Case Report

Sclerosing angiomatoid nodular transformation of spleen with calcifying fibrous pseudotumor: A rare case with unusual association

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ABSTRACT

Sclerosing angiomatoid nodular transformation (SANT) of the spleen is a rare benign vascular lesion of the spleen that was first described in 2004. SANT is associated with other concurrent diseases, mostly malignancies. Calcifying fibrous pseudotumor (CFPT) is a tumor-like lesion usually arising from soft tissue or peritoneal sub-serosa. Both SANT and CFPT are considered to be variants of the inflammatory myofibroblastic tumor. We report the rare case of a 24-year-old female presenting with a left abdominal mass that was clinically diagnosed as an extraintestinal gastrointestinal stromal tumor (GIST). Histopathological examination revealed SANT of spleen and CFPT. We report this case due to its rarity of occurrence and unusual association of SANT with CFPT.

Key words: Calcifying fibrous pseudotumor, Inflammatory myofibroblastic tumor, Sclerosing angiomatoid nodular transformation, Spleen

INTRODUCTION

Sclerosing angiomatoid nodular transformation (SANT) is a non-neoplastic vascular lesion of the spleen characterized by multiple nodules having a central vascular core containing capillaries, sinusoids, and small veins, which are surrounded by a fibrosclerotic zone with the presence plasma cells indicating association with IgG4-related sclerosing disease. In 2004, this vascular lesion in the spleen was first described by Martel *et al*. [1]. The patients with SANT have a high prevalence (20%) of concurrent diseases with most of them being malignancies at other sites such as renal cell carcinoma, colonic carcinoma, gastric carcinoma, lung cancer, and leukemia [2]. Very few cases of SANT associated with calcifying fibrous pseudotumors (CFPTs) have been reported in the literature [2]. CFPTs are rare benign lesions arising from the soft tissue or peritoneal subserosa and are considered to arise from the inflammatory myofibroblastic tumor (IMT) [3].

To date, six cases of SANT associated with multiple calcifying fibrous tumors were reported from Taiwan [2,4]. To the best of our knowledge, the present case is the first case to be reported in the literature from India.

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CASE REPORT

A 24-year-old female presented with a complaint of the left-sided abdominal mass for the past 1 year with a history of associated dull aching and non-radiating pain in the left side of the abdomen for 1 month. There was no history of fever, bladder/bowel disturbances, vomiting, loss of appetite, and loss of weight.

General examination revealed a pulse rate of 80/min, blood pressure of 116/78 mm hg, and respiratory rate of 14/min. Abdominal examination revealed a 16×10 cm hard, mobile, and non-tender mass palpable below the left hypochondrium.

Routine hematological examinations were within normal limits except for the erythrocyte sedimentation rate of 100 mm/h. Computed tomography (CT) abdomen showed a well-defined large lobulated mixed-density lesion showing calcifications with heterogeneous enhancement post-contrast, in the retroperitoneum on the left side extending from the left hypochondrium till L4 displacing spleen anterosuperiorly. The lesion was completely encasing the spleen, body of the pancreas, portal vein, splenic vein and splenic artery, and extending up to the abdominal wall (Fig. 1). A clinical diagnosis of retroperitoneal extraintestinal gastrointestinal stromal tumor (GIST) was considered.

During surgery, approximately 30×20×20 cm retroperitoneal tumor encasing the spleen and extending inferomedially

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displacing bowel loops, sigmoid colon, descending colon, left kidney, pancreas, duodenum, and stomach was noted. Growth appeared to be infiltrating the body, neck, and tail of the pancreas. Partial resection of the tumor was done leaving the tumor attached to the pancreas and sent for histopathological examination.

We received a retroperitoneal tumor excision specimen with an attached spleen measuring 29×22×22 cm. The cut section revealed a grey-white solid firm lesion measuring 15.5×12×12 cm having whorling appearance, with an attached spleen which was tan-brown measuring 13.5×10.5×10 cm. The spleen was nodular in appearance (Fig. 2).

Microscopy revealed a spleen with nodules having central vascular spaces lined by endothelial cells surrounded by the fibrotic zone. At the periphery of nodules, chronic inflammatory cells with plasma cells and few lymphocytes were seen (Fig. 3a). Adjacent to the splenic parenchyma, a grey-white lesion showed that spindle-shaped fibroblasts embedded in a collagenous stroma. Focal chronic inflammatory cells were seen. Foci of psammomatous calcifications were noted (Fig. 3b and c).

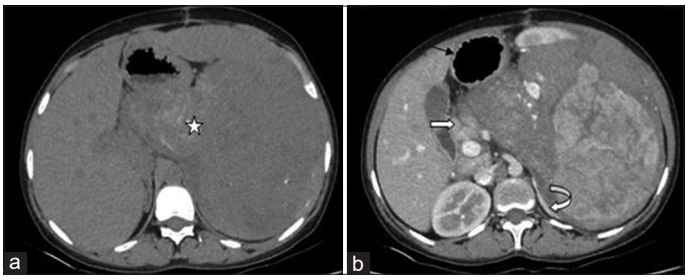

Figure 1: Non-contrast CT (a) and contrast-enhanced CT abdomen axial image (b) showing large heterogeneously enhancing soft-tissue density lesion in the spleen with amorphous cloud like calcification (star) within and lesion is displacing stomach anteriorly and to right (black arrow), pancreas posteroinferiorly (white arrow) and to right and left adrenal medially (curved arrow)

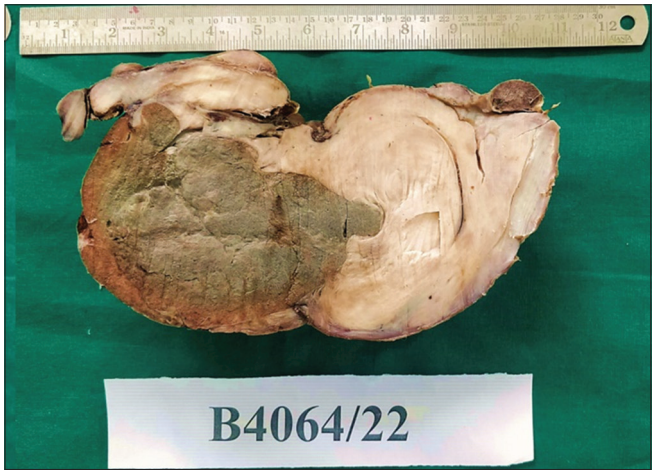

Figure 2: Excision specimen with tan-brown spleen showing nodularity and adjacent attached grey-white solid firm lesion having whorly appearance

Immunohistochemistry was performed with CD34, CD31, CD138, IgG4, ALK, and Actin. In the spleen, endothelial cells in the central core of nodules stained positive with CD34 and endothelial cells in the sinusoids stained positive with CD31. Plasma cells present in the periphery of nodules and in the fibrotic lesion stained positive with CD138 and IgG4. Spindle cells in the fibrotic zone were negative for ALK and actin. Based on the above morphological features and immunohistochemistry, a diagnosis of SANT of the spleen associated with CFPT was made. The post-operative period was uneventful.

DISCUSSION

SANT is a rare benign vascular lesion in the spleen which was first described in 2004. Before its identification, this lesion was reported as hemangioma, hemangioendothelioma, or hamartoma [5]. SANT showed slight female predominance [6] and usually present between 30 and 60 years of age [7]. However, in our case, the patient was of a 24-year-old female.

Most of the patients are asymptomatic and the lesion was detected incidentally during imaging. Some of them presented with abdominal discomfort, pain, palpable mass, pelvic pain, thrombocytopenia, anemia, night sweats, and long-standing fever [7]. CT imaging of the spleen shows a well-circumscribed solitary, hypodense, or isodense mass in the plain CT images with or without a central calcification [8] and showed a "spoke-and-wheel" pattern on multiphasic imaging in case of SANT [9].

Morphological features of SANT are well-circumscribed and bosselated mass with tan-white or red-brown nodules separated by fibrotic stroma on gross examination. Microscopic examination reveals multiple nodules composed of vascular spaces lined by endothelial cells, surrounded by dense fibrocollagenous tissue with few chronic inflammatory cells in the internodular zones of SANT. Inflammatory cells, siderophages, plasma cells, myofibroblasts, and erythrocytes can be present in these nodules. Cytologic atypia, necrosis, mitotic figures, and histiocytic giant cells will be absent in these lesions [7].

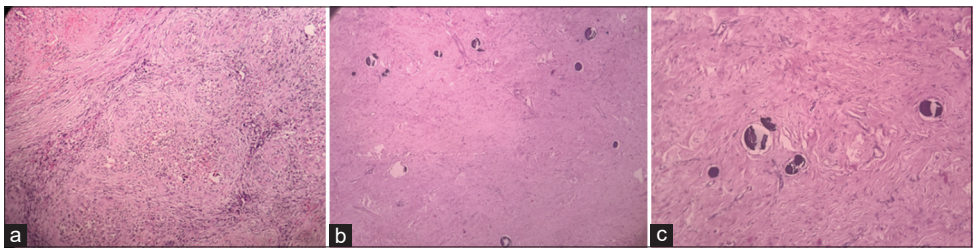

Figure 3: (a) Spleen with nodules having central vascular spaces lined by endothelial cells surrounded by the fibrotic zone with lymphoplasmacytic infiltrate (H and E, ×100). (b) Grey-white lesion showing spindle shaped fibroblasts embedded in collagenous stroma with focal psammomatous calcifications in some foci (H and E, ×100). (c) Grey-white lesion showed spindle shaped fibroblasts embedded in collagenous stroma with few chronic inflammatory cells and focal psammomatous calcifications (H and E, ×400)

SANT consists of three distinct types of vessels, that is, small veins, sinusoids, and capillaries. Endothelial cells of the small veins stain with CD31 but are negative for CD8 and CD34. Sinusoidal endothelial cells are CD31 positive, CD34 negative, and CD8 positive. Endothelial cells of capillaries are usually CD34 and CD31 positive but negative for CD8. As SANT has an overgrowth of these vessels, it is also considered a variant of splenic hamartoma [2].

Littoral cell angioma (LCA) is considered as differential diagnosis. LCA presents grossly as a nodule with sponge-like vascular spaces comprising of anastomosing sinusoids lined by tall endothelial cells which express both histiocytic markers like CD68 and KP-1 and also endothelial markers like CD31 and CD34. However, endothelial cells are negative for CD8.

Pathogenesis of SANT is still unclear due to the limited number of cases. SANT was considered a variant of hamartoma as angiomatoid nodules comprised of red pulp only which has undergone a peculiar pattern of sclerosis. Some of them proposed that SANT is a reactive lesion rather than a neoplasm. Some considered SANT a variant of the inflammatory pseudotumor because of the presence of granulation tissue like or angiomatoid core and fibro myxoid cortex. SANT contains myofibroblasts and a few inflammatory cells in the peripheral sclerotic regions, unlike the conventional inflammatory pseudotumor. However, usually, splenic inflammatory pseudotumors contain the EBV genome which is not present in SANT. However, SANT is considered a reactive lesion as it is associated with concurrent diseases (20%) at other sites, most of them being malignancies [2]. In our case, the patient has SANT associated with CFPT encasing the spleen and tail of the pancreas.

In 1988, CFPT was first reported by Rosenthal and Abdul-Karim among two children [10]. The tumor usually arises from the soft tissue or peritoneal subserosa. These lesions in the soft tissue tend to occur in childhood, whereas, lesions from the peritoneal subserosa are seen in both children and elderly patients.

Grossly, CFPT appears as a well-circumscribed grey-white lesion. Microscopic examination of these lesions reveals spindle-shaped fibroblasts in dense hyalinized collagen showing lymphoplasmacytic infiltrate and psammomatous calcifications. Immunohistochemically, spindle-shaped fibroblasts are positive for factor XIIIa and Vimentin. They stain variably with SMA and CD68 but are negative for Bcl-2, CD117, ALK, Calretinin, EMA, and S-100. Histological feature of CFPT overlaps with IMT and hence, is considered to represent a late sclerosing stage of the IMT [11]. IMTs are more cellular when compared to CFPT and lacks calcifications. Cells of IMT express ALK which is absent in CFPT. Due to the above distinct histological and immunohistochemical features, some of the researchers consider CFPT as a separate entity. Although CFPT has been included in benign tumors of soft tissue and bone in the World Health Organization classification, the neoplastic nature of this lesion remains controversial [12].

Differential diagnosis of CFPT includes desmoplastic fibroblastoma, fibromatosis, and GIST. Desmoplastic fibroblastoma is a multinodular and hypocellular lesion with hyalinized stroma and spindle-shaped cells. However, it lacks inflammatory cells and calcifications which distinguish it from CFPT. Fibromatosis has an intermediate biologic behavior with an ill-defined and infiltrating border. Histologically, it also has hyalinized stroma with spindle cells but lacks inflammatory cells and calcifications. Cells in fibromatosis show β-catenin positivity which is absent in CFPT [13]. GIST often expresses CD117 and DOG1 which are not expressed in CFPT. Our case was clinically diagnosed as extraintestinal GIST on imaging which was further diagnosed as SANT of the spleen with CFPT based on morphological features and immunohistochemistry.

Clinically CFPT and SANT are benign lesions with favorable prognoses. Recurrence has been reported in CFPT, but SANT does not show recurrence after splenectomy [2]. The recurrence rate for CFPT has been estimated to be approximately 10% [14]. Recurrence was reported in one case after 15 months of surgical resection [15].

CONCLUSION

SANT and CFPT are two benign entities that may have common etiologic factors contributing to the development of these lesions. Both lesions are considered to be closely related to the IMT. However, further molecular studies are required to understand the pathology of these lesions. We report this case due to the rarity of these lesions with the unusual association.

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