Case Report
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Sclerosing Angiomatoid Nodular Transformation of the Spleen: A Case Report

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Objectives: Sclerosing Angiomatoid Nodular Transformation (SANT) of the spleen is a rare benign vascular lesion with unknown etiology. Our purpose is to present our experience with this condition and review the available literature regarding it. **Methods:** This report depicts a pathologically proven case of SANT in a 32-year-old man with a history of two previous old injuries who presented with weight loss, vomiting and with left upper quadrant pain and an enlarged spleen. **Results:** The patient was successfully treated by splenectomy and diagnosed with SANT based on histological and immunohistochemical findings postoperatively. **Conclusion:** Most patients with SANT are asymptomatic. Imaging studies are essential for detection and the management of SANT. However, the final diagnosis can only be made by histopathology. SANT does not recur after splenectomy.

Keywords: Spleen, Hamartoma, CD34, Splenectomy

Introduction

Sclerosing Angiomatoid Nodular Transformation (SANT) of the Spleen is very rare benign vascular neoplasm, which is established firstly as SANT in 2004 by Martel et al[1].To date, 177 cases of SANT had been reported in English literature; however, the exact incidence and pathogenesis are still unclear. SANT occurs predominantly in females with a median age 46 years (range 0-82 years)[2-4]. Generally, a solitary nodule is detected, but a few cases of SANT with multiple nodules had been reported[5]. The majority of patients (46.6%) were asymptomatic at presentation; the remaining patients had symptoms such as abdominal pain, abdominal or back discomfort, fatigue, weight loss, fever, and splenomegaly[6]. Many patients diagnosed with SANT have had a pre-existing or simultaneous malignant neoplasm, including breast cancer, ductal carcinoma of the pancreas, uterine clear cell carcinoma, colon cancer with liver metastasis, rectal cancer, hypopharynx, and thyroid carcinoma etc[2,7-9]. Because SANT is

rare, it is not well-known to clinicians, surgeons, radiologists, or pathologists.[5] Thus, SANT is often misdiagnosed as inflammatory pseudotumor, hamartoma, and hemangioendothelioma[1,10]. Here we present the histopathological and immunohistochemical evidence used to diagnose SANT in a 32 year-old-man with a history of two old injuries and who subsequently presented with left upper quadrant pain.

Case Report

A 32-year-old male presented to the Department of Surgery, The University Hospital of Mongolian National University of Medical Sciences (MNUMS) with left upper quadrant pain, discomfort, and tenderness. The discomfort was intermittent but had become more progressively worse with 13 kg weight loss, with vomiting after eating or exercising for the previous two months. He fell from the 4th floor of building while doing a construction job seven years before presenting to our clinic. Six months before presentation, he was involved in an accident, and computed tomography (CT) (Siemens, Germany) was performed to rule out internal injury. The imaging study showed a hypertensive solitary mass with 10 x 7 cm in his spleen. Follow-up CT of the abdomen performed after five months later demonstrated a slight size increase of the mass up to 12 cm in largest dimension (Figure 1A). The physical examination revealed no pathological findings except weight loss. Laboratory values upon admission showed a hemoglobin of 11.6g/dl, hematocrit 34.7%, mean corpuscular volume 76.4fL, mean corpuscular haemoglobin 25.6 pg, mean corpuscular haemoglobin concentration 33.4 g/dl, red blood cell count (RBC) 15.43 x 10^3/uL, neutrophils 12.63 x 10^3/uL, lymphocytes 1.35*10^3/uL, monocytes 1.41 x 10^3/uL, eosinophils 1.01 x 10^3/uL, and basophils 1.03 x 10^3/uL. The remaining laboratory data, including liver function test, viral markers, electrolyte, urine analysis, and coagulation factors, were within the normal ranges. The patient underwent open splenectomy under the provisional diagnosis of spleen tumor or hemorrhagic mass.

On gross examination, the spleen measured 13 x 12 x 6 cm and weighed 165 g. The cut section showed relatively well-defined multinodular hemorrhagic nodular mass with central scaring, measuring 11 x 9 x 4.5cm (Figure 1B). The resected tissue underwent routine processing for hematoxylin and eosin staining, and light microscope examination. Microscopically, the lesion was surrounded by a thick fibrous capsule and divided by fibrous and fibrosclerotic stroma into multiple nodules with hemosiderophages, myofibroblasts, and inflammatory cells. Within the nodules, slit-like fissures, round, variable-sized blood vessels with extravasated red blood cells, hemosiderin pigment, and focal calcification were present (Figures 2 A-D, 3A, and 3B). Neither nuclear atypia nor mitosis was observed. By immunohistochemical staining, consistent well-formed capillaries were positive for CD34 hematopoietic stem cells (Figure 3C). Also, scattered macrophages are positive for CD68, which is a marker for macrophages and monocytesin contrast to

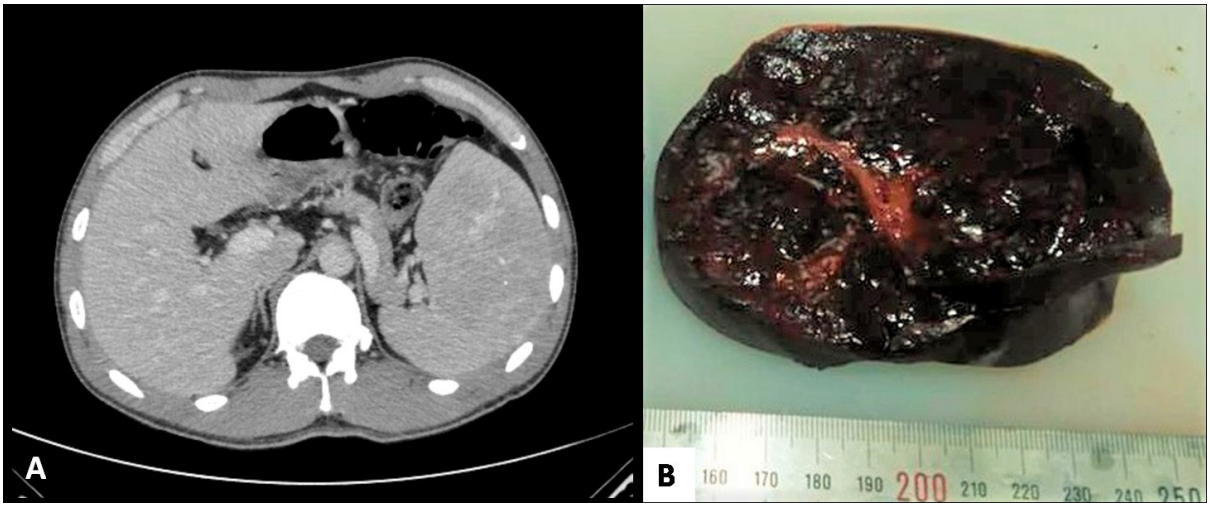

Figure 1. A) CT scan showing enlarged spleen and B) The gross specimen showing multinodular hemorrhagic nodular mass with a radial-scarring pattern of fibrosis.

other inflammatory cells (Figure 3D). Based on histopathological and immunohistochemical findings, the diagnosis of SANT was concluded. The patient's condition improved after surgery, and there was no recurrence within18 months by routine check-up.

Discussion

Martel et al. established SANT as a new separate entity with their description of 25 cases[1]. SANT had previously been diagnosed as other diverse vascular lesions such as hemangioma, lymphangioma, hemangioendothelioma, and angiosarcoma or inflammatory lesions, including inflammatory pseudotumor[2,11].

To date, 177 cases of SANT have been described in English literature. Until recently, SANT was known to occur only in the spleen and only in adults. Then Zavatta et al. reported a SANT in the adrenal gland[10]. Subsequently, SANT was identified in an infant that presented with an abdominal hemorrhage, splenomegaly, anemia, and coagulation abnormalities[4]. Based on the literature review, SANT occurs predominantly in females a with median age 46 years (range 0-82 years)[2-4].

Most patients presenting with SANT (46.6%) were asymptomatic; the remaining patients had symptoms such as abdominal pain, abdominal or back discomfort, fatigue, weight loss, fever, and splenomegaly[6]. Approximately percent of patients diagnosed SANT had pre-existing or simultaneous malignant neoplasm, including breast cancer, ductal carcinoma of the pancreas, uterine clear cell carcinoma, colon cancer with liver metastasis, rectal cancer, hypopharynx, and thyroid carcinoma

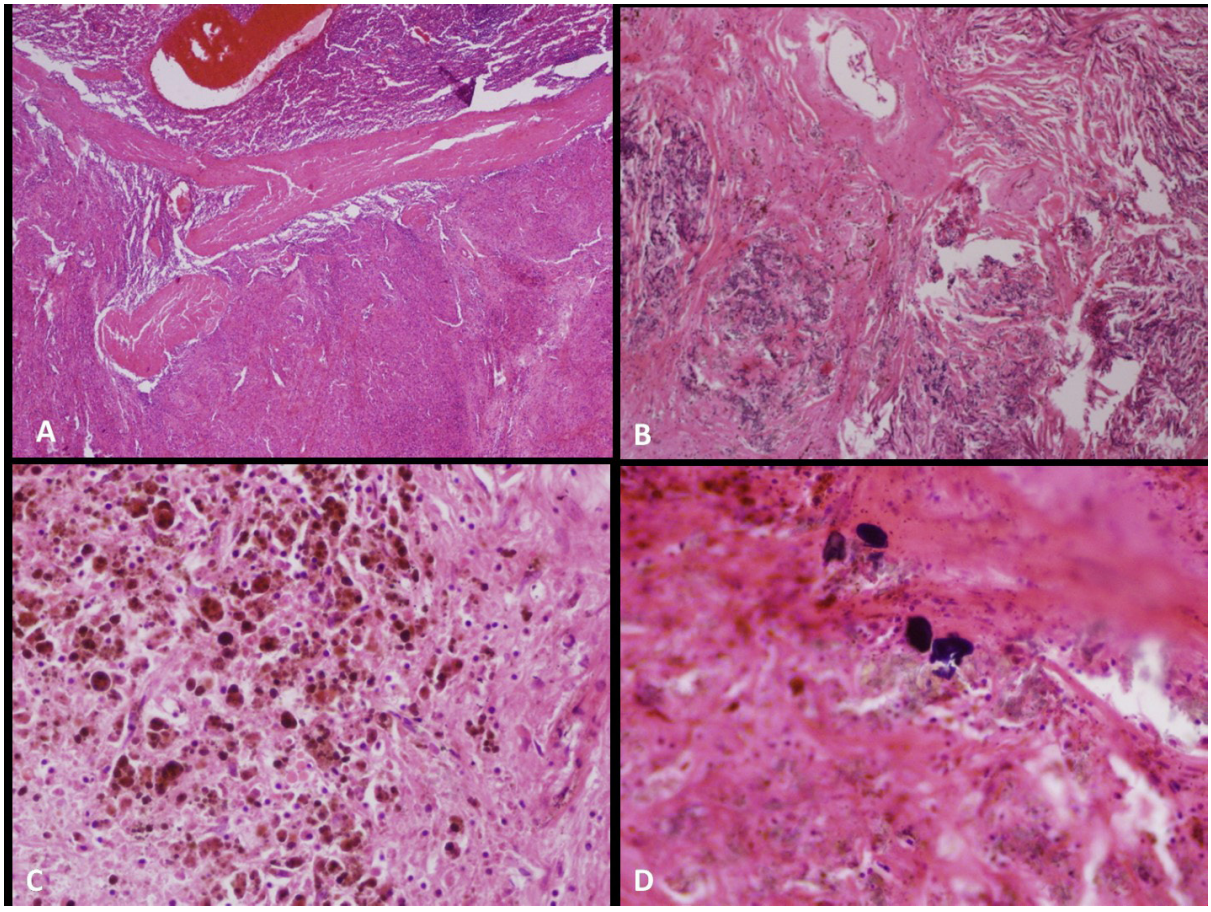

Figure 2. Histopathological findings of SANT. (A) A dense fibrous capsule surrounds the tumor and separated by fibrosclerotic stroma into multiple angiomatoid nodules. The proliferation of collagen fibers and slit-like, regular or irregular shaped vascular spaces are common as shown (H&E, 4x). (B) The tumor is composed of thick collagen fibers arranged in haphazard appearance (H&E, 40x). (C) Angiomatoid nodules show prominent red cell extravasation and hemosiderosis (H&E, 40x). (D) Within the fibrosclerotic stroma, scattered psammoma bodies as shown (H&E, 40x).

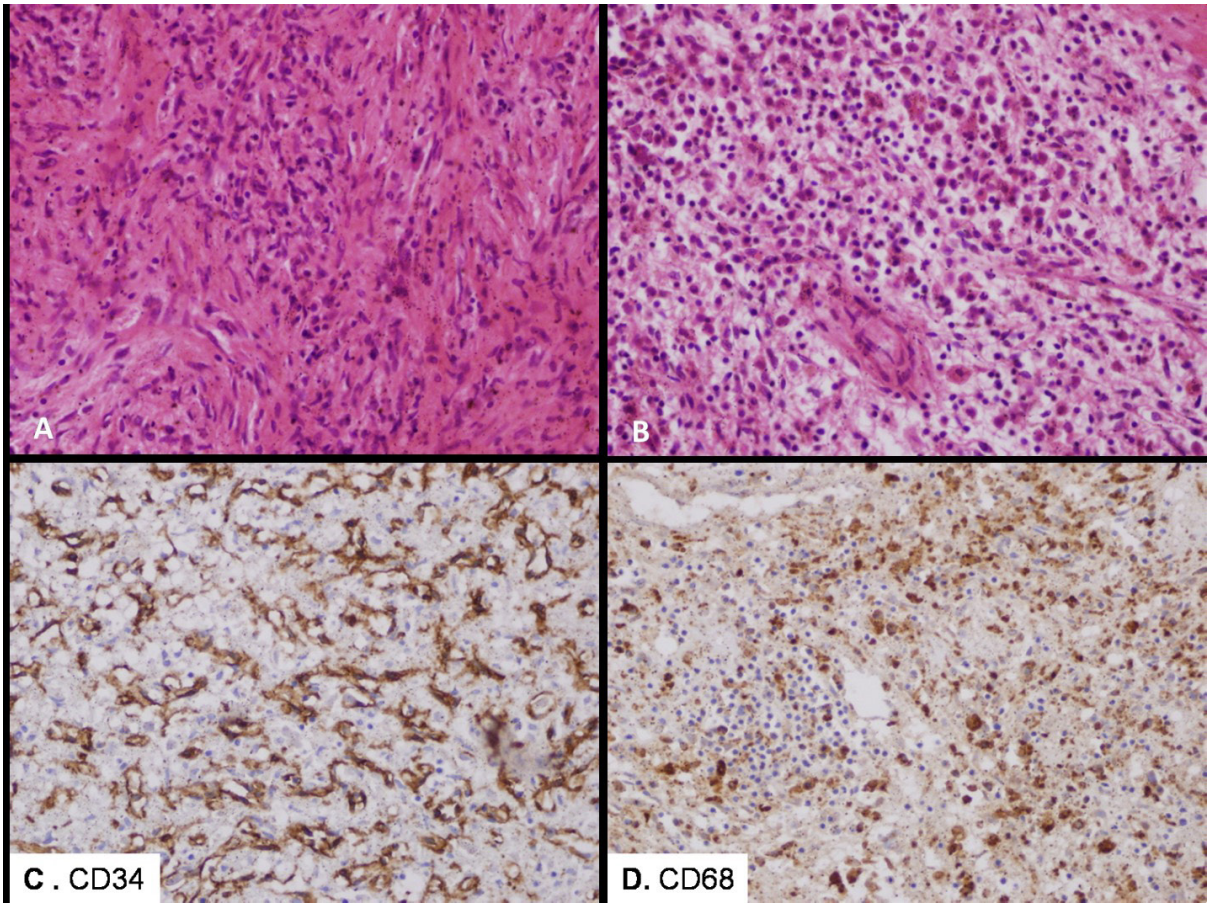

Figure 3. Immunohistochemical findings of SANT. (A). At higher magnification, nodules are composed of myofibroblast-like spindle cells (H&E, 40x) (B) The spindle cells are accompanied by mixed inflammatory cells, including lymphocytes, plasma cells and scattered eosinophils which is reminiscent if inflammatory pseudotumor (H&E, 40x). (C). CD34 is selectively stained in narrow capillaries. Many vascular channels are CD34 negative, including splenic sinusoidal and small veins (CD34, IHC 40x). (D). CD68 is expressed in a few scattered macrophages compared with other inflammatory cells (CD 68, IHC 40x).

etc[2,7-9]. The mean maximal lesion diameter was 49.5 mm, ranged between 3.83 mm to 175 mm in 71 cases[2]. In our case, the patient was a young male with two injuries within seven years. Two out of seven cases reviewed by Peilong et al. had a history of traumatic injuries as well as our case; however, the correlation between SANT and traumatic injuries has not yet been determined[12]. Compared to the previous examples, the size of our patient's lesion was relatively large (11 x 9 x 4.5 cm). This gradual increase in tumor size was related to progressive worsening of symptoms, such as abdominal discomfort, weight loss, and vomiting after meals[1]. This suggests that larger tumor size was associated with clinical symptoms.

Splenic neoplasms are often incidentally identified in imaging studies, such as in our patient who had a CT scan after being in a car accident. Ultrasound imaging findings of SANT are non-specific, usually described as heterogenous hypo or hyperechogenic mass[13]. The contrast CT findings in SANT shows a heterogeneous hypodense mass in early portal venous phase imaging or peripheral nodular enhancement on arterial phase imaging and a hypervascular rim during portal venous phase imaging. The radial scarring pattern of fibrosis is mostly associated with the pathological macroscopic findings on CT, and this pattern could be more prominent on MRI[14-16]. The decreased signal on longer gradient-echo images may be related to secondary hemorrhage and hemosiderin deposition within mass[17].

On gross pathology, previous studies have reported that SANT is mostly solitary, well-circumscribed, multinodular

angiomatoid nodule with central radial scarring. These features were identified in our case, as well. Microscopically, the following characteristic findings are required to diagnose as SANT; at low magnification, a relatively good circumscribed lesion surrounded by dense fibrotic capsule usually with a centrally located fibrosclerotic scar. The lesion may grow in a multinodular pattern which is separated by thin connective tissue. The individual nodules typically show different histologic characteristics, such as slit-like, regular, and irregular vascular spaces lined by plump endothelial cells and interspersed by a group of spindle or oval cells. The presence of numerous red blood cells and hemosiderosis as well as scattered inflammatory cells, including plasma cells, and lymphocytes are characteristic. The internodular stroma consists of myxoid to dense fibrous tissue with plump myofibroblasts and scattered psammoma bodies[1,2,5,18,19]. On immunohistochemical staining, three types of vessels have been observed, which are characteristic of SANT. Capillary vessels are positive for CD34 and CD31 but are negative for CD 8. Sinusoid vessels are positive for CD31 and CD8, but negative for CD34. Small veins are positive only for CD31 and negative for both CD34 and CD8[1]. Our case contained histopathological as well as definitive immunohistochemical features characteristic of SANT. Also, the above findings support that SANT is a distinctive non-neoplastic, benign vascular lesion.

Some researchers have been suggesting that SANT may be related to IgG4–associated inflammatory pseudotumor or Epstein-Barr Virus (EBV) infection in endothelial cells[5]. Chang et al. summarized that SANT is polyclonal benign lesion rather than neoplasm based on only 2 out of 22 cases having an increased level of IgG4+ cells suggestive of a tumor and did not show inflammatory pseudotumor-like morphology[20]. Nomura et al. found no relationship between EBV and SANT using Epstein-Barr virus by in-situ hybridization in 28 cases of SANT[2].

To date, all cases of SANT have been cured by surgical excision without recurrence or metastasis. Histopathological examination is strongly recommended for the diagnosis and treatment of all splenic lesions. Also, laparoscopic splenectomy could be used as a treatment for SANT as a feasible and minimally invasive procedure.

Finally, the main identifying attributes are its solitary onset, a well-circumscribed lesion with a multinodular angiomatoid appearance and heterogeneous immunostaining profile using vascular immunohistological markers. To date, histopathological examination remains the gold standard for the diagnosis of SANT.

Conclusion

This case report describes a case of SANT in a young man who had two old injuries. The clinical findings were not specific. The abdominal CT had characteristic features of SANT, but splenic hemorrhage and malignancy were considered in the differential diagnosis. The condition could only be definitively diagnosed by histopathological examination.

Conflict of Interest

The authors state no conflict of interest.

Acknowledgments

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