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Case Report

Sclerosing angiomatoid nodular transformation of spleen: an uncommon benign lesion of spleen

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ABSTRACT

SANT (sclerosing angiomatoid nodular transformation) is a rare benign vascular tumour of spleen. SANT can mimic benign and malignant conditions of spleen. There are no definite radiological features. It has characteristic histopathology and immunohistochemistry findings which help us to differentiate it from other angiomatoid and tumor-like lesions. Splenectomy is the treatment of choice as it is diagnostic and therapeutic at the same time. We present a case of 22 years female with left upper quadrant pain since, 2 months. Magnetic Resonance Imaging revealed well-defined hypodense mass measuring 6.3×6.1×5.8cm in the spleen, with provisional diagnosis of hemangioma. Laproscopic splenectomy was done and a diagnosis of SANT was made on histology and immunohistochemistry. This case shows us that SANT should be considered in the differential diagnosis of splenic solid lesions.

INTRODUCTION

Solid tumors of the spleen are rare, with an incidence of 0.007%. Sclerosing angiomatoid nodular transformation (SANT) of the spleen is a rare benign primary tumor of the spleen with unknown etiology. It is characterized by benign proliferation of vascular tissue within the red pulp of the spleen.[1] Some theories suggested in the evolution are- (1) abnormal inflammatory response, (2) dysimmune disorders (IgG4 related), (3) perturbations in red pulp blood flow.[2] SANT lesions were originally thought to occur predominantly in females. Currently with increased awareness of this lesion and a greater number of cases are being reported. 44.3% of the cases are males, with increased incidence between 30 and 60 years of age.[1] Most patients are asymptomatic, splenomegaly being a rare presentation. Absence of definitive imaging signs and various growth patterns makes it challenging to come to a proper pre-operative diagnosis of SANT. Splenectomy can be both diagnostic and treatment modality.[3,4] Accurate diagnosis can be obtained on histopathology and immunohistochemistry studies of the splenectomy specimen.

CASE REPORT

A 22 years old female presented with intermittent dull-aching left upper quadrant abdominal pain since, one month, partially relieved on medications and with no constitutional symptoms. Hematological parameters, liver and kidney function tests were unremarkable. Abdominal Ultrasound revealed a space occupying lesion in the spleen. MRI showed well defined hypodense lesion measuring 6.3×6.1×5.8 cm in the spleen hemangioma (Figure 1). Laproscopic splenectomy suggestive for further evaluation was done.

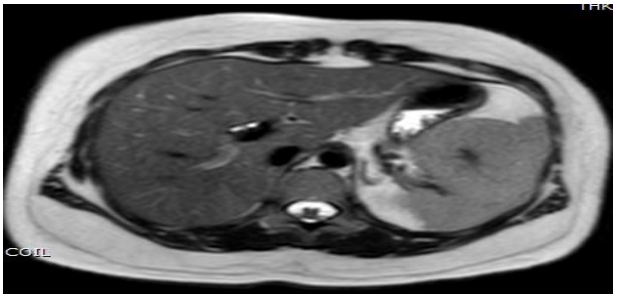

Figure 1: Axial T2W image demonstrating circumscribed isointense lesion in spleen with central hypointense scar.

On gross examination, splenectomy specimen measuring 12×8×5.5 cm with cut section showing a well circumscribed non-encapsulated bosselated mass measuring 6.5×5×5 cm. Cut section of the mass showed a scar composed of red brown to grey brown area separated by fibrotic stroma. The lesion was slightly firm than the rest of the spleen (Figure 2).

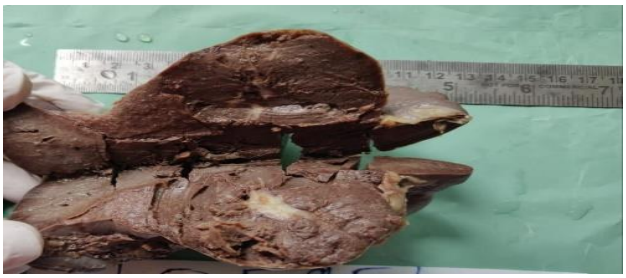

Figure 2: Splenectomy specimen showing well circumscribed mass and a scar on cut section.

On microscopy sections revealed a thick dense connective tissue capsule. The subcapsular area showed replacement of the splenic parenchyma by well-circumscibed multinodular pattern of vascular spaces surrounded by dense hyalinised collagen. The nodules were composed of vascular spaces of varying sizes lined by endothelial cells interspersed by few hemosiderophages and sparse inflammation composed of lymphocytes and few plasma cells. Occasional giant cell reaction seen. No nuclear atypia, no mitosis and necrosis seen (Figure 3-5).

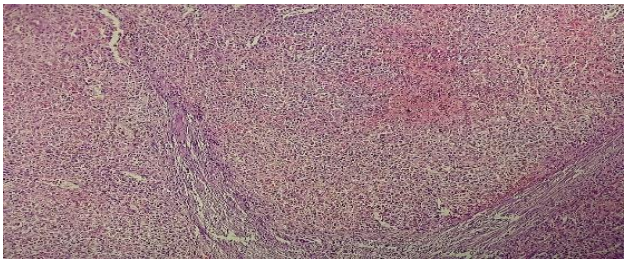

Figure 3: Splenic parenchyma showing nodule formation. H and E 10X.

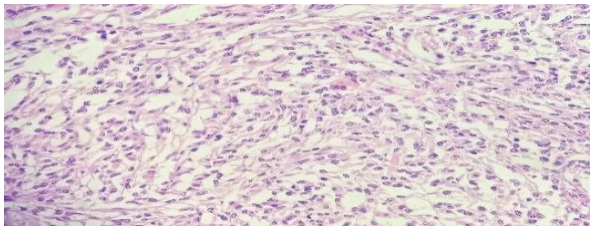

Figure 4: Section shows varying sizes of vascular spaces lined by endothelial cells with intervening collagen. H and E 40X.

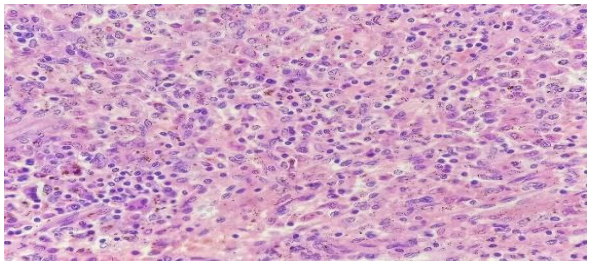

Figure 5: Nodules show haemosiderin laden macrophages with interspersed inflammatory cells. H and E 40X.

Further evaluation with immunohistochemistry showed CD34 and CD31 positivity highlighting well-formed blood vessels. CD31 immunostain highlighted capillaries, veins and sinusoid like spaces within the nodules like a complex network. CD 34 immunostain highlighted the capillaries. SMA highlighted smooth muscle fibres (Figure 6-8). CD8, CD30 and ALK-1 were negative.

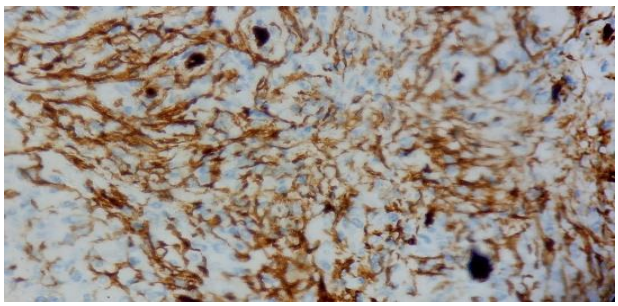

Figure 6: Immunohistochemistry- CD34 positive.

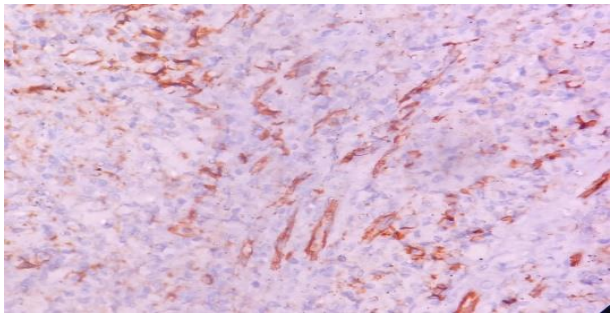

Figure 7: Immunohistochemistry- CD31 positive.

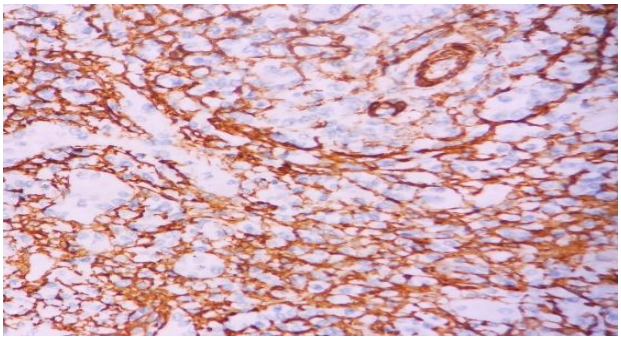

Figure 8: Immunohistochemistry- smooth muscle actin positive.

Serum IgG4 levels were normal. There was no evidence of increased plasma cells on light microscopy. Hence IHC for IgG4 was not done. Based on the characteristic macroscopic features, H and E and IHC findings the final diagnosis was that of SANT. Patient is currently asymptomatic and there is no evidence of recurrence on follow-up.

DISCUSSION

Splenic lesions are of an incidental nature. Benign vascular tumors are the second most common tumors of the spleen after lymphoma. Close differentials for SANT include hamartoma, hemangioma, littoral cell tumor, a lymphangiom, extramedullary hematopoesis, inflammatory pseudotumor, hemangioendothelioma and from malignant lesions like angiosarcoma and myeloma. The incidence of SANT is low and less than 200 cases have been reported since 2004.[5] SANT predominantly affects middle aged population with a median age of 44yrs with a near equal gender ratio.[6]

In 1993, Krishnan et al described it as 'Splenic cord capillary angioma'. Later the disease was described as 'multinodular hemangioma'. In 2004, the SANT entity was given by Martel et al in a study of 25 cases. According to Martel et al, SANT arises from red pulp of spleen rather than white pulp.[7]

The most common presentations are incidental finding of an asymptomatic splenic mass, abdominal pain or discomfort and splenomegaly.[7] The etiology of SANT is obscure. Some papers have reported relationship between systemic inflammatory reactions, Epstein- Barr virus infection, trauma, splenic hematomas and SANT.[2,8]

Ultrasonographic features of SANT have been poorly described. On USG, it usually appears as a heterogenous hypoechoic mass with acoustic shadowing at the center.[6]

Computed Tomography reveals a well circumscribed mass that is hypodense and early peripheral enhancement which extends in a spoke wheel pattern towards the center with progressive central enhancement. This pattern is due to central stellate fibrous stroma with fibrous septa separating angiomatoid nodules.[9,10]

MRI of SANT on T2-weighted imaging show the lesion as a spoke-and-wheel pattern, which is similar to the pattern obtained by multiphase imaging with CT and may be useful for the diagnosis of SANT.[6] Pre-operative diagnosis of SANT is difficult with no specific or sensitive method available to rule out malignancy and other differential diagnosis. Ultrasound guided core needle biopsy of the spleen may be performed but bleeding or dissemination of the tumour may be a complication of this procedure. Laproscopic splenectomy is the recommended procedure for diagnosis and treatment.

Macroscopic features of SANT show a well-circumscribed un-encapsulated lesion with a central white scar. Microscopically a multinodular growth pattern with nodules composed of a variable mixture of vascular spaces surrounded by dense collagen fibrosis and fibroid rims is seen. Internodular stroma show myxoid to dense fibrous tissue with scattered plump myofibroblasts, lymphoplasma cells and siderophages.[11] These findings indicate gradual progression of angiomatoid nodules to collagenized fibres. Few studies suggest that the fusiform cells in the nodules are considered to be myofibroblasts with expression of SMA found to be inside and around the angiomatoid nodules extending to the junction between the lesion and splenic tissue and infiltrated the nodules and residual splenic tissue.

Few studies hypothesized that certain factors such as inflammation, trauma and hemorrhage can lead to myofibroblast proliferation, splenic tissue division and encapsulation, small vessel growth in the interstitial space and vascular structures in the sinusoidal endothelial cells, fibrosis and hyaline degeneration.[12]

On immunohistochemistry the classical appearance of SANT is characterized by three distinct type of blood vessels. The first type are well formed cord capillaries arranged in a lobular pattern and are CD 34+/CD8-/CD31+. The second type are splenic sinusoids which are negative for CD34 and stain positive for CD8 and CD31. The third type are small veins arranged in mesh like pattern and are CD34-/CD8-/CD31+. None of the cells in the lesion stain positive for CD23, CD30, ALK-1 and EMP-LMP.[6,7,13] SANT and IgG4-related sclerosing lesions has been seeking attention in the recent times. IgG4-related sclerosing lesions have shown sclerosing inflammation and infiltration of numerous IgG4+plasma cells with increased serum IgG4 levels. Clinically, few patients with SANT have high levels of IgG4 and on microscopy they have dense IgG4+plasma cells within the fibrous stroma thus sharing common features with IgG4-related sclerosing lesions.[5,14]

SANT should be distinguished from its various differential diagnosis. Inflammatory pseudotumors

consist of proliferating fibroblasts and mixed inflammatory cells consisting of lymphocytes, plasma cells and histiocytes but do not posses angiomatoid nodules as seen in SANT. Splenic hamartoma, a neoplastic condition shows highly proliferated red pulp with irregularly arranged cells and has no multiple angiomatoid nodules and proliferating myofibroblasts.[6]

Littoral cell angioma has sinus shaped lumens with different sizes that are mutually linked in a labyrinthine manner or papillae inside coated with endothelial- like cells and lacks fibrosis and hardening as seen in SANT.[14,15] Follicular dendritic cell tumors, in which fusiform tumor cells are arranged alternately, in a lymphocytic background but angiomatoid nodules are not seen. CD21 and CD23 are expressed by the follicular dendritic cells.

Hemangiomas are common benign tumors that arise from sinusoidal epithelial cells and lack the typical trivascular pattern of proliferation seen in SANT.[16] Lymphangiomas arise from the lymphatic endothelium showing cystic spaces lined by single or multi-layered endothelium.[17] Angisarcoma is a common primary malignant tumor of the spleen showing irregular anastomosing vascular channels with marked cytological atypia and invasion. Absence of nodular growth pattern and presence of invasion, atypia and mitosis helps us to differentiate it from SANT.[6] All the conditions mimicking SANT lack the nodular pattern of SANT and each stain for only a single type of vascular channel.

CONCLUSION

SANT of the spleen in a rare benign pathological condition. It can mimic other benign and malignant splenic lesions. Pre-operative correct diagnosis is difficult. Possibility of SANT should be considered in the differential diagnosis when solitary lesions are identified on imaging. Splenectomy is the treatment of choice because it is diagnostic and therapeutic in a definitive way. It is confirmed on microscopy by multiple angiomatoid nodules separated by collagenous bundles. Hence a thorough histological evaluation with ancillary IHC markers are necessary for a definitive diagnosis.

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