of immunosuppression or human immunodeficiency virus (HIV). Biopsies were taken from the gastric body, antrum, duodenum, terminal ileum, right and left colon, and rectum. A 3 mm sessile rectal polyp was excised.

Histologically, there was no evidence of autoimmune gastritis or microscopical colitis. The incidental rectal polyp contained a circumscribed but unencapsulated submucosal lesion abutting the deep aspect, with intact overlying normal rectal mucosa. The vaguely lobulated lesion was formed by multiple anastomosing sinusoidal capillary-sized spaces lined by often hyperchromatic endothelial cells with frequent hobnail morphology, reminiscent of splenic parenchyma (Fig. 1). The endothelial cells lacked significant atypia, multilayering, mitoses and necrosis. There were thin intervening bands of mildly cellular fibrous stroma without significant inflammatory infiltrate. There were occasional fragmented red blood cells and hyaline globules within spaces possibly within macrophages.

Immunohistochemistry demonstrated diffuse positive staining for endothelial marker CD34 (Fig. 2) but no expression of lymphatic marker D2-40, GLUT-1, CD8, or HHV8. Background staining for smooth muscle actin (SMA) hampered assessment although there was some staining for endothelial markers (e.g., CD31, CD34, factor VIII, ERG, FLI1), smooth muscle actin (supportive pericytic cells bordering endothelial cells), and Ki-67 (low endothelial proliferation). There were occasional lymphocytes but no acute inflammation or plasma cells. Margins are minimally invasive, with focal extension to larger vessels and surrounding soft tissues. There may be hyaline globules (secondary lysosomes whose degradation has been halted so lysosomes overfill with phagocytosed proteinaceous material), mimicking other malignancies. Other features may include sclerosis, haemorrhage, fatty change, calcification, intravascular fibrin thrombi, and extramedullary haemopoiesis.

On immunohistochemistry, AH stains positively for endothelial markers (e.g., CD31, CD34, factor VIII, ERG, FLI1), smooth muscle actin (supportive pericytic cells bordering endothelial cells), and Ki-67 (low endothelial proliferative activity). AH has negative staining for GLUT-1 (juvenile haemangioma), CD8 (splenic sinusoids), D2-40 (lymphatic), HHV-8 (Kaposi sarcoma), keratins AE1/3, epithelial membrane antigen, placental alkaline phosphatase, and melanocytic markers.

On electron microscopy, AH usually has well preserved structures down to the level of organelles, coarse internal granular structures in homogeneously electron-dense matrix, and homogeneous electron-dense globules and increased primary lysosomes in endothelial cytoplasm.

Next generation DNA sequencing has demonstrated recurrent driver mutations in the G-protein signal transduction pathway, including frequent activating somatic mutations in the GNAQ and GNA14 genes.

The discovery of recurrent GNAQ and GNA14 mutations implicates this pathway in its pathogenesis. Sixty to eighty percent of AH are asymptomatic and detected incidentally during examination or imaging for non-specific symptoms. Sometimes, patients may present with complications from local compression by AH. For instance, renal AH may present with haematuria, back pain, lower urinary tract symptoms, or arise in the context of pre-existing end stage renal failure. Ovarian AH has manifested with apoplexy, ascites, elevated serum CA-125, and endometrial hyperplasia or carcinoma. There have also been reports of AH associated with extramedullary haemopoiesis and therefore polycythaemia. Radiological findings are non-specific and cannot differentiate between AH and malignancy. AH typically appear as well-defined, exophytic masses with chunky calcification, surrounding fat stranding, and heterogeneous enhancement in the arterial phase of contrast. Macroscopically, AH are usually solitary but sometimes multifocal solid-cystic tumours that are well circumscribed, non-encapsulated, grey to red/brown, spongy, and measure 1–80 mm (mean 22 mm).

Microscopically, AH are classically well circumscribed, partially encapsulated, and embedded within oedematous, fibrous or myxoid stroma. They have a diffuse or vaguely lobulated growth pattern of tightly packed anastomosing capillary-sized vessels with intravascular papillary areas, classically resembling splenic parenchyma. They are lined by endothelial cells with often hobnail morphology and minimal atypia or mitotic figures. There may be mild to focally moderate chronic inflammation with numerous B and T lymphocytes but no acute inflammation or plasma cells. Margins are minimally invasive, with focal extension to larger vessels and surrounding soft tissues. There may be hyaline globules (secondary lysosomes whose degradation has been halted so lysosomes overfill with phagocytosed proteinaceous material), mimicking other malignancies. Other features may include sclerosis, haemorrhage, fatty change, calcification, intravascular fibrin thrombi, and extramedullary haemopoiesis.
tions in heterotrimeric G-protein alpha-subunit GNAQ at codon 209. These findings differentiate AH from angiosarcoma and suggest an underlying neoplastic (rather than reactive) process driven by GNAQ and GNA14 mutations via the mitogen-activated protein kinase (MAPK) signalling pathway.7 AH has several differential diagnoses depending on the site of occurrence, including splenic parenchyma,1 angiosarcoma, intravascular papillary endothelial hyperplasia (IPEH), angiomyolipoma, Kaposi sarcoma, retiform haemangioendothelioma, and papillary intralymphatic angioendothelioma (PIA).4 AH classically resembles splenic parenchyma (seen elsewhere in the abdomen after splenic rupture), which has CD8+ lymphoid tissue organised in a sinusoidal anastomosing pattern.7 Well differentiated angiosarcoma can occur in any organ but is particularly aggressive in the gastrointestinal tract. Angiosarcoma is usually large, broadly infiltrative, highly cellular with significant cytologic atypia, necrosis, hyaline globules, endothelial cell multilayering, and endothelial marker positivity.7 AH can be distinguished from angiosarcoma by its lack of endothelial atypia and spindling, multilayering, papillary endothelial tufting, and mitotic activity.

Intravascular papillary endothelial hyperplasia (IPEH) is an intravascular tumour rarely organised into a haematoma, with papillary morphology lined by hyperplastic endothelium and staining positive for CD31, CD34 and FLI1.7 Angiomyolipoma is another differential which belongs to a family of lesions called perivascular epithelioid cell tumours (PEComas). Angiomyolipoma features vessels, smooth muscle and fat, stromal cells radiating off the outer edges of large blood vessel walls, and diffuse positivity for smooth muscle and melanocytic markers (e.g., HMB-45, Melan-A).3 Kaposi sarcoma, occurring in the dermis and subcutaneous tissue, contains slit-like vascular spaces in an infiltrative growth pattern, plasma cells, periodic acid–Schiff diastase-positive hyaline globules in endothelial cells, and positive staining for CD31, CD34, D2-40, ERG, and HHV-8.4 Retiform haemangioendothelioma also occurs in the dermis and subcutaneous tissue, and has a monomorphic reticulin-like growth pattern, hobnail morphology, fibrosis, papillae with hyaline collagenous cores, chronic inflammation with lymphohistiocytic infiltrate, and positive staining for CD31, CD34 and ERG.4 PIA is a subcutaneous tumour usually of the limbs, featuring intraluminal papillary tufts, hobnail morphology, and positive staining for D2-40, VEGFR3 and CD31.4 Other mimics of AH include granulation tissue, pyogenic granuloma, and littoral cell angiomat of the spleen.3

Current literature indicates that AH shows benign behaviour, does not metastasise, and rarely recurs after complete excision.9 Given its excellent prognosis, recommended treatment for AH is conservative if small or asymptomatic, and surgical resection only if symptomatic.4 Whilst AH is benign, it is underdiagnosed preoperatively and overtreated since it shares radiological and pathological features of aggressive malignancies such as well differentiated angiosarcoma. AH presents a diagnostic challenge, especially in small core biopsies, but pathological diagnosis is easier if diagnosticians are aware of its classical features distinguishing it from malignancy, even when arising in unusual locations.

By sharing this rare case of colonic AH, we aim to increase clinicians’ awareness of the distinguishing features of AH to
facilitate accurate diagnosis and avoid overly aggressive treatment for this benign entity.

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