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Case report

Hamartoma of the spleen with haematological symptoms

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Summary. We report the case of a 29 year old male patient with a splenic hamartoma suffering from infections, anaemia and thrombocytopenia. Shortly after surgical removal of the tumour the blood cell count was within normal range. Hamartomas of the spleen are rare benign tumour-like lesions composed mainly of vascular elements. Most of them remain small in size and asymptomatic and are therefore incidental findings at laparotomy or autopsy. However, occasionally they present with symptoms, among which haematological disturbances appear in very few cases; only 16 cases of splenic hamartomas with haematological symptoms are described in the literature. The major symptoms were anaemia and/or thrombocytopenia as well as frequent infections. After removal of these lesions the symptoms disappeared.

Key words: Spleen – Hamartoma – Haematological symptoms – Anaemia – Thrombocytopenia

Introduction

Primary neoplasms of the spleen are very rare. However, tumour-like lesions, commonly termed hamartomas, occur, mostly remaining small in size and causing no clinical symptoms. They are thus nearly always incidental findings at laparotomy or autopsy. In rare cases the lesions become larger and/or show clinical symptoms, occasionally including haematological disorders such as anaemia, thrombocytopenia or pancytopenia (see Table 1). In the present communication a 29 year old male patient with anaemia and thrombocytopenia caused by a large splenic hamartoma is presented, with a review of relevant literature.

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Case report

In May 1982 a 26 year old male patient consulted an internist because of frequent infections, persisting fatigue and nightly sweating. Three weeks earlier the patient had had a tonsillectomy for chronic tonsillitis, the supposed cause of his frequent infections. On physical examination tenderness was found in the left epigastrium. Signs of anaemia (pallor, dry skin and ripped finger nails) were seen. The red cell count was decreased to 3.8 mill/mm^3, haemoglobin to 11.3 g/dl, and platelets were 98000/mm^3. Leucocytes and differential blood cell count were normal. Palpation of the abdomen revealed no mass. The lymph nodes were not enlarged.

No specific cause for the anaemia was detected. Thus, the patient was treated symptomatically with iron. Subsequently the anaemia improved, but reappeared after cessation of therapy. During the following three years the red blood cell count was between 3.8 and 4.3 mill/mm^3, haemoglobin ranged between 10.4 and 11.6 g/dl and Hb/E was 27 pg. The serum level of iron was between 22 and 56 µg/dl and that of LDH was between 59 and 88 mU. The blood sedimentation rate was increased. The total leucocyte count and the differential count were always normal.

In March 1985 the patient was admitted to the University Hospital of Graz. He was in good general condition, at physical examination heart and lungs were normal. No palpable mass could be detected in the abdomen. Lymphnodes were not enlarged. Laboratory tests at admission: red cell count 4.6 mill/mm^3, haemoglobin 12.2 g/dl, Hb/E 26.5 pg, leucocytes 9150 mm/^{3}, differential count normal, reticulocytes 14‰, platelets 109000/mm^3. There were no significant abnormalities in other investigations. Serological tests for HIV- and HTLV-infections were negative.

In a urogram a tumour was found in the left epigastrium, which could be separated from the left kidney. By sonography, a tumour measuring 15 cm in diameter was localized between the left kidney, the spleen and the left lobe of the liver. At computer-assisted tomography a tumour, about 15 cm in diameter was found in the left epigastrium. This could not be separated from the spleen and showed calcifications and a necrotic area in its central portion (Fig. 1); enlarged lymph nodes were not found. A sonographically guided fine needle biopsy of the tumour revealed a richly cellular mesenchymal tumour of suspected malignancy, infiltrated by inflammatory cells.

In order to obtain a precise diagnosis, an explorative laparotomy was performed in April 1985. At operation, a ball-shaped tumour was found, closely attached to the spleen and

Table 1. Published cases of splenic hamartomas with haematological symptoms

Authors	Sex f/m	Age (years)	Clinical symptoms	Largest diam. of hamartoma	Weight of the spleen (in g)	Recovery after splenectomy
Videbaek 1953	f	30	anaemia, thromboc.	mult., 6 cm	nd	recovered
Schrijver and Verdonk 1957	f	31	anaemia	sing., 19 cm	750	recovered
Hardmeier 1962	f	50	anaemia, thromboc.	size of 2 fists	1790	recovered
Sen Gupta and Mukerjee 1963	f	nd	anaemia	nd	2280	recovered
Wexler and Abrams 1964	m	4	anaemia	sing., 7 cm	300	recovered
Benjamin et al. 1965	f	29	anaemia, thromboc.	nd	4560	recovered
Pinkhas et al. 1968	m	50	anaemia, thromboc.	mult., some mm	3900	+
Ross and Schiller 1971	f	54	thromboc.	sing., about 16 cm	1430	recovered
Santagati et al. 1974	f	26	pancytop.	sing., 10 cm	920	recovered
Shalev and Ariel 1978	m	24	anaemia, thromboc.	mult., 5 cm	2400	recovered
Silverman and LiVolsi 1978	m	9	anaemia	sing., 10 cm	500	recovered
Iozzo et al. 1980						
Case 1	f	12	pancytop.	mult., up to 5 cm	795	recovered
Case 2	m	9	pancytop.	mult., up to 5 cm	994	recovered
Pardo-Mindan et al. 1983	f	68	anaemia, thromboc.	about 17 cm	1780	recovered
Morgenstern et al. 1984	m	22	anaemia	mult., 0.2–1.5 cm	900	recovered
Scully et al. 1985	m	69	thromboc.	mult., up to 6 cm	710	recovered
Present case	m	29	anaemia, thromboc.	sing., 15 cm	730	recovered

Abbreviations:
f = female; m = male; thromboc. = thrombocytopenia; pancytop. = pancytopenia; nd = no data available; mult. = multiple; sing. = single; diam. = diameter; +11 months after splenectomy a polycythaemia developed

well separated from the liver, the diaphragm, the left kidney and the transverse colon. The tumour apparently originated from the splenic hilus and was covered at its lateral aspect by the remainder of the spleen in a hood-like fashion. Its blood supply arose exclusively from the splenic pedicle.

The tumour and the remaining spleen were removed and the tumour mass was congested and friable. The other abdominal organs, paticularly the liver, were normal on surgical exploration.

The postoperative course was uncomplicated and the patient was discharged from the hospital on the 8th day after surgery. Immediately after operation anaemia and thrombocytopenia disappeared. Blood chemistry values remained within normal ranges during a follow-up-period of 10 months.

Material and methods

Tissues for histological examination were fixed in 10% phosphate-buffered formaldehyde solution (pH 7.4) and processed conventionally. Sections of 5 μm thickness were cut and stained with haematoxylin-eosin, Gomori's stain for demonstration of reticulin fibers and Prussian blue for visualization of haemosiderin-associated iron.

For electron microscopy tissue was fixed in 2.5% glutaraldehyde in 0.1 M Na-cacodylate buffer (pH 7.25) for 4 h and postfixed in 1% OsO_4 for 2 h. The specimens were then dehydrated and embedded in Epon 812 following standard procedures. Semithin and ultrathin sections were cut with a Reichert OM U4 ultracut microtome. The ultrathin sections were stained with uranyl acetate and lead citrate and examined at 80 kV in a Philips EM 400 electron microscope.

Results

The spleen weighed 730 g. A spherical tumour originated from its hilus and was covered by the remainder of the spleen in hood-like fashion (Fig. 2). In cross sections a well circumscribed tumour, 15 cm in diameter, was seen. It was reddish-brown and showed a central star-like scar with hyalinized and focally calcified areas (Fig. 3). The normal splenic tissue was compressed and revealed a prominent follicular pattern.

On light microscopy the lesion showed a vascular pattern consisting of capillaries (Fig. 4) and sinusoid-like structures (Fig. 5). These vessels were lined by endothelial cells and surrounded by extravasated erythrocytes, reticulum cells, macrophages, lymphocytes and numerous plasma cells. Granulocytes were interspersed. Reticulin fibers were seen in irregular distribution (Fig. 6). The fibrotic areas were composed of elastic and collagen fibers with calcified necroses (Gandy-Gamna bodies). Normal lymph follicles were absent, but lymphocytes, densely arranged around small vessels, could be seen. The nodule also contained large thin- and thick-walled vessels. The nontumour splenic tissue was without histological abnormalities.

On electron microscopy the vascular spaces were lined by flattened or ovoid endothelial cells. The endothelial cells adhered to a basement membrane and showed few organelles in their cytoplasm (Fig. 7). Lymphocytes, granulocytes, plasma cells, macrophages and even platelets were closely attached to the basement membranes.

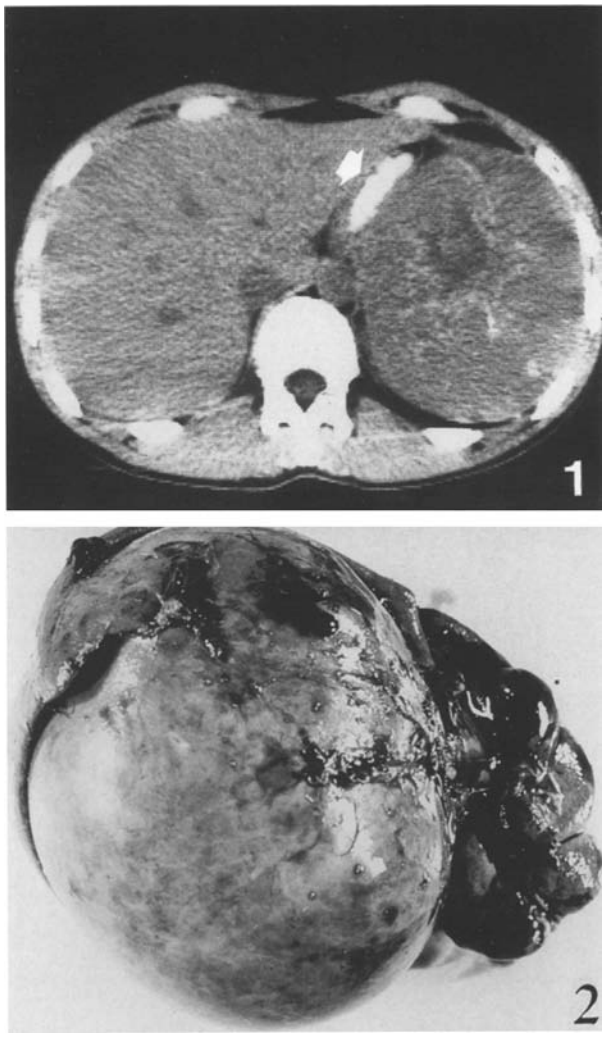


Fig. 1. Computer-assisted tomography of the upper abdomen. *Right side*: large tumour with necrosis and calcification in central areas. *Left side*: liver. Between tumour and liver the stomach, visualized by contrast medium, is detectable (*arrow*)

Fig. 2. Ball-shaped tumour originating from the spleen. The remainder of the spleen covers the tumour in a hood-like fashion

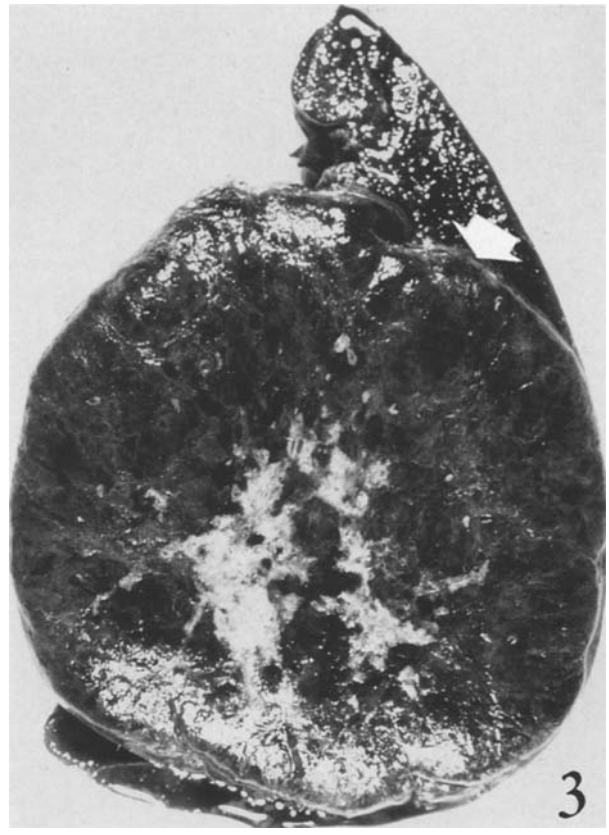
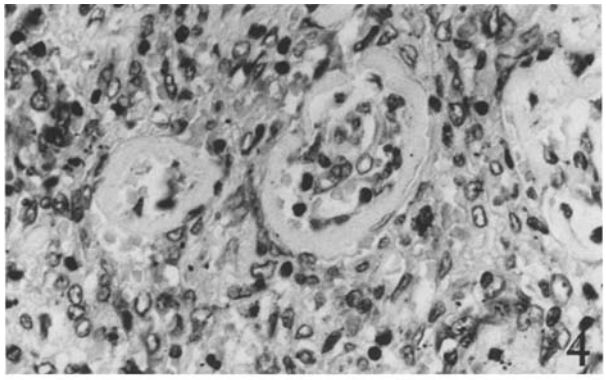


Fig. 3. On a cross section the tumour shows central hyalinized and calcified areas and is surrounded by a peripheral fibrous pseudocapsule (*arrow*)

Discussion

Hamartomas of the spleen are rare tumour-like lesions (see Bersch 1972; Silverman and LiVolsi 1978). In very few cases hamartomas have been associated with haematological symptoms such as anaemia (Schrijver and Verdonk 1957; Sen Gupta and Mukerjee 1963; Wexler and Abrams 1964; Silverman and LiVolsi 1978; Morgenstern et al. 1984) thrombocytopenia (Ross and Schiller 1971; Scully et al. 1985) or anaemia and thrombocytopenia (Videbaeck 1953; Hardmeier 1962; Benjamin et al. 1965; Pinkhas et al. 1968; Shalev and Ariel 1978; Pardo-Mindan et al. 1983; present case) and pancytopenia (Santagati et al. 1974; Iozzo et al. 1980). They present in all age groups; the mean age, however, was higher in females (37.5 years) than in males (27 years). Also the mean weight and diameters were higher in females (1788.12 g/12.16 cm) than in males (1304.25 g/6.25 cm) suggesting that hormonal factors may have some influence on the growth (Benjamin et al. 1965). The lesions were either multiple (Videbaeck 1953; Pinkhas et al. 1968; Shalev and Ariel 1978; Iozzo et al. 1980; Morgenstern et al. 1984; Scully et al. 1985) or singular (Schrijver and Verdonk 1957; Hardmeier 1962; Wexler and Abrams 1964; Ross and Schiller 1971; Santagati et al. 1974; Silverman and LiVolsi 1978; Pardo-Mindan et al. 1983; present case), but multiplicity was not related to the extent of the haematological symptoms. All symptomatic hamartomas were of the red pulp type which is mainly composed of vascular channels resembling splenic sinusoids. Because of the numerous irregular vessels demonstrable by angiography one should be aware of an erroneous diagnosis of a



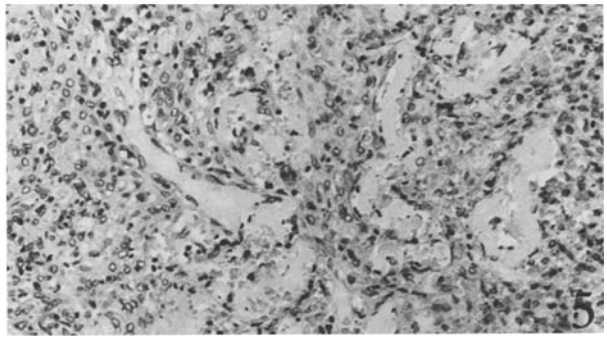
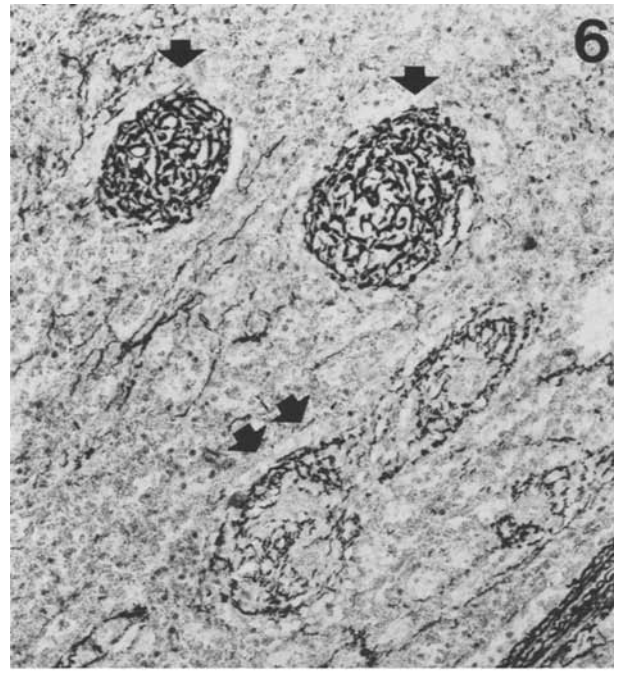


Fig. 4. Capillary-like blood vessels with thickened wall

Fig. 5. Thin-walled sinusoid-like blood vessel

malignant tumour (Wexler and Abrams 1964; Graham et al. 1969). The bone marrow of the patients revealed a hyperplastic pattern except two cases (Pardo-Mindan et al. 1983; Scully et al. 1985). In some cases hepatosplenomegaly (Videbaeck 1953; Schrijver and Verdonk 1957; Ross and Schiller 1971; Santagati et al. 1974; Silverman and LiVolsi 1978; Iozzo et al. 1980) was found. Anaemia, thrombocytopenia and pancytopenia in patients with hamartomas are due to increased numbers of hamartomatous vascular channels, which lead to decreased circulation by extension of the vascular space. Consequently, blood cells are pooled and can be destroyed more easily when compared with normal splenic tissue. This assumption was underlined impressively by studies with heat-treated ^{51}Cr labelled red blood cells, which revealed a higher rate of sequestered cells in the lesion than in remaining splenic tissue (Teates et al. 1972). Moreover, in hamartomas red blood cells were found in rouleaux formation which impeded passing of the cells through the sinusoidal wall. In all cases of splenic hamartomas combined with haematological symptoms the disorder disappeared immediately after removal of the spleen. Thus, a real hypersplenism was present (Crosby 1962). However, the existence of only sporadic cases of splenic hamartomas combined with hae-



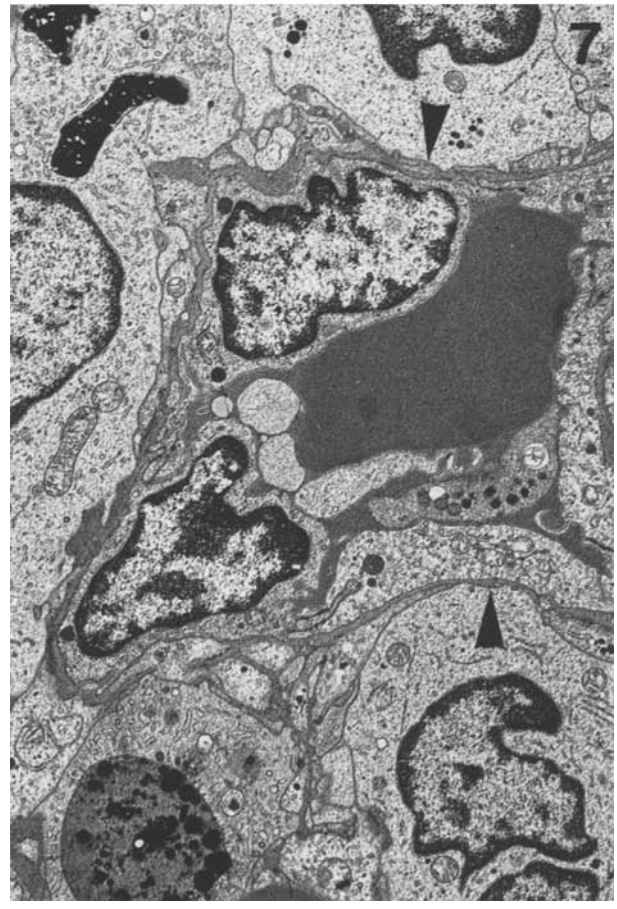


Fig. 6. Reticulin fibers arranged in more (*one arrow*) or less (*two arrows*) spherical order indicating lymphocytic aggregates (Gomori's stain)

Fig. 7. Vascular space lined by endothelial cells which adhere to a basement membrane (*arrowheads*) EM 5000 ×

matological disturbances indicates, that other unknown cofactors also play a role in inducing anaemia and/or thrombocytopenia. These cofactors are obviously independent of weight and size of the lesion, since Hodge and Wilson (1947) reported a harmatoma of 13130 g and Coe and von Drashek (1952) of 23 cm in diameter without haematologic symptoms. Silverman and LiVolsi (1978) even hypothesized that splenic hamartomas may not be causally related to haematological disorders and may be innocent bystanders in an otherwise diseased spleen. This is in contrast to our light microscopic studies of the non-hamartomatous splenic tissue which revealed no morphological changes which could be held responsible for the haematological disturbances. Why only few cases of splenic hamartomas are combined with haematological disorders is unclear.

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