ABSTRACT. An 11-year-old girl with low-grade fever, night sweats, thrombocytopenia, and an 8-year history of progressive splenomegaly underwent an elective splenectomy. Pathologic diagnosis was multiple splenic hamartoma. The patient’s symptoms resolved after the splenectomy. Since first described by Rokitansky in 1861, ~140 cases of splenic hamartoma have been described in the literature. Most of the splenic hamartomas were discovered incidentally. A minority of these lesions were associated with hematologic symptoms such as pancytopenia, anemia, and thrombocytopenia. Only 20 of the reported cases of splenic hamartoma occurred in pediatric patients. However, compared with the adult patients, nearly half of these cases in pediatric patients was associated with symptoms. Splenectomy and partial splenectomy have relieved these symptoms. With advances in imaging, splenic hamartomas are being discovered with increasing frequency. A multimodal radiologic work-up has enabled some cases of splenic hamartoma to be diagnosed preoperatively. Inclusion of this benign entity in the differential diagnose of symptomatic splenomegaly in a pediatric patient is important in the preoperative management and counseling of the patient and family. In patients who have discrete lesions, consideration of this entity preoperatively may avoid total splenectomy. Pediatrics 1998;101(5). URL: http://www.pediatrics.org/cgi/content/full/101/5/e10; splenic hamartoma, pancytopenia, hypersplenism, splenomegaly, hemangiomases.

ABBREVIATIONS. ANA, antinuclear antibody; CT, computed tomography; EBV, Epstein–Barr virus; MRI, magnetic resonance imaging.

Rokitansky, according to Friedreich, first described splenic hamartomas >100 years ago in 1861. Since then, ~140 cases of true hamartomas have been reported or mentioned in the literature.

Synonyms have included splenomas, spleen within a spleen, hemangiomas, postrumaar scars, fibrotic nodules, and hyperplastic nodules. They are usually asymptomatic, particularly in the adult population, and are discovered either incidentally during work-up of other problems or during postmortem examination. It appears that Von Falkowski reported the first case of splenic hamartoma in a pediatric patient in 1914. Approximately 20 of the reported cases of splenic hamartoma have been in pediatric patients (<16 years of age). An association with hematologic disorders or other symptoms is rarely reported. Therefore, splenic hamartomas are seldomly included in the differential diagnoses of a left upper quadrant mass in pediatric patients.

In 1953, Videbaek first reported the association of splenic hamartoma with hematologic disorders in a 30-year-old woman who had onset of symptoms in childhood. Thirty such symptomatic cases have been reported since then. Symptoms reported most frequently include pancytopenia, anemia, and thrombocytopenia. Less commonly, fever, malaise, and weight loss have been reported. Nine cases of symptomatic splenic hamartoma have been described in pediatric patients. The symptoms observed in the pediatric patients are similar to those in the adult patient population. In addition, growth retardation, night sweats, and recurrent infections have been reported in the pediatric patient population. Here, we report an example of symptomatic splenic hamartoma in a pediatric patient who had an 8-year span of clinical course from the time of initial presentation to the time of diagnosis.

CASE REPORT

The patient was an 11-year-old girl with an 8-year history of progressive splenomegaly who was admitted for elective splenectomy. She was first seen in 1988 at 3 years of age for splenomegaly. Complete blood count findings were normal. She then developed severe thrombocytopenia. Work-up revealed both direct and indirect platelet antibodies. Antinuclear antibody (ANA) was <1:20. A bone marrow aspirate showed abundant marrow megakaryocytes. A liver spleen scan demonstrated splenomegaly, without a shift in radionuclide uptake. Computed tomography (CT) images showed splenomegaly. Immune thrombocytopenia subsequently was diagnosed. The patient responded to intravenous gammaglobulin therapy with a rise in platelet count from 11 000/mm3 to 152 000/mm3 in 3 days. Biopsies of a subcutaneous buttock mass and a left axillary lymph node revealed capillary hemangioma and reactive hyperplasia, respectively. During the next several years, the spleen continued to enlarge. There were intervening episodes of urinary tract infection at 4 years of age, Epstein-Barr virus (EBV) infection (documented by EBV IgG titer of 640, EBV-EA titer of 320, and EBNA antibody titer of 40), and unclassified gommerulonephritis at 7 years of age. Sonograms and repeat CT images showed splenomegaly and no focal lesions.

When seen in March 1996 at 11 years of age, the patient had symptoms of periodic low-grade fever and night sweats. Physical examination showed both weight and height to be less than the fifth percentile for age. The spleen was then 11 cm below the left costal margin (Fig 1). White blood count was 3800/mm3, with a normal differential. The hemoglobin was 7.8 g/dL, and the hematocrit was 22.8%. The red cell indices were as follows: mean corpuscular volume 70.2 fl, mean corpuscular hemoglobin 24.1 pg, and mean corpuscular hemoglobin concentration 34.3 dL. The platelets count was 90 000/mm3. The reticulocyte count was 6%. The erythrocyte sedimentation rate was elevated at 54 mm/h. Prothrombin time was 44.6 and partial thromboplastin time 39.9. Lactate dehydrogenase was normal. Total bilirubin was slightly elevated at 1.4 mg/dL, with direct fraction of 0.1 mg/dL. Bone marrow findings were consistent with the diagnosis of hyperplasia. Chest x-ray was normal. Tuberculin skin test, coccidio- mycoses, and ANA serology were noncontributory. A splenic arteriogram showed irregular distribution of contrast material and marked splenomegaly (Fig 2). The patient underwent elective splenectomy in March 1996. During the operation, the spleen was noted to be enlarged. An accessory spleen was identified at the hilum, along with large periselnic lymph nodes. The postoperative course was uneventful, and the platelet count increased to...
within normal range. Examination of the patient 9 months later showed an increase in both height and weight and resolution of fever and night sweats. The complete blood count and erythrocyte sedimentation rate returned to within normal range.

**PATHOLOGIC FINDINGS**

The resected spleen weighed 921 g (expected weight for height is 128 g) and measured $20 \times 15 \times 8$ cm. The hilum showed several lymph nodes at $\leq 8$ mm each. An accessory spleen, measuring 1.5 cm, was present. Cut surface of the spleen showed several large bulging circumscribed solid nodules that measured up to 4.5 cm (Fig 3). The largest nodule contained a central tan–white stellate scar. Numerous similar but smaller nodules ranging from a few millimeters to 1.2 cm were noted throughout the spleen.

Histologically, the nodules were less defined and merged imperceptibly with the surrounding splenic parenchyma. The nodules were composed of irregularly arranged sinusoids admixed with intervening pulp cord-like elements (Fig 4). Endothelial cells similar to sinusoidal lining cells lined these channels. These lining cells, by immunoperoxidase stains, showed reactivity for CD8 and factor VIII-related antigen, consistent with splenic type endothelium. There was no reactivity to CD34, which highlights the cord capillaries. The pulp-like elements consisted of lymphocytes and macrophages along with few immunoblasts (Fig 5). There was focal stromal sclerosis, hyalinization, and hemosiderosis. Foreign body giant cells were present with engulfed pigments. Foci of extramedullary hematopoiesis were
observed. No lymphoid follicles of the white pulp were identified within these nodules. The rest of the spleen and the accessory spleen showed normal components of red and white pulp. The hilar lymph nodes showed mild sinus histiocytosis.

EBV EBER1 transcripts by in situ hybridization test demonstrated a latent EBV transcript in rare lymphoid cells of the spleen and hilar lymph node. This result suggested that the patient was a virus carrier from previous viral exposure. However, the splenomegaly was not a result of proliferation of EBV-infected lymphocytes.

The vascular spaces are lined by cells with ultrastructural features consistent with endothelial cells. These rounded cells rest on basement membrane material that is present only intermittently. At higher magnification, the organelles of these cells are noted to consist of abundant Golgi complex, membrane bound vesicles, and mitochondria. Occasional Weibel–Palade bodies are seen in the lining cells of the vascular channels (Fig 6).

DISCUSSION

Primary nonlymphomatous tumors of the spleen are uncommon. Most are either cysts or hemangiommas. Hamartomas of the spleen are rarely reported entities. The incidence of splenic hamartomas has been reported to be 3 in 200 000 splenectomies. With the use of modern radiologic imaging techniques such as sonography, CT, radionuclide scintigraphy, and MRI, splenic hamartoma may not be as uncommon as thought previously. In fact, one third of the cases reported in the past 135 years occurred just in the last decade.

Approximately one sixth of these cases were described in patients <16 years of age. The majority of

Fig 3. A cut surface of the spleen showing circumscribed nodules of various sizes.

Fig 4. The nodule is composed of irregularly arranged sinusoids admixed with intervening pulp cord-like elements (hematoxylin–eosin, 100 ×).
patients were asymptomatic, with the hamartoma being an incidental finding. A minority of the patients who were symptomatic had symptoms of hypersplenism and, less commonly, fever, night sweats, and malaise. Additional unique symptoms noted in the pediatric population include growth retardation and recurrent infections (Table 1).

Although a hemangioma may be considered a form of hamartoma, the term splenic hamartoma usually is designated for circumscribed intrasplenic lesions composed of tissue resembling normal red pulp. The capillary hemangiomas of the spleen may closely resemble splenic hamartoma such that some investigators think that the two are virtually identical.1,8

Immunohistochemical staining can be used to distinguish splenic hamartoma from capillary hemangioma by their respective staining characteristics.9-11 Because the hamartoma is of splenic sinusoidal origin, the component cells show reactivity for T-lymphocytes markers, such as CD8, as well as for the endothelial cell markers, such as factor VIII-related antigen. In contradistinction, the hemangioma that is a tumor of vascular origin, shows reactivity for endothelial cell markers only.

The first ultrastructural features of splenic hamartomas are described. Fig 5 shows the pulp-like elements consisted of lymphocytes, macrophages, and few immunoblasts (hematoxylin–eosin, 400 ×).

Fig 5. The pulp-like elements consisted of lymphocytes, macrophages, and few immunoblasts (hematoxylin–eosin, 400 ×).

Fig 6. Electron micrograph (30 400 × magnification) of an endothelial cell with organelles that include Weibel–Palade bodies (dart).

Fig 6. Electron micrograph (30 400 × magnification) of an endothelial cell with organelles that include Weibel–Palade bodies (dart).
toma have been reported to consist of endothelial cells with Weibel–Palade bodies. The current case showed similar ultrastructural features, with occasional Weibel–Palade bodies identified.

The multimodal approach currently available in medicine has enabled some cases of splenic hamartomas to be diagnosed preoperatively. The first such case diagnosed preoperatively was in an 11-month-old male reported in 1977 by Kuykendall, using radionuclide scintigraphy, sonography, and arteriography. Recently, in 1996, Thompson et al reported a case of symptomatic splenic hamartoma in a pediatric patient, diagnosed preoperatively by using a combination of radiologic imaging, consisting of sonography, radionuclide scintigraphy, CT, and MRI. A single hamartoma was present in both of these cases.

Single and discrete splenic hamartoma have been removed by conservative surgical approach, ie, by partial splenectomy. In the case of symptomatic single splenic hamartoma treated by partial splenectomy, there was resolution of the patient’s symptoms afterward.

In our patient, periodic sonography, radionuclide scintigraphy, and CT were performed during the 8-year course, along with preoperative splenic arteriography and splenoportography. All of these studies only reaffirmed the clinical impression of splenomegaly, without focal lesions identified. MRI was not performed in our case. Because our patient had multiple splenic hamartomas throughout the spleen, it probably was unlikely for this diagnosis to be made preoperatively. A conservative surgical approach likewise was not feasible in our patient because of the multiplicity of the lesions.

The association of splenic hamartoma with other hamartomatous entities such as tuberous sclerosis is known. The relationship of splenic hamartoma and accessory spleen is speculative because this piece of information is not available in most of the cases reported. In Morgenstern’s series, accessory spleens were noted in one third of the cases.

In summary, splenic hamartoma should be included in the differential diagnoses of symptomatic splenomegaly and of splenic nodules discovered incidentally in pediatric patients. In cases of a single discrete splenic hamartoma, the use of multimodal radiologic imaging may help to pinpoint the diagnosis preoperatively. In addition, single and discrete hamartoma may be treated by conservative partial splenectomy.

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