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CASE REPORT

A case of sclerosing angiomatoid nodular transformation of the spleen

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Key words

SANT • Spleen • Morphology

Summary

Sclerosing angiomatoid nodular transformation of the spleen is a rare benign vascular lesion with extensive sclerosis and unknown aetiology. Although its pathogenesis is not clear, it has been postulated that it may represent a peculiar hamartomatous transformation of red pulp in response to an exaggerated non-neoplastic stromal proliferation. However, it is unclear whether SANT is the end stage of a variety of benign splenic conditions including inflammatory pseudotumour, hamartoma or hematoma. Considering that the lesion is benign, splenectomy is curative. We report a new case of SANT, discussing differential diagnosis, immunohistochemical profile and pathogenesis.

Introduction

Sclerosing angiomatoid nodular transformation of the spleen (SANT), first described by Martel and colleagues in 2004 [1], is a rare benign vascular lesion with extensive sclerosis and unknown aetiology. It involves exclusively the spleen and is often discovered incidentally during imaging analysis, as patients are usually asymptomatic. Although its pathogenesis is not clear, it has been postulated that it may represent a peculiar hamartomatous transformation of red pulp in response to an exaggerated non-neoplastic stromal proliferation [2]. Considering that the lesion is benign, splenectomy is curative. These lesions may pose diagnostic difficulties pre-operatively because they may mimic malignant tumours both clinically and radiologically, such as angiosarcoma. Vascular tumours are the most common neoplasms of the spleen, and include several different entities, some of which are unique to that organ. SANT is a novel vascular lesion of the spleen, and it must be differentiated from other vascular tumours or tumour-like lesions of the spleen, including granuloma, hamartoma, littoral cell angioma and inflammatory pseudotumour. We report a new case of SANT, discussing differential diagnosis, immunohistochemical profile and pathogenesis.

Case report

A 71-year-old man presented with an accidentally discovered solitary splenic nodule during routine screening. He had no significant past medical history. Laboratory findings, including Mono Test, were within normal limits. A computerized tomography (CT) scan showed a 7 cm exophytic lesion of the spleen, with patchy enhancement. Magnetic resonance imaging (MRI) with gadolinium showed contrast enhancing of the lesion with subtle calcifications in the upper part of the mass (Fig. 1). Therefore, the patient was treated with splenectomy. At gross examination, the spleen measured 10 x 7 x 2.5 cm and weighed 120 gm. A 7 cm mass with an exophytic growth and a broad-based implant was observed at the superior pole of the spleen. The cut surface of the lesion showed multiple firm nodules separated by fibrous septae (Fig. 2). At histological examination, the lesion was sharply distinct from the adjacent parenchyma of the spleen and was formed of variably sized nodules surrounded by thick fibrosclerotic stroma (Fig. 3). Some nodules showed fibrous obliteration, but the majority were composed of a haphazardly distributed sieve-like complex of vascular spaces (Fig. 4). The spleen parenchyma spared by SANT showed normal features of the red and white pulp. The first consisted of a complex network of venous sinuses and the cords

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Fig. 1. Magnetic resonance imaging showed contrast enhancing of the lesion with subtle calcifications in the upper part of the mass.

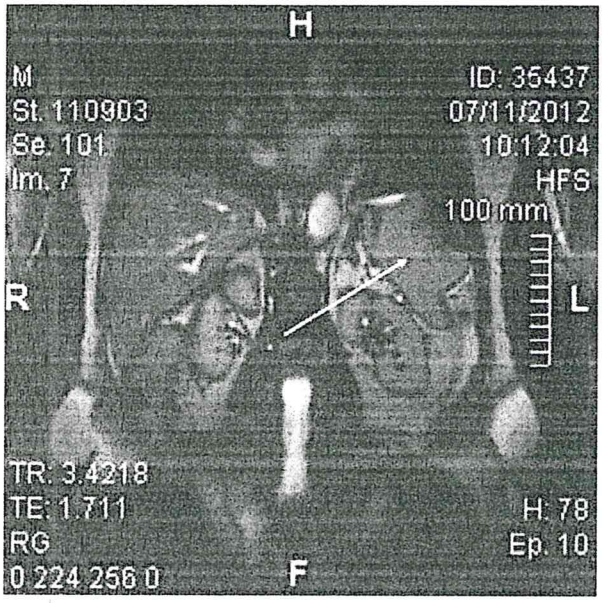


Fig. 2. A 7 cm mass with an exophytic growth and a broad-based implant was observed.

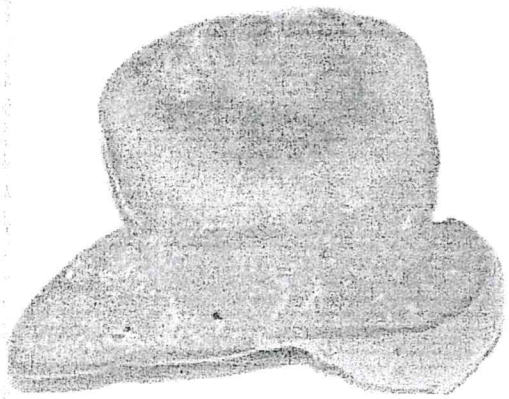


Fig. 3. The lesion was formed of variably sized nodules surrounded by thick fibrosclerotic stroma (H&E 50X).

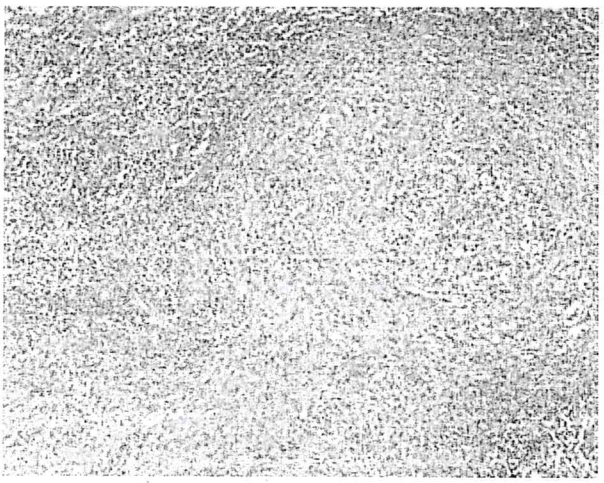


Fig. 4. Lesions were composed of a haphazardly distributed sieve-like complex of vascular spaces (H&E 100X).

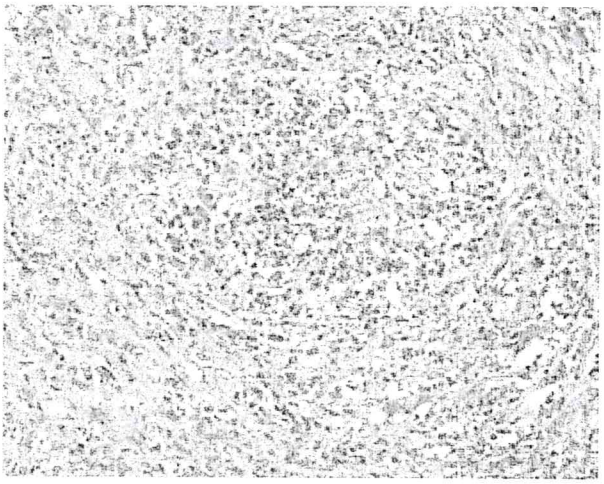
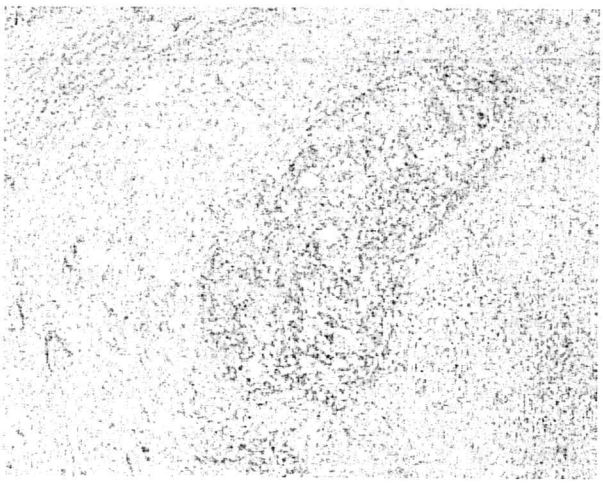


Fig. 5. CD31 immunostaining highlights the abundant vascular spaces (capillaries, sinusoid like spaces and veins) along with numerous single cells within the nodules (50X).

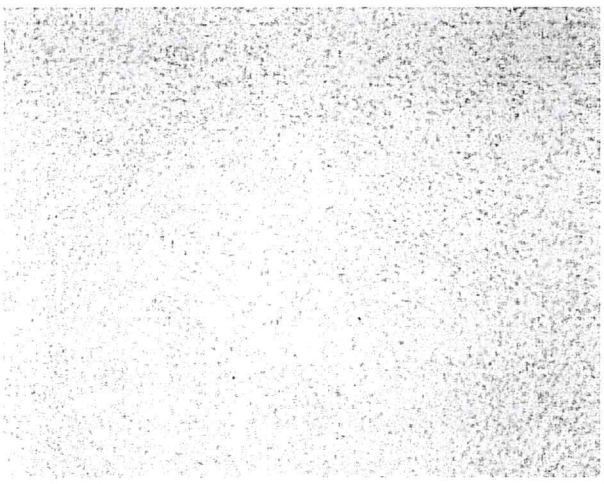


of Billroth. The second was made up of T lymphocytes located in the periarteriolar lymphoid sheath and B lymphocytes located eccentrically to this sheath in the form of primary lymphoid follicles. Immunostaining revealed three distinct types of vessels: CD34+/CD8-/CD31+ capillaries, CD34-/CD8+/CD31+ sinusoids and CD34-/CD8-/CD31+ small veins (Figs. 5, 6). Mitoses, necrosis and atypical cells were absent. Staining for HHV-8 was negative. A diagnosis of sclerosing angiomatoid nodular transformation of the spleen (SANT) was made. The patient is alive and well after one year follow-up.

Discussion

SANT is a benign, nodular vascular proliferation of splenic red pulp with sclerosis. It usually affects mid-

Fig. 6. CD34 immunostaining highlights the capillaries (50X).



dle-aged adults and shows a female predominance. Martel [1] first described sclerosing angiomatoid nodular transformation (SANT) of the spleen as altered red pulp tissue that had been entrapped by a non-neoplastic stromal proliferative process, and that was distinguished from splenic vascular tumours. However, it is unclear whether SANT is the end stage of a variety of benign splenic conditions including inflammatory pseudotumour, hamartoma or haematoma [2]. Weinreb reported both the expression of CD30 in endothelial cells and EBV encoded small RNA in spindle cells in SANT, thus implying that SANT might be associated with a cytokine mediated inflammatory process induced by EBV [3]. The histogenesis of the lesion is uncertain, but it has been postulated to be an exaggerated stromal response and outflow disruption in the spleen leading to hyperplasia of the proximal vascular bed and, thus, its nodular transformation. At gross examination, SANT is a solitary, well-circumscribed nodule that is distinct from the surrounding splenic parenchyma. Histologically, angiomatoid nodules of the SANT are composed of spindle cells, inflammatory infiltrate and proliferating endothelial cells. These nodules are enveloped concentrically by collagen fibres. The inflammatory infiltrate is formed of lymphocytes, plasma cells and histiocytes. The angiomatoid nodules of the SANT are composed of several morphologically and immunophenotypically distinct blood vessels: a cord capillary-like type that co-expresses CD34 and CD31 but not CD8, a sinusoid- like type that expresses CD8 and CD31 but not CD34, and small veins that express only CD31 [4]. Differential diagnosis of SANT includes granuloma, littoral cell angioma, haemangioma, hamartoma, angiosarcoma, inflammatory myofibroblastic tumour (IMT) and metastatic carcinoma [5 6]. The angiomatoid nodules of SANT closely resemble granulomas considering that both are characterized by a fibrous stroma, cells with plump nuclei and small prominent nucleoli, accompanied by lymphocytes. However, the first is characterized by a capillary meshwork, erythrocytes in the stroma, dispersed haemosiderin pigment and the absence of well-formed granulomas with typical epithelioid histiocytes. In contrast to SANT, littoral cell angioma shows a monotonous blood vessel composition, a prominent pseudopapillary growth pattern and the absence of sclerosis. The immunohistochemical profile of littoral cell angioma is unique, with coexpression of histiocytic and endothelial markers. Sinusoidal endothelial cells are positive for CD31, factor VIII and CD68, and negative for CD34 and CD8. Haemangiomas, although rare, are the most common benign vascular lesion of the spleen and are composed of cord-type capillaries lined by flat endothelial cells. In contrast to SANT, haemangioma is formed of a morphologically uniform blood vessel proliferation. In haemangioma neither spindle cell proliferation or fibrosis are observed.

Endothelial cells in haemangiomas are positive for CD31 and CD34, and negative for CD8. Haemangioma lacks the distinct nodular architecture of SANT. Splenic hamartomas are also rare. They are composed of disorganized red pulp elements presenting a tumour-like mass. Hamartomas are characterized by endothelial cells with features of splenic sinusoids, which are positive for CD31 and CD8, and negative for CD34. Haemangioendothelioma is a low-grade malignant vascular neoplasm that shows an infiltrative rather than a defined tissue tumour interface. It consists of ill-defined vascular channels bordered by moderately atypical cells, having a low mitotic index. Angiosarcoma is characterized by pleomorphic cells, nuclear irregularity and mitosis. Intracytoplasmic lumens and rosette-like microacinar formations can be noted. Inflammatory myofibroblastic tumour is another mimic of SANT that may involve the spleen. Inflammatory myofibroblastic tumour is characterized by proliferation of spindle cells with fibroblastic/myofibroblastic features and a mixed inflammatory cell infiltrate composed of histiocytes, lymphocytes, plasma cells and neutrophils in a collagenous stroma. A vascular granulation tissue-like pattern may be seen. The spindle cells may be immunoreactive with smooth muscle actin and/or CD68 or follicle dendritic cell markers. Metastatic carcinomas have also been reported to cause nodular transformation as a reactive response in the spleen. Any significant cytological atypia or the presence of epithelial cell features such as gland formation or cellular sheets should raise suspicion of a malignant tumour.

In conclusion, clinicians, radiologists and pathologists must recognize that distinguishing SANT from other vascular neoplasms of the spleen, especially from malignant tumours, is essential since total surgical excision represents the treatment of choice of SANT, after which there are no instances of recurrent disease.

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