Sclerosing Angiomatoid Nodular Transformation of the Spleen: A Case Report

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Background: Sclerosing angiomatoid nodular transformation (SANT) of the spleen is a non-tumorous benign lesion that originates in the spleen and It is rare.
Case Presentation: A 59-year-old man visited his physician for a checkup. Ultrasonography showed a mass in the spleen, and the patient was referred to our hospital. He tested negative for tumor markers and soluble interleukin-2 receptor (sIL-2R). Abdominal computed tomography revealed a 51-mm hypovascular mass that was slowly enhanced from the portal venous to the equilibrium phases, at the inferior extremity of the spleen. Abdominal magnetic resonance imaging showed a spoke-wheel pattern. Fluorodeoxyglucose positron emission tomography indicated a mild tumor accumulation, with a standardized uptake value max of 5.3. These results led to the suspicion of SANT, angioma, and angiosarcoma. Because the onset of malignant diseases could not be excluded, laparoscopic splenectomy was performed. A brown, round mass, without a capsule but with clear boundaries, was macroscopically observed on the cut surface. In addition, white fibrosis was found in the mass. Histopathological examination revealed nodular angioma lesions, and the proliferation of fibrotic interstices and inflammatory cells was observed between the lesions. Immunohistological examination revealed proliferation in the 3 types of narrow capillaries inside angiomatoid nodules;CD31 + / CD34+/CD8–, CD31+/CD34–/CD8+, and CD31+/CD34–/CD8– cells; therefore, the patient was diagnosed with SANT.
Conclusions: Here, we reported one patient who developed the typical symptoms of SANT. SANT is easily diagnosed by histopathological examination; however, its causes remain unknown. More cases with SANT are required for further analysis.

Key words: spleen, laparoscope, sclerosing angiomatoid nodular transformation

BACKGROUND

Sclerosing angiomatoid nodular transformation (SANT) of the spleen is a non-tumorous benign lesion that originates in the spleen. The term was first reported by Martel *et al*. [1], in 2004. SANT is often identified incidentally, although clinical symptoms develop in some cases. Because imaging prior to surgery is insufficient to accurately exclude the possibility of malignant diseases, patients with suspected SANT undergo surgery, and histopathological examinations are performed. The conditions associated with this disease remain unknown.

CASE PRESENTATION

Case patient: 59 years of age, Male.
Chief complaints: Ultrasonography at a checkup showed a mass.
History of present illness: The patient was referred to our hospital due to a mass in the spleen, revealed by ultrasonography during a checkup by his physician.
Past medical history: hypertension
Blood test findings: White blood cells (WBC), 7,100 μl (4000–8000 μl); hemoglobin (Hb), 14.6 g/dl (13.5–17.5 g/dl); platelets (Plt), 17.3 × 10^6/μl (14–40 × 10^6/μl); carcinoembryonic antigen (CEA), 1.5 ng/ml(0–5 ng/ml); carbohydrate antigen 19–9 (CA19–9), 14.1 U/ml (0–37 U/ml); Soluble interleukin-2 receptor (sIL-2R), 368 U/ml(157–474 U/ml); Immunoglobulin G (IgG), 973 mg/dl (870–1700 mg/dl); IgG-4, 68.9 mg/dl (11–121 mg/dl); Epstein-Barr virus-viral capsid antigen antibody immunoglobulin G (EB-VCA-G), 40-fold (10 fold); Epstein-Barr virus-viral capsid antigen antibody immunoglobulin M (EBV-VCA-M), 10-fold (10-fold).
Abdominal ultrasonography: A 58 mm × 49 mm low-echo tumor was found in the spleen. A scar-like lesion, with linear high echo was observed near the central region of the tumor. Insufficient blood flow signals were detected on color Doppler flow imaging, confirming a hypovascular tumor (Fig. 1).
Abdominal contrast-enhanced computed tomog-

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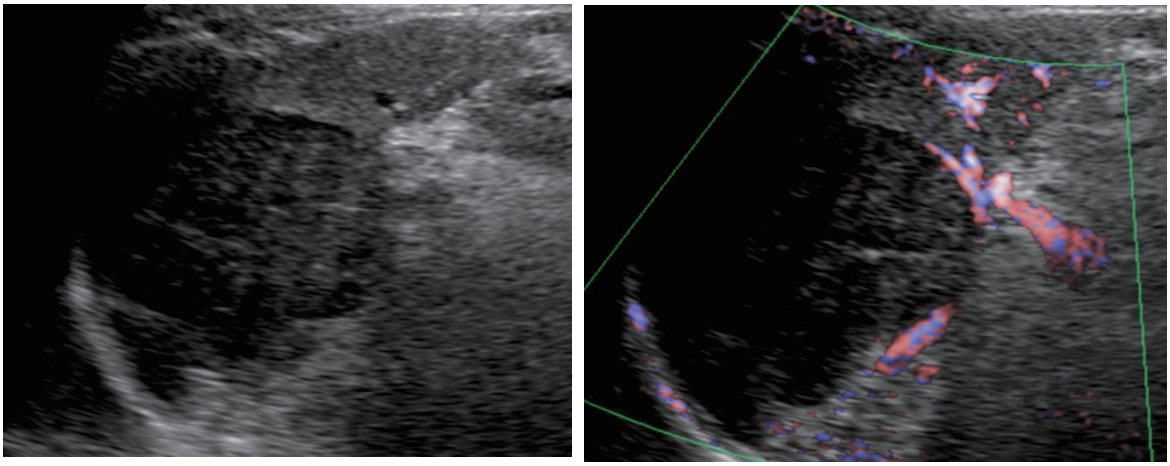

Fig. 1 Abdominal ultrasonography
A 58 mm × 49 mm low-echo tumor was found in the spleen. A scar-like lesion, with linear high echo at the central portion of the tumor was observed. Blood flow signals were insufficient, confirming a hypovascular tumor.

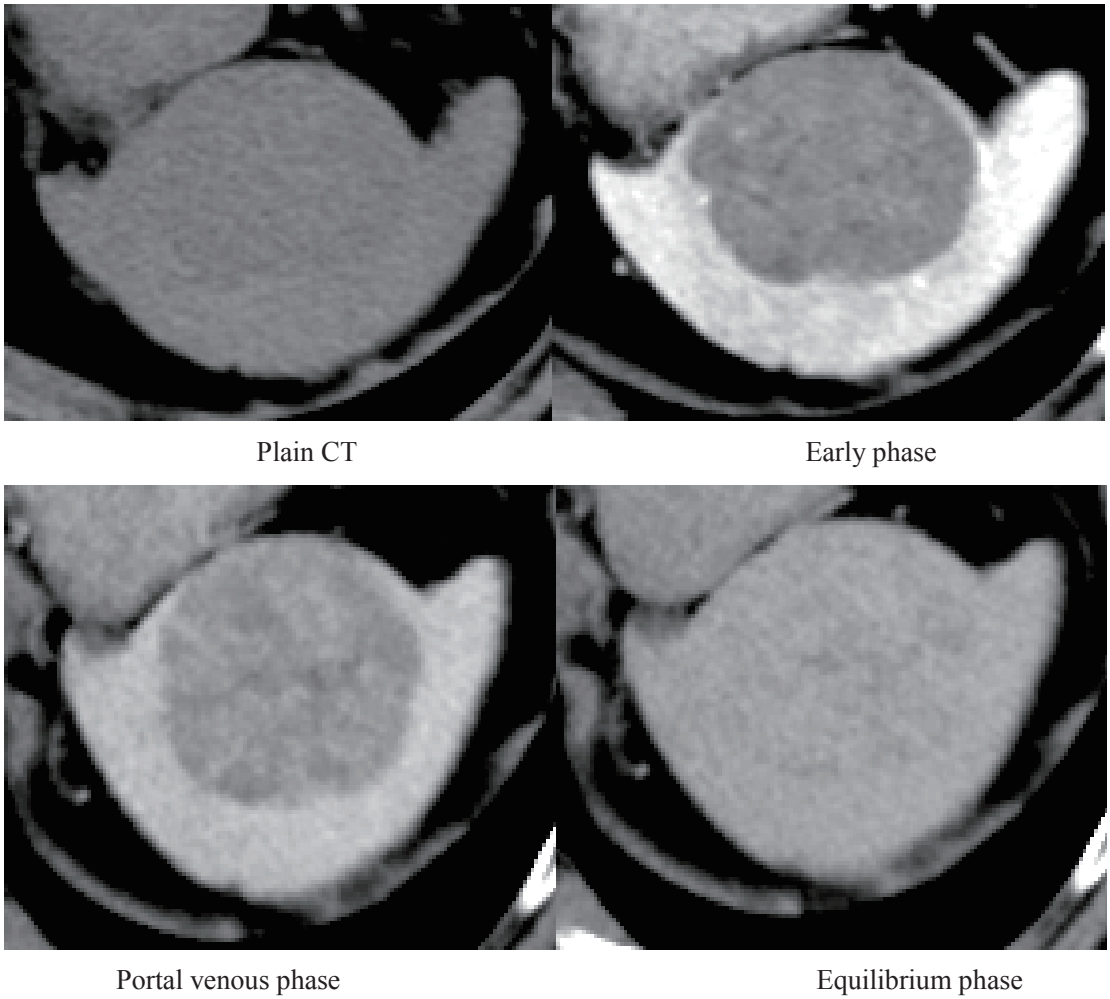

Fig. 2 Abdominal contrast-enhanced computed tomography
Plain computed tomography (CT) revealed a 51-mm, low-density mass, relative to the splenic parenchyma at the inferior extremity of the spleen. The mass was slowly enhanced between the portal venous and equilibrium phases.

raphy (CT): Plain CT revealed a 51-mm, low-density mass, relative to the density of the splenic parenchyma, at the inferior extremity of the spleen. Although the early phase of the CT showed low density, the mass was slowly enhanced between the portal venous and equilibrium phases (Fig. 2).

Abdominal magnetic resonance imaging (MRI): The mass presented low signal intensity on both T1- and T2-weighted imaging, and in diffuse weighted images (DWIs). In addition, the mass was gradually enhanced on contrast-enhanced MRI, during the equilibrium phase, and revealed a spoke-wheel pattern (Fig. 3).

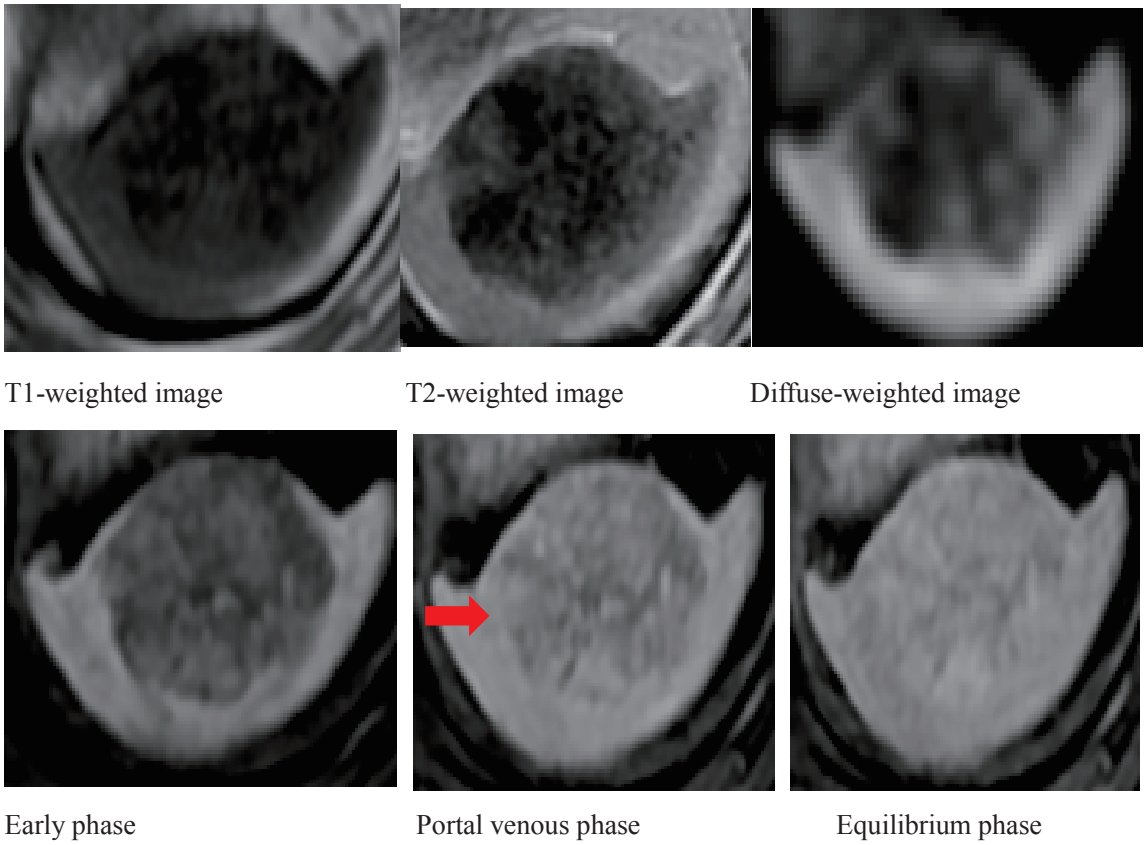

Fig. 3 Abdominal magnetic resonance imaging
Low signal intensity on T1- and T2-weighted images and a diffuse-weighted image
The mass was gradually enhanced on contrast-enhanced MRI, between the portal venous and equilibrium phases, showing a spoke-wheel pattern. (red arrow, ➡).

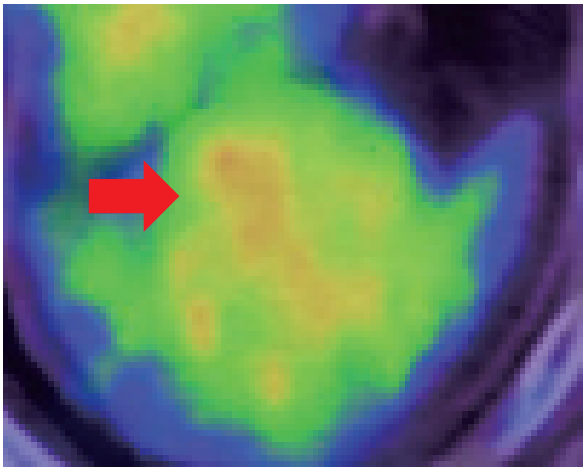

Fig. 4 Fluorodeoxyglucose-positron emission tomography
A mild tumor accumulation, a maximum standard uptake value (SUV_{max}) of 5.3 was observed in the spleen (red arrow, ➡).

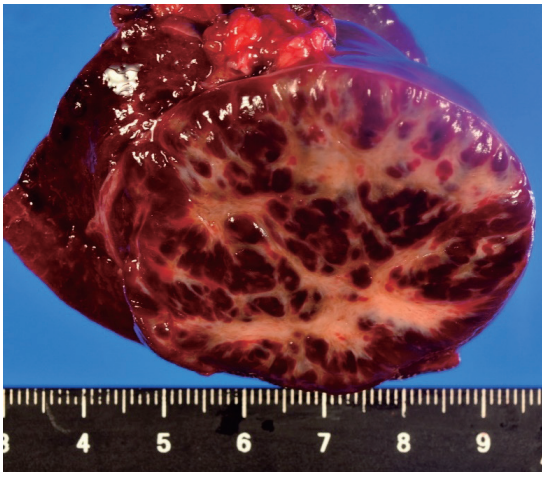

Fig. 5 Macroscopic findings
A brown, round mass, without a capsule but with clear boundaries, was observed on the cut surface. White fibrosis was found in the mass.

Fluorodeoxyglucose-positron emission tomography (FDG-PET): A mild tumor accumulation, with a maximum standardized uptake value of 5.3, was observed in the spleen (Fig. 4).

Explanation of Upper and Lower Gastrointestinal Endoscopy: No abnormality was found on endoscopy.

The above results led to the suspicion of SANT, angioma, and angiosarcoma. However, because the onset of malignant disease could not be excluded, laparoscopic splenectomy was performed.

Surgical findings: Surgery was performed by inserting ports into incisions near the umbilicus, forming an inverted trapezium shape. No findings suggestive of malignant disease, such as ascites, peritoneal dissemination, or lymphadenopathy, were observed in the abdominal cavity. An elastic, hard mass was identified at the inferior extremity of the spleen. The splenic artery and vein and the short gastric artery and vein were treated. Consequently, a 5-cm incision was made at the umbilicus to extract the spleen.

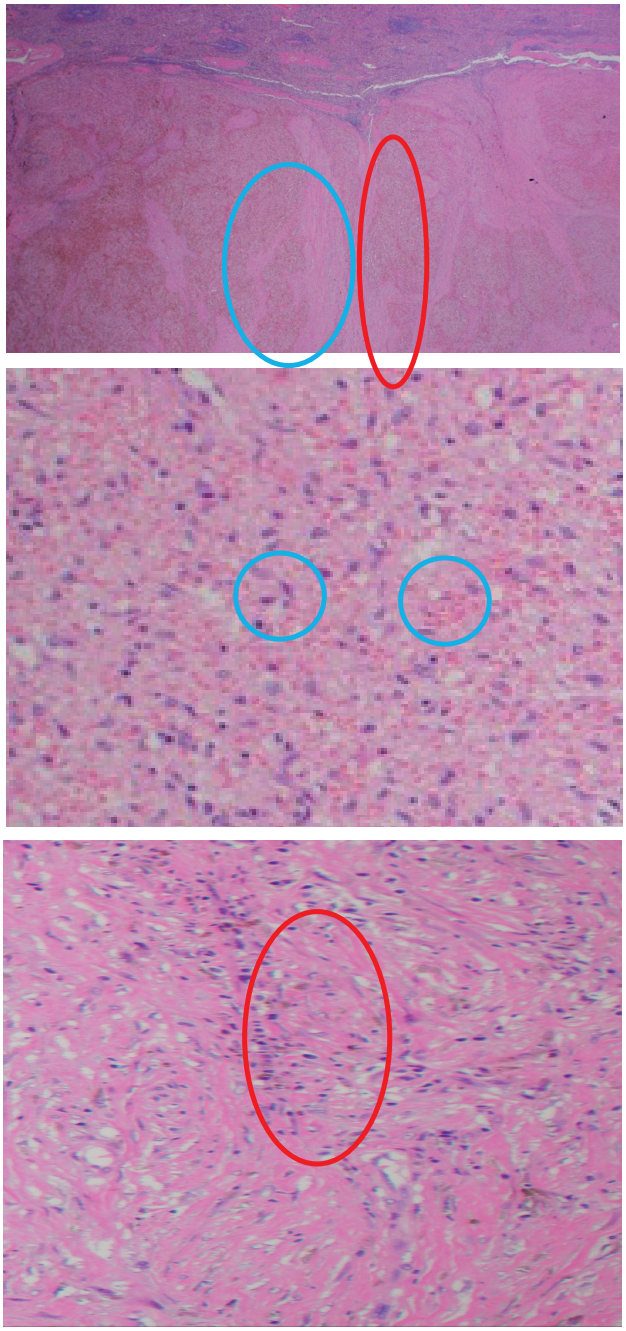

Fig. 6 Histopathological findings
Nodular angioma lesions were observed . Bundles of collagen, with a septal wall shape, was observed (red circle, ○). Narrow capillaries and spindle cells aggregate and proliferate (blue circle, ○).

Macroscopic findings: A brown, round mass, without a capsule but with clear boundaries, was macroscopically observed on the cut surface. In addition, white fibrosis was identified within the mass (Fig. 5).
Histopathological findings: Nodular angioma lesions were observed. The proliferation of fibrotic interstices and inflammatory cells, especially small lymphocytes, was observed between the lesions. Narrow capillaries and spindle cells aggregated and proliferated in the nodules (Fig. 6).
Immunohistochemistry: Most vessels inside angiomatoid nodules were positive for CD34 and CD31. Only a few vessels in the tumor were positive for CD8. The tumor presented with 3 types of narrow capillaries: CD31+/CD34+/CD8−, CD31+/CD34−/CD8+, and CD31+/CD34−/CD8−) (Fig. 7). These blood vessels were mixed.
The final diagnosis: Sclerosing angiomatoid nodular transformation.
Postoperative progress: The patient started eating on postoperative day 1. He was discharged on postoperative day 7. He was able to walk independently.

CONCLUSIONS

In 1978, this disease was first described and considered a splenic hamartoma by Silverman and LiVolsi. [2] In 1993, Falk *et al.* [24] designated it "splenic cord capillary angioma," which was later redefined as a special kind of splenic hamartoma by the same authors. As described in "Rosai and Ackerman Surgical Pathology, the disease is a "multinodular hemangioma" [25].

SANT was first reported by Martel *et al.*, in 2004, after the examination of a series of 25 cases. This disease is characterized by a non-tumorous, benign lesion that originates from the spleen, presenting with multinodular hemangioma lesions containing 3 types of vessels [1]. Epidemiologically, some studies have reported that SANT more commonly develops in women than in men [2]; however, more recent findings have suggested that the previously reported age and gender predilections may be neutralized as additional cases are accumulated [19]. Most patients with SANT are asymptomatic; therefore, their symptoms are not identified and they are not diagnosed unless they receive a checkup [1, 3, 4]. There are no clear reports on the frequency, size, or location of symptoms, and most of them are reports of obstruction to passage due to excretion into the digestive tract. One study reported the occurrence of SANT originating from the accessory spleen [4]. The symptoms associated with SANT include abdominal distention and vomiting [5], and the development of anemia occurs in some patients [6]. No reports regarding spontaneous ruptures in adult patients with SANT were found in the literature; however, Pelizzo, *et al.* described such an incidence in a 9-week-old female infant [7].

Plain CT revealed a low-density mass, relative to the density of the splenic parenchyma, which is a characteristic of previously described imaging findings in patients with SANT. In addition, CT revealed low enhancement in the arterial phase, although the mass was slowly enhanced between the portal venous and equilibrium phases, until a spoke-wheel pattern ultimately appeared. In some patients, classification is observed in the mass [8]. The mass presented with low signal intensity on both T1- and T2-weighted MRI, and in DWI. Enhanced MRI also showed a spoke-wheel pattern [8]. PET-CT showed mild tumor accumulation, preventing the exclusion of malignant disease during the differential diagnosis of SANT [9]. Ma *et al.* [8] evaluated CT and MRI of 12 SANTs. It is reported that 90% of the low density was recognized by CT. MRI also reported that the T1 weighted image had a low signal intensity of 75%, and the T2 weighted image/diffusion weighted image had a low signal intensity of 100%, and the spoke-whell pattern was 58%. This case also had similar test results.

The differential diagnosis of SANT includes both benign and malignant diseases. Benign forms include

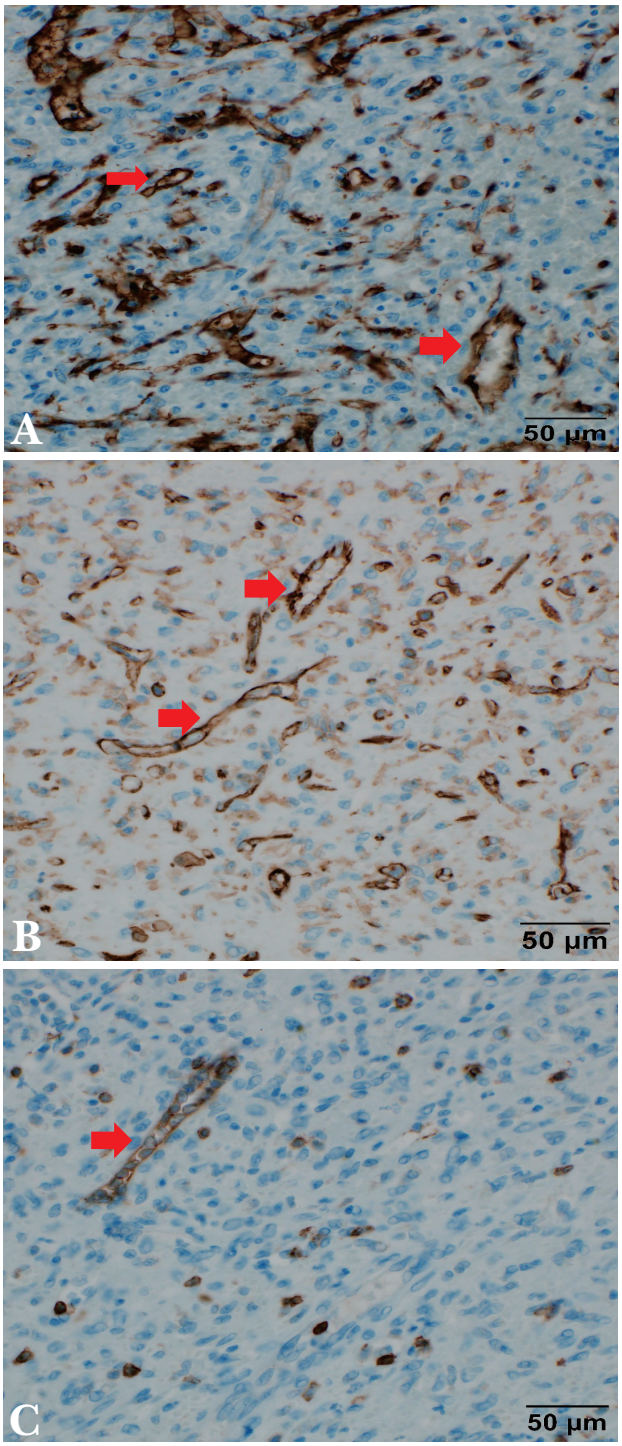

Fig. 7 Immunohistochemistry
A) Immunostaining for CD34 (red arrows, ➡) narrow capillaries in the angiomatoid nodules.: CD31+/CD34+/CD8−
B) Immunostaining for CD31 (red arrows, ➡) numerous cells in the angiomatoid nodules express this marker: CD31+/CD34−/CD8−
C) Immunostaining for CD8 (red arrow, ➡) some sinusoid-like structures in the angiomatoid nodules:CD31+/CD34−/CD8+

angioma, hamartoma, lymphangioma, littoral cell angioma, and inflammatory pseudotumor, whereas malignant diseases include angiosarcoma, malignant lymphoma, and metastatic splenic tumor. To distinguish SANT from these diseases, MRI is generally used; MRI findings for angioma and hamartoma include high signal intensity on T2-weighted images [10], whereas the MRI findings for littoral cell angioma show low signal intensity on T2-weighted images and multiple lesions in the spleen [11]. For inflammatory pseudotumor, MRI reveals low signal intensity, on both T1- and T2-weighted images, reflecting the abundance of fibrosis components. In addition, during dynamic contrast-enhanced (DCE)-MRI, delayed enhancement has been observed in the center and the margins of tumors [12]. According to Lewis *et al*., MRI findings for angioma include high signal intensity on T2-weighted images and cystic lesions, associated with bleeding and necrosis. The MRI findings for malignant lymphoma include isointense to low signal intensity on T2-weighted images; however, almost no contrast enhancement is observed. The MRI findings for metastatic splenic tumor include multiple lesions, and patient's medical history may help when attempting to differentiate SANT from this disease [11].

These results suggest that the diagnosis of SANT based on imaging findings alone may be difficult. Some reports have described the combined use of ultrasound and CT-guided percutaneous needle biopsy; however, this is an uncommon procedure, due to the potential risk of dissemination when bleeding occurs or the tumor is malignant [13]. Immunohistochemical examinations of the resected tumors can assist with the definitive diagnosis; therefore, surgical resection is commonly performed.

Currently, laparoscopic splenectomy, which is a minimally invasive method, is commonly used in SANT cases [5]. Jin *et al*. [14]. statistically compared open splenectomy, laparoscopic splenectomy, and laparoscopic partial splenectomy for a number of parameters, and the results showed no significant differences regarding the amount of bleeding, length of hospital stays, or incidence of postoperative complications among these procedures. The period of drain placement was longer, and platelet count was slightly lower after laparoscopic partial splenectomy was performed, compared with other procedures [14]. Whether surgery should be performed to remove small lesions in asymptomatic SANT patients is controversial. The rate of postoperative complications and mortality were approximately 30% and 4% or lower, respectively, depending on patient's condition and the co-occurrence of blood diseases [15]. Identified long-term risks encountered by splenectomy patients include *Streptococcus pneumonia* infections [16]. The mortality associated with overwhelming post-splenectomy infection (OPSI) can be as high as 70% [17]; however, these diseases can be prevented by vaccination [18]. To date, no recurrence of SANT has been reported.

In many SANT cases, a brown, round mass, without a capsule but with clear boundaries, can be macroscopically observed on the cut surface. In addition, white fibrosis can be identified in the center of the mass. During inflammatory pseudotumor, fibrosis proliferates and appears white, whereas fibrosis is unnoticeable and appears reddish-brown in hamartoma. These findings can be used when performing differential diagnoses.

Histopathological examination revealed both small and large nodular growth patterns, consisting of cord-type, narrow capillaries, and inflammatory cell

infiltration, which was predominantly associated with the proliferation of fibrotic interstices, small lymphocytes, and histiocytes. Immunohistological examination revealed the growth of 3 types of narrow capillaries, indicating similar morphologic and immunostaining features as normal red pulp.

These 3 vessels were positive for CD31; however, they can be distinguished from other CD31 cells because presentation of CD34 and CD8 are different, resulting in different morphologic features and distributions. 1. Immunostaining for CD34: There is a selective staining of the narrow capillaries in the angiomatoid nodules. Many vascular channels are negative. (CD31+/CD34+/CD8–). 2. Immunostaining for CD8: Some sinusoid-like structures are highlighted in the angiomatoid nodules. (CD31+/CD34–/CD8+). 3 Immunostaining for CD31: Numerous cells in the angiomatoid nodules express this marker. (CD31+/CD34–/CD8–) [1]. Some studies have reported that endothelial cells in cord capillaries are positive for CD68 and CD30, in some patients [19, 20]. Spindle cells in the interstitial space are positive for alpha-smooth muscle actin (α-SMA), which are similar to myofibroblast characteristics [21].

The nature of SANT has been controversial, although some hypothesize that SANT is a response to hamartoma, inflammatory pseudotumor, and trauma [1]. Some studies have demonstrated a relationship with immunoglobulin G4-related diseases and Epstein–Barr virus infections [22, 23]. SANT is a polyclonal, reactive lesion rather than a neoplasm. [23]. This case was normal for serum IgG4.

Here, we reported one patient, who developed the typical symptoms of SANT. SANT can be easily diagnosed by histopathological examinations; however, its nature remains unknown. More SANT cases must be examined for further analysis.

DECLARATIONS

List of abbreviations

Sclerosing angiomatoid nodular transformation of the spleen; SANT, Carcinoembryonic antigen; CEA, Carbohydrate antigen 19−9; CA19−9, Solubleinterleukin-2receptor; sIL-2R, Immunoglobulin G; IgG, Epstein-Barr virus-viral capsid antigen antibody immunoglobulin G; EB-VCA-G, Epstein-Barr virus-viral capsid antigen antibody immunoglobulin M; EBV-VCA-M.CT; computed tomography, magnetic resonance imaging; MRI, Fluorodeoxyglucose-positron emission tomography; FDG-PET,

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

COMPETING INTERESTS

Not applicable.

FUNDING

Not applicable.

AUTHORS' CONTRIBUTIONS

HY wrote this paper. TT performed the autopsy, reviewed the pathological findings, and revised the manuscript. HI reviewed the medical image findings. HI, MM, EN, and HM helped to writeI writing the manuscript. All authors read and approved the final manuscripmanuscript.

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Authors' information.

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