



Sclerosing Angiomatoid Nodular Transformation of the Spleen: A New Entity or a New Name?

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ABSTRACT

Sclerosing angiomatoid nodular transformation of the splenic red pulp has been described quite recently; many of the lesions previously diagnosed as splenic exuberant granulation tissue, multinodular hemangioma, and inflammatory pseudotumor could actually belong to this category. The lesion has been well reported intermittently in the past, but new cases with still newer associations keep appearing from time to time. There are no known risk factors and no inciting triggers have been proven. We report two such cases- one of which has extensive extramedullary haematopoiesis; a feature that has never been reported earlier. Clinico-morphological and radiological features along with pathogenesis are discussed in detail.

Key Words: Spleen, Extramedullary haematopoiesis, Hemangioma

INTRODUCTION

Vascular tumors are common in spleen. Recently, a distinct subset of these tumors with characteristic morphology and typical immunoprofile has been designated as "Sclerosing Angiomatoid Nodular Transformation" (SANT). Herein we describe two cases of SANT with characteristic histomorphology and immunoprofile. One of our cases was associated with extensive extra-medullary haematopoiesis in the spleen - a finding that has never been reported in literature.

CASE REPORTS

Case 1

A 35-year-old gentleman presented to the hospital with left upper quadrant discomfort since 6 months and gradually increasing lump in upper abdomen since 4 months. History of fever, weight loss or night sweats was absent. Per-abdomen examination revealed splenomegaly 6 cm below coastal margin. Haematological parameters and liver function tests were unremarkable except for mildly elevated serum lactate dehydrogenase levels (124 U/L). Ultrasound abdomen revealed splenomegaly with nodular mass lesion in the lower part of spleen. On computed tomography (CT) scan, there was splenomegaly with a large isodense mass (Hounsfield scale = 40-55 HU) measuring 8.5 X 7.3 cm at the lower medial pole of spleen. Contrast enhanced CT (CECT) showed minimal heterogeneous enhancement with calcifications (Figure 1A-D). Few sub-centimetre lymph nodes at portal,

porto-caval and para-aortic regions were noted. High resolution CT scan of the chest was normal. The bone marrow evaluation showed normoblastic erythropoiesis, normal and orderly myelopoiesis, and morphologically unremarkable megakaryopoiesis. However, the overall cellularity for age was reduced. Rest of the haematological work up was unremarkable. In view of the solitary nature of the mass, the patient underwent splenectomy.

Grossly the spleen measured 13 X 7 X 7 cm and weighed 260 grams. The external surface was congested with discrete nodularity at lower pole. Cut surface showed well circumscribed mass measuring 6 cm in diameter, with a bulging cut surface and fibrous septa traversing throughout, thus dividing it into yet discrete complete or incomplete nodules (Figure 2A and inset). Light microscopy recapitulated the nodular appearance seen at gross. Within the nodules, there was slit like arrangement of capillary sized vessels lined by plump endothelial cells. Few of these vessels were slit like with sclerosed and hyalinised walls. The nodules were separated by fibro-sclerotic stroma with hemosideophages, fibroblasts and lymphomononuclear cells. Striking feature was the presence of extensive extramedullary haematopoiesis composed of mainly myeloid, few megakaryocytic and erythroid precursors. Histochemical stains- reticulin, Masson's trichrome, Periodic Acid Schiff (PAS) and Perls' stains were used to highlight the collagen rings surrounding the nodules, hemosiderin deposits and hematologic precursors

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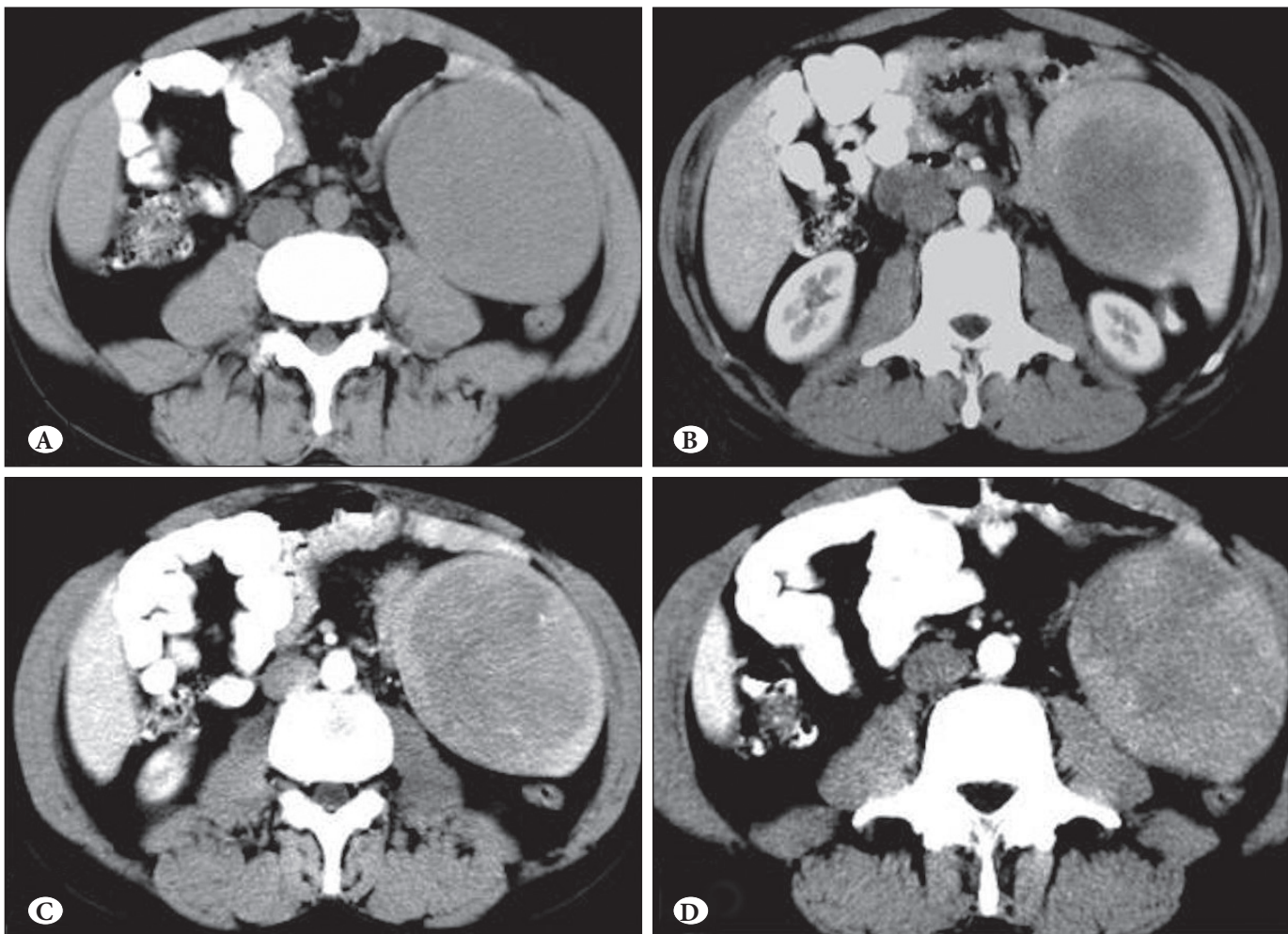


Figure 1: CT scan image of abdomen in arterial phase (A) Plain and (B-D) after contrast administration showing enlarged spleen extending well below the kidney. There is a definite mass lesion, isointense to the normal splenic parenchyma, with heterogenous contrast enhancement.

(Figure 2B-F). A diagnosis of sclerosing angiomatoid nodular transformation with extensive extramedullary haematopoiesis was given.

Immunohistochemistry (IHC) was performed with CD31, CD34, CD68, smooth muscle actin (SMA) and myeloperoxidase (MPO). The vasculature within nodules was a variable admixture of CD31 and CD34 positive vessels (Figure 3A-F) indicating their derivation from sinusoidal, capillary like and vein like elements.

Case 2

A 12-year-old girl presented to this hospital in 2005 with upper quadrant discomfort since 6 months. Ultrasound revealed splenomegaly. CECT abdomen showed a hypodense soft tissue mass without contrast enhancement at the upper pole. ^{99m}Tc -sulphur colloid single photon emission tomography computed tomography (SPECT/

CT) scan revealed normal tracer activity within the liver and spleen with no active uptake within the lesion. Other investigations including colour Doppler, bone marrow evaluation, electro-cardiogram and blood investigations were unremarkable. The patient was taken up for splenectomy. Grossly, the mass had a nodular, firm to hard, gray white cut surface (Figure 4A). Microscopy revealed nodular appearance of variable sized vascular channels lined by plump endothelial cells. The nodules were surrounded by bands of sclerosis (Figure 4B). At that time, it had been designated as multinodular hemangioma. However in view of the recent concept of SANT, review of H&E stained sections along with relevant immunohistochemistry was done. There was nodular arrangement of vascular channels with a characteristic immunoprofile as described for case 1. The diagnosis has been revised as SANT.

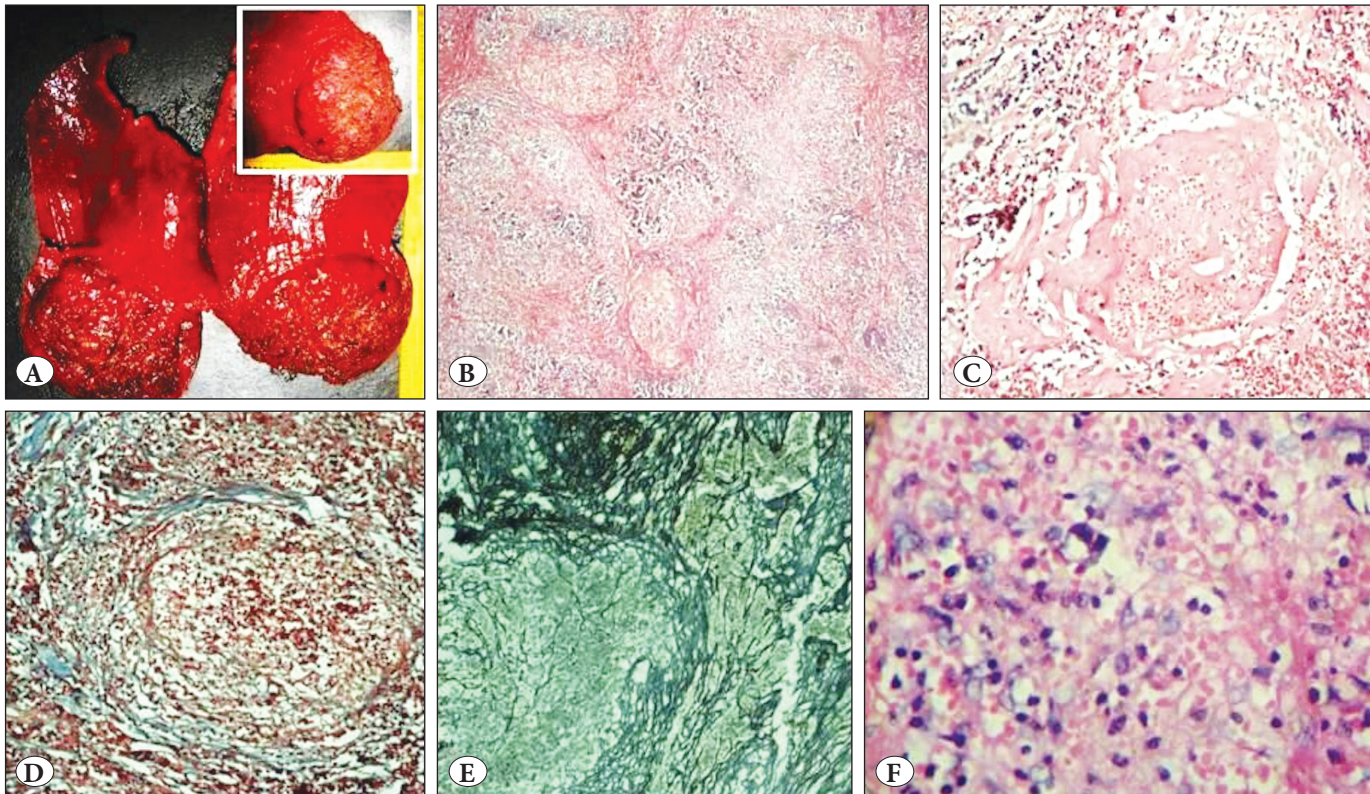


Figure 2: (A) Gross photograph with the bulging lesion at the lower pole; inset shows intersecting fibrous strands dividing it into still smaller nodules. (B) Low power photomicrograph showing variable sized nodules (H&E x40) (C) The nodules are composed of channel/slit like vasculature (H&E x100) (D) & (E) Masson's trichrome and reticulin stains to highlight the collagenous network and nodular configuration (Masson's trichrome x40) (F) Photomicrograph showing myeloid precursor cells along with a megakaryocyte (H&E x400).

Both the patients were given standard pre and post splenectomy precautions. They are symptom-free and on follow up (Case 1-11 months, Case 2- 5 years). The follow up bone marrow evaluation of case 1 was similar to the previous one without any symptoms thereof.

DISCUSSION

Vascular neoplasms in spleen are common and may exhibit a variety of biological behaviour. These include those with a benign course (littoral cell angioma, hemangioendothelioma and hemangiopericytoma) and those that are frankly malignant (angiosarcoma) (1).

The characteristic morphology of multiple angiomatoid nodules forming a space-occupying lesion in spleen is currently called as sclerosing angiomatoid nodular transformation (SANT). Though known to exist as early as 1978, many of these cases have been previously diagnosed as splenic exuberant granulation tissue, hamartomas, multinodular hemangiomas or even as inflammatory pseudotumors (2-4).

Herein we describe two cases of SANT, extramedullary hematopoiesis in one of our cases was an association never earlier reported. The characteristic gross features of this case prompted us to revise the diagnosis of the earlier case.

SANT as a distinct entity was initially described by Martel in 25 patients and recently by Diebold in 16 splenectomy specimens (4,5). The female: male ratio reported is 2:1 and mean age is 48 years (range, 22–74 years). The size ranges from 3 to 17 cm in diameter (5).

Clinically, the patients are usually asymptomatic. They may have variety of unrelated coexisting conditions. Associated haematological conditions that have been reported include leucocytosis, polyclonal gammopathy, increased erythrocyte sedimentation rate and myelodysplastic syndrome (5,6). Possibly the transient bone marrow suppression leading to extra-medullary hematopoiesis could have triggered red pulp transformation in this case. Apart from this explanation, the patient did not have any haematological abnormality that could offer explanation for other associations as mentioned above.

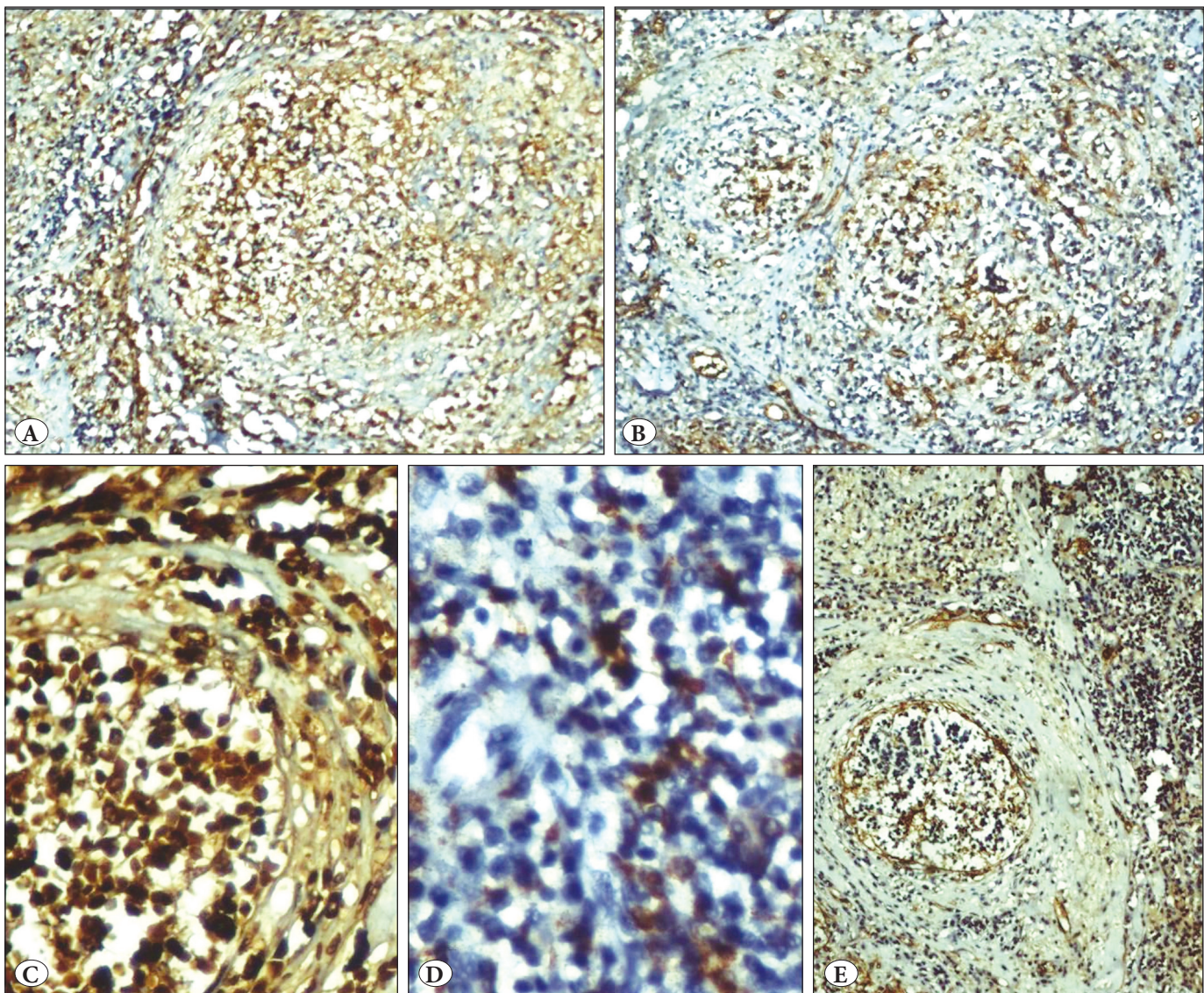


Figure 3: Immunohistochemistry with (A) CD 31 positivity in few slit like vessels within the lesion (x100) (B) CD34 positivity in small calibre vessels (x100) (C) Myeloperoxidase (MPO) marking the hematopoietic cells (x400) (D) CD68 highlighting few scattered macrophages (x400) and (E) Smooth muscle actin (SMA) positive musculature surrounding nodules surrounded by bland fibrosis (x400).

The mass is usually detected during radiological work-up for other unrelated conditions. Grossly, the mass shows multiple individual and confluent variable sized nodules with diameter ranging from 3 to 17 cm. This classic appearance was a clue to diagnosis in this present case and diagnosis was suspected on gross examination.

Microscopically, the nodules show a variable admixture and sieve like arrangement of vascular spaces that represent an admixture of cells lining splenic sinusoids, capillaries and veins (4). The degree of circumscription of nodules by collagen and the quality of the intervening stroma (whether fibromyxoid, sclerotic or hyaline) may vary

between individual tumours. This is well reflected in their pattern of immunostaining for CD34, CD31 and CD8. Angiomatoid nodules of SANT are composed of vessels or vascular spaces lined by cells showing either of the three immunotypes 1) CD34+/CD31+/CD8- indicating capillary derivation 2) CD34-/CD31+/CD8+ indicative of splenic sinusoidal lining cells and 3) CD34-/CD31+/CD8- indicating small veins. The splenic red pulp also has similar pattern of expression; thus indicating that nodules of SANT recapitulate the normal splenic red pulp. The microscopic features and immunoprofile of other close differentials have been well described in literature (2).

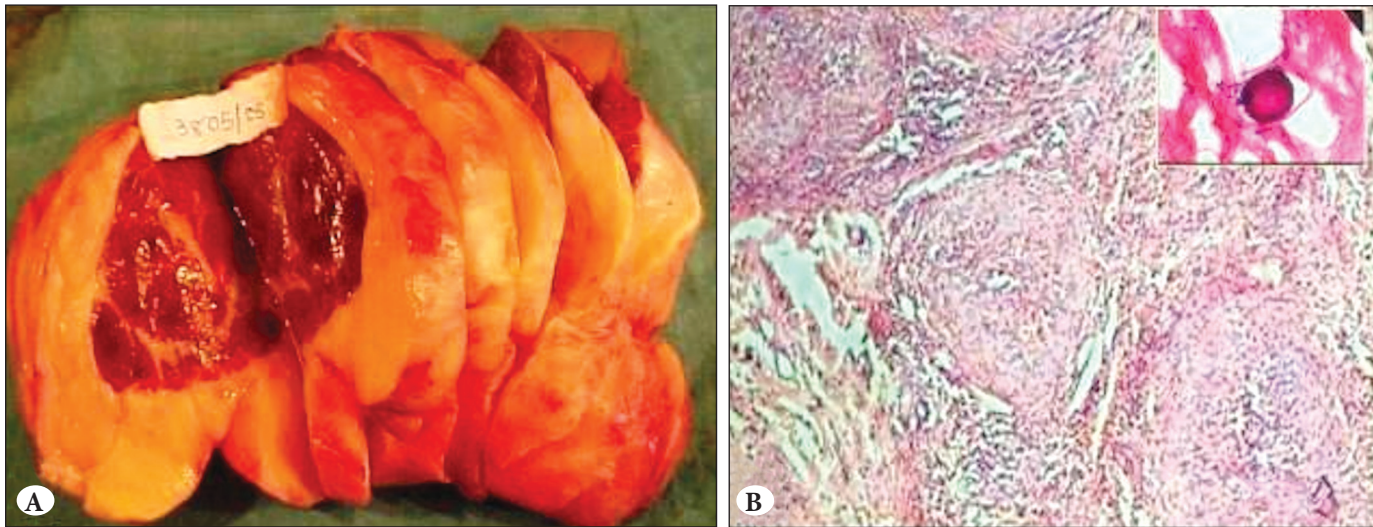


Figure 4: (A) Splenectomy specimen of Case 2 showing a nodular tumour occupying the upper pole. (B) Photomicrograph of the same case showing nodular arrangement of vasculature with surrounding bands of sclerosis. Inset shows focal psammomatous calcifications (H&E x100).

CD68 positivity in SANT favours non-neoplastic origin of this entity and may be indicative of active phagocytosis due to increased splenic proliferative activity (7). Radiological features of SANT have now been well described (6,8). Plain and contrast enhanced CT features in our cases correlated with those already reported. On CT scanning, the lesions are usually isodense or hypodense when compared with splenic parenchyma. Magnetic resonance imaging with contrast and ^{99m}Tc -sulfur colloid scanning in case 1 would have helped us in pre-operative assessment of extensive extra-medullary hematopoiesis, but it was not done. This is a common scenario in a developing country like ours where this investigation is not routinely available.

The combined effect of a stagnant splenic circulation (due to passive congestion) and local metabolic effects as anoxia are triggers for formation of angiomatoid nodules. Damaged endothelial cells when coupled with myofibroblast and neocapillary proliferation, lead to fibrin deposition and granulation tissue formation akin to wound repair. The end result is an exuberant (and to a little extent organised) proliferation and transformation of the red pulp to form SANT.

The differential diagnosis of SANT includes hemangioma, littoral cell angioma, splenic hemangioendothelioma, inflammatory myofibroblastic tumor, hamartoma and nodular transformation of splenic red pulp in response to metastasis. Hemangiomas in the spleen are usually smaller than 2 cm and of the cavernous type. Littoral cell angioma is a tumor of the littoral cells, which exhibit both endothelial and histiocytic phenotype. The cells are

negative for CD34 unlike the mixed immune-expression of SANT. Unlike other body sites, hemangioendothelioma in the spleen is a controversial entity. In addition to the presence of characteristic intracytoplasmic red blood cells, cells of hemangioendothelioma are variably positive for CD34. Many previously described splenic multinodular hemangiomas and hamartomas could in the present times be categorised as SANT. The former lesions are benign, whereas the outcome of SANT is intermediate between benign tumors and malignant sarcomas. With classic gross and histopathological features as in this case, we consider the name 'SANT' more appropriate as it better conveys the intermediate prognostic significance.

Extensive extramedullary haematopoiesis is unreported in these cases. Probably our first case had transient bone marrow suppression which could have caused the spleen to take up haematopoiesis, though this feature is not well characterised in adults. It is unclear as to whether extra-medullary haematopoiesis in this case could have incited the excessive organised red pulp transformation. Further reported cases will help better demographic and clinical characterisation of SANT.

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