

Sclerosing angiomatoid nodular transformation presenting with abdominal hemorrhage: First report in infancy

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Abstract

A limited number of sclerosing Angiomatoid Nodular Transformation (SANT) have been reported in pediatric age. We describe the first case of SANT occurring in a nine-week-old female infant that was admitted to our unit for severe abdominal distension and rectal bleeding. Enlarged spleen was detected on physical examination. Laboratory investigations revealed severe anemia and coagulation abnormalities. Abdominal ultrasound and computed tomography revealed ascites and splenomegaly with a large mass at the lower medial splenic pole. A diagnosis of intra-abdominal hemorrhage was presumed and an exploratory laparotomy was performed. A complete transformation of the giant splenomegaly to bossellated masses and multiple bleeding capsular ruptures without subcapsular hematoma were found and an urgent splenectomy was performed. At histology, a SANT was diagnosed (CD34, CD31, CD8 positivity). The postoperative follow up was uneventful. SANT may also occur in infancy with a potentially life-threatening presentation. Splenectomy may represent the only treatment in severe cases.

Introduction

Sclerosing Angiomatoid Nodular Transformation (SANT) is a rare, benign, entity of the spleen characterized by prominent vascular proliferation associated with sclerosis. Although its etiology remains unknown, SANT predominantly affects females, usually affecting middle-aged adults.^{1,2} Most lesions are found incidentally upon imaging carried out for other causes, whereas some patients may present with abdominal pain. To date, a limited number of pediatric cases have been reported.³⁻⁶

We describe the first case of SANT occurring in an infant and presenting with a severely distended abdomen, splenomegaly, anemia, coagulation abnormalities and rectal bleeding. A review of the literature regarding SANT pediatric cases is also reported.

Case Report

A nine-week-old female infant, with an unremarkable birth-medical history, was admitted to the Pediatric Surgery Department for severe abdominal distension and rectal bleeding. Three days prior to admission the mother noted poor feeding, diarrhea and vomiting. The infant's condition worsened one day before hospital admission, with the appearance of progressive abdominal distention and rectal bleeding. The infant was born at term (weight 3.200 kg) by cesarean section (CS) (due to a previous maternal CS). No antenatal concerns or postnatal medical problems were reported; however, the mother reported a family history of Mediterranean anemia and maternal diabetes.

Abdominal distension (Figure 1) and an enlarged spleen (more than 5 cm below the costal arch) were detected upon physical examination. The baby (weight 5.5 kg) looked markedly pale, and was afebrile (36°C); eupneic (54 breaths/minute) with good oxygen saturation at room air (99%), the heart rate was 160 beats/minute with hypertension (105/52 mmHg). Laboratory investigations revealed severe anemia (Hb 4.6 g/dL), thrombocytopenia ($54 \times 10^3/\mu\text{L}$) and coagulation abnormalities: fibrinogen 50 mg/dL vn 150-45 and prothrombin time (PT) 15.7 sec vn 9-12.5; PT% 60 vn 70-120. Liver function tests were normal. A plain abdominal X-ray revealed multiple air fluid levels in the distended small intestine. Abdominal ultrasound showed ascites and splenomegaly (11 cm in longitudinal diameter) with a bossellated mass in the lower part of spleen. Computed tomography (CT) revealed

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corpuscolated liquid in the abdominal cavity, hepatomegaly and splenomegaly (longitudinal diameter 9.5 cm) with a large isodense mass, without intraparenchymal contrast enhancement, at the lower medial pole of the spleen (Figure 1).

Based on the triad of pallor, anemia and abdominal distension, in addition to the imaging and biochemical findings a diagnosis of intra-abdominal hemorrhage was hypothesized. The infant received several blood transfusions and underwent monitoring for 24 hours in the Pediatric Intensive Care Unit. The subsequent increase in abdominal distension, appearance of respiratory distress, and persistent abdominal hemorrhage un-responsive to blood transfusions were then considered indications for an exploratory laparotomy.⁷ During surgery, a great amount of bloody ascites (more than 1.5 L) were aspirated. Considering the complete transformation of the spleen to bossellated masses of different dimensions (varying from 1 to 2 cm in

diameter) and the multiple bleeding capsular ruptures without subcapsular hematoma an urgent splenectomy was performed.

At gross pathologic evaluation the lesion was composed of multiple red-brown nodules diffusely distributed, without a coalescent scar. At histological evaluation the mass showed a multinodular architecture composed of numerous, convoluted, congested vessels without significant atypia of the endothelium. Subtle sclerotic tissue surrounded the vascular structures and an abundant lymphoid infiltrate was intermingled among the vessels. By immunohistochemistry, endothelial cells expressed the vascular markers CD34 and CD31 and positivity for CD8, whereas podoplanin (D2 40), CD21, CD35 e CD 68 were negative. Smooth muscle actin (SMA) stained the perimeter of the vascular structures. No infection by HHV8/ORF73 or EBV/EBER and IgG4 were detected by immunohistochemistry and *in situ* hybridization, respectively (Figure 2). The lymphoid infiltrate contained both CD20-positive B and CD3-positive T cell components with no evidence of lymphoproliferative disease.

Elevated polymorphonuclear leukocyte counts were detected after splenectomy; however, no infectious complications occurred and the monthly postoperative follow up has been uneventful. Vaccination against the most common pathogens that can cause post-splenectomy infection and antibiotic prophylaxis were prescribed, together with parental education on the consequences of splenectomy.

Discussion and Conclusions

SANT of the spleen is a benign, non-hematolymphoid tumor that arises in the red pulp of the spleen (Tracher, Abbot).^{8,9} Since its first description in 2004 by Martel *et al.*,² 155 cases of SANT have been reported in adults (Cipolla, cao),^{10,11} while only four cases have been reported in pediatric patients (Table 1). Zhang *et al.*⁶ described a 3-year-old child injured in a car accident with a postsplenectomy SANT diagnosis; Vyas *et al.*⁴ presented a case of SANT with inflammatory pseudotumor-like areas in an 11-year-old child with a history of trauma presenting with a rapidly growing splenic lesion; Agrawal *et al.*³ described SANT in a 12-year-old girl with upper quadrant discomfort which lasted six months; Kuybuli *et al.*⁵ reported a case of SANT in an 11-year-old girl with growth retardation and increased sedimentation rate, mimicking chronic inflammatory disease.

The present report describes the first SANT case in infancy. Patients with SANT are usually asymptomatic or have non-specific abdominal pain. Most cases are found incidentally on radiographic examination or during surgery for an unrelated condition.¹² On the contrary, our case displayed life-threatening intra-abdominal bleeding with severe and rapid abdominal distension and coagulation abnormalities. This was a particularly unusual presentation requiring splenectomy as a life-saving treatment.

The pathogenesis of SANT remains unclear.^{1,2} It has been hypothesized that passive congestion of the splenic pulp secondary to trauma or unknown causes leads to sinus endothelial cell damage, fibrin deposition, and inflammation resulting in

pseudotumor appearance or SANT.² Other authors have proposed that SANT represents a peculiar hamartomatous transformation of the splenic red pulp in response to exaggerated non-neoplastic stromal proliferation.¹³ Finally, SANT has also been reported to be associated with Epstein-Barr virus (EBV) infection,¹⁴ and immunoglobulin (Ig)G4-related sclerosing disease.^{15,16} A significantly higher number of IgG4+ plasma cells and an increased IgG4/IgG ratio has also been reported in some studies.^{15,17,18}

In our case, EBV was not found and although we did not measure serum IgG4 levels, immunochemical staining for IgG4 showed only extremely rare plasma cells. Therefore, we ruled out the hypothesis of a SANT IgG4-associated disease.



Figure 1. Clinical and imaging features. A) severe abdominal distension at admission; B) large isodense splenic mass and abdominal hemorrhage at computed tomography.

Considering the patient's age, the role of genetic or gestational risk factors, such as gestational diabetes, cannot be excluded in the pathogenesis. Considering the early presentation in our case, a long-term post-splenectomy follow-up to detect possible hepatic involvement of SANT over time is recommended.

The differential diagnosis of SANT includes consideration of several other benign as well as malignant vascular lesions of the spleen, such as hemangioma, lymphangioma, littoral cell angioma, hamartoma, lymphangiomatosis, lymphangiomatosis, hemangioendotheliomas, angiosarcoma and inflammatory pseudotumor (IPT).¹⁹ The preoperative differential diagnosis to exclude other splenic tumors or malignant lesions is difficult.²⁰ A thorough histopathologic examination and immunohistochemical analysis are necessary to make a diagnosis of SANT. The characteristics of SANT with regard to the immunohistochemical profile

include three distinct types of blood vessels and endothelial cells stained with CD34, CD8 or CD31, respectively: i) CD34+/CD31+/CD8- indicative of capillary derivation; ii) CD34-/CD31+/CD8+ indicative of splenic sinusoidal lining cell involvement and iii) CD34-/CD31+/CD8- indicative of small vein involvement.^{3,19} The phenotypic profile of our case suggested a genetic component.

In our case, splenectomy was the only curative option for the management of SANT and is the treatment of choice in symptomatic patients. SANT patients have a good prognosis, with no recurrence after splenectomy.

In conclusion, SANT may also occur in infancy and present with potentially life-threatening conditions. Although splenectomy increases the patient's risk for infection, particularly in neonates, infants and small children, it represents a life-saving treatment. In early onset SANT in infants,

long term follow-up is recommended to detect further multi-organ involvement.

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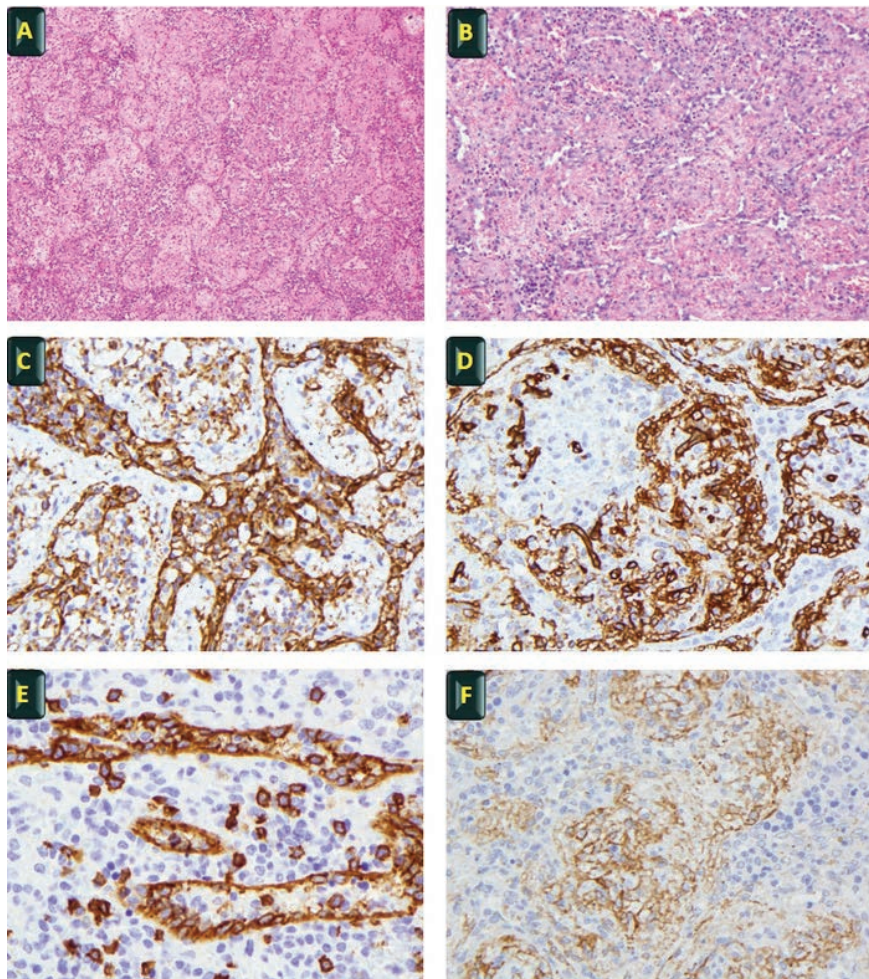


Figure 2. Histological evaluation. A-B) H&E - typical vascular appearance of SANT (x20, Panel A; and x40, Panel B); C-D) Diffuse positivity of vascular channels for CD 31 (x40, Panel C) and CD34 (x40, Panel D); E-F) Vascular channels positive for CD8 (x40, Panel E) and sclerosis (x40, Panel F)

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