Image Quiz for Surgeons

Chirurgia (2012) 107: 670-674
No. 5, September - October
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Splenic Sarcoidosis – a Case Report

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Rezumat

Sarcoidoza splenică

Pacientă în vârstă de 66 de ani, internată pentru o splenomegalie gradul III-IV, cu hipersplenism hematologic şi anemie secundară medie/mare, diagnosticată în clinica de hematologie, unde s-a infirmat un sindrom mieloproliferativ. Se intervine chirurgical şi se practică splenectomie, toaletă şi drenajul lojei splenice. Examenul histopatologic stabileşte diagnosticul de sarcoidoză splenică. Evoluţie bună postoperatorie. Sunt discutate principalele probleme etiopatogenice, diagnostice şi terapeutice, pe care sarcoidoza, boală rară, de etiologie neprecizată, le ridică.

Cuvinte cheie: sarcoidoză, hipersplenism hematologic, splenectomie

Abstract

Patient aged 66 years, was admitted for splenomegaly grade III/IV, haematological hypersplenism and medium / large secondary anemia, diagnosed in the hematology clinic, where a myeloproliferative syndrome was denied. Was performed splenectomy, splenic lodge toilet and drainage. Histopathology was established the diagnosis of splenic sarcoidosis. Good postoperative evolution. Main issues discussed are etiopathogeny, diagnostic and therapeutic, that this rare disease of unknown etiology is giving.

Key words: sarcoidosis, haematological hypersplenism, splenectomy

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Introduction

Sarcoidosis, known as Besnier-Boeck-Schaumann disease or syndrome, is a granulomatous inflammatory disease of unknown etiology that occurs mainly in young people. The most frequent clinical manifestation of the disease is characterized by: symmetrical lymphadenopathy in lung hilum, lung parenchymal infiltration, ocular and skin lesions.

Although the lung is the most common interested, the disease can affect any organ and/or system. The diagnosis is established only histopathological, by observing noncaseating granulomas.

Sarcoidosis may be limited or multivisceral disease, chronic or episodic and may have periods of remission and relapse.

Splenic localization of sarcoidosis is rare, sporadic cases are reported in literature. Therefore, we present a clinical observation, which we encountered in our clinic.

Case report

A 66 years old, female, was admitted for: splenomegaly III-IV degree, haematological hypersplenism, secondary

anemia. The diagnosis has been established in the Hematology clinic, where it also was put the indication of splenectomy, a mieloproliferativ process being unconfirmed.

Anamnestic we remember that patient noted the appearance of a palpable abdominal formations in the left hypochondrium and flank. On physical examination we reveal a slender and painless abdomen on the flank and left hypochondrium and a lump of firm consistency, well defined, which median reaches the xifoombilical line and lower goes well below the navel.

Ultrasound founds a fatty liver, 230/90 mm spleen, relatively homogeneous, with splenic vein in the hilum of 10 mm caliber, right renal ptosis grade I. CBC: anisocytosis, moderate poikilocitoză (mycrocytes, ovalocytes), mild hypochromia. Other laboratory findings within normal limits. Chest radiography finds bilaterally parahilare microalcifications, EKG without pathological changes and esogastroduodenal endoscopy was normal.

We perform surgical intervention and we find a III/IV degree splenomegaly (lower pole is below the navel) with high consistency, with significant perisplenic adherential sindrome. Body size were 25/15/9 cm. Accessory spleens were found in the hilum, gastrosplenic ligament and left flexure of the colon, and whose size varied between 0.7 and 1.2 cm. Was practiced in hilum splenectomy and removal of accessories spleens, toilet and drainage of splenic lodge. Favorable postoperative evolution. Discharged surgically cured on 18th postoperative day. Prolongation of existing hospitalization was due to a postsplenectomy platelet crisis, which required treatment with anticoagulant (Reviparina 0.6 ml) sc/day and antiplatelet medication (aspirin 75 mg/day) until platelets number normalisation.

Thr pathology exam diagnose splenic sarcoidosis based on the presence of numerous sarcoid granulomas type without caseating necrosis and without tendency to confluence (Fig. 3, 4). The granulomas consisted of epithelioid cell with eosinophilic pale cytoplasm with round/ovalar shape nuclei, with visible nucleoli and multinucleated giant cells. At their periphery there is a fine crown of small/average lymphocytic cells (Fig. 5, 6). Granulomatous lesions are relatively evenly distributed throughout the parenchyma. PAS staining, performed to identify any fungal or parasitic infections was negative. Ziehl-Nielsen staining, to exclude tuberculosis splenic infection, was also negative.

The clinical and haematological follow-up, last one in January 2012, saw a steady favorable postoperative evolution, without complications or recurrence of the disease.



Figure 1. *Piece of splenectomy, 25/15/9 cm. Sarcoid granulomas are noted (white-yellowish nodules)*

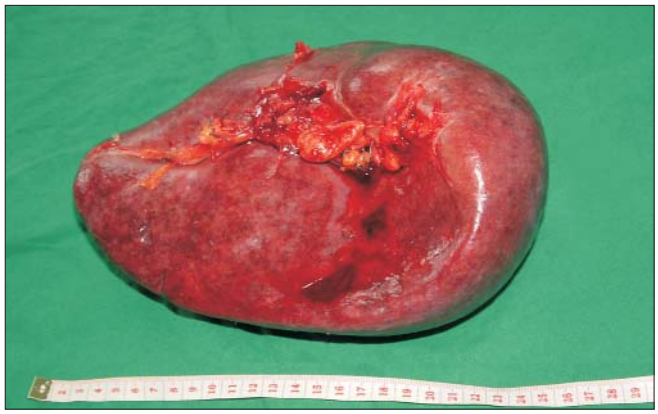


Figure 2. *Part of splenectomy - the hilarious. Sarcoid granulomas numerous surface*

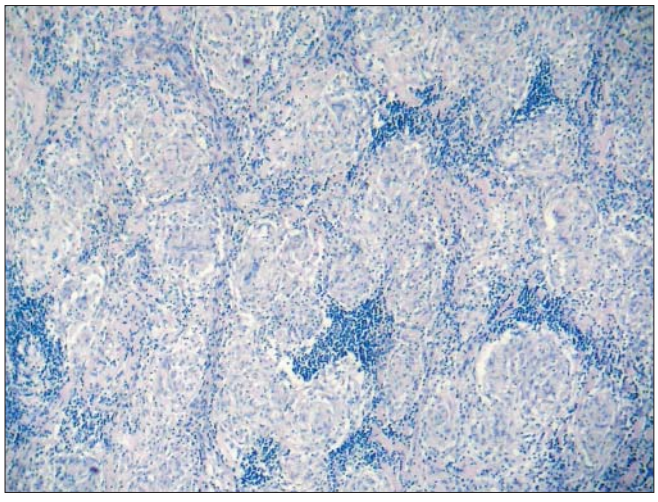


Figure 3. *Conglomerate of sarcoid granulomas type splenic white pulp with debris. HE staining, Ob 10 x 10*

Discussions

Sarcoidosis is considered a chronic inflammatory reaction following an exaggerated immune response to an unknown antigen. The defining element of the desease is sarcoidosis granuloma formed following an immune response to an antigen persistence, hard degradable (1).

The onset interested cells are of type Th1 phenotype who are secreting cytokines, including gamma interferon, interleukins IL-2, IL-12, tumor necrosis factor alpha (TNF-α), which promotes granuloma formation as a local response to the action of aggressor immune factor. CD-4 lymphocytes in combination with other immunologically active cells (such as

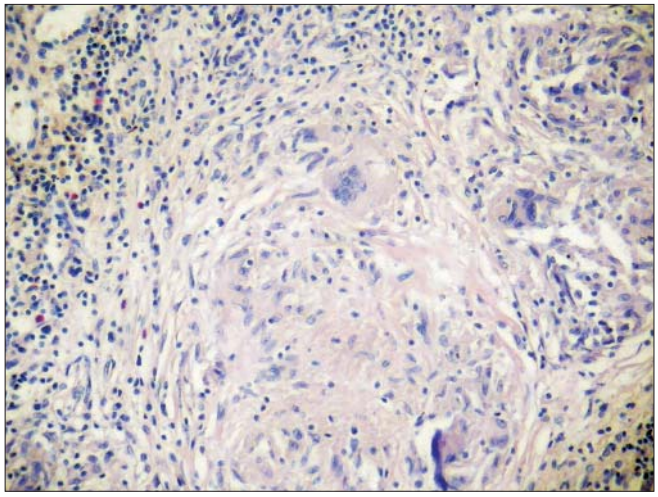


Figure 4. *Sarcoid granuloma and giant cell asteroid body outline. HE staining, Ob 10 x 20*

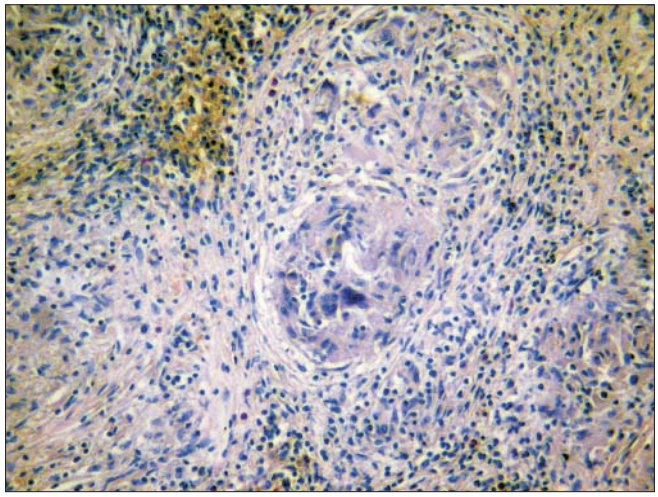


Figure 5. *Sarcoid granulomas showing epithelioid cells and giant cells with peripheral lymphocyte crown (without necrosis) and remaining red pulp. HE staining, Ob 10 x 20*

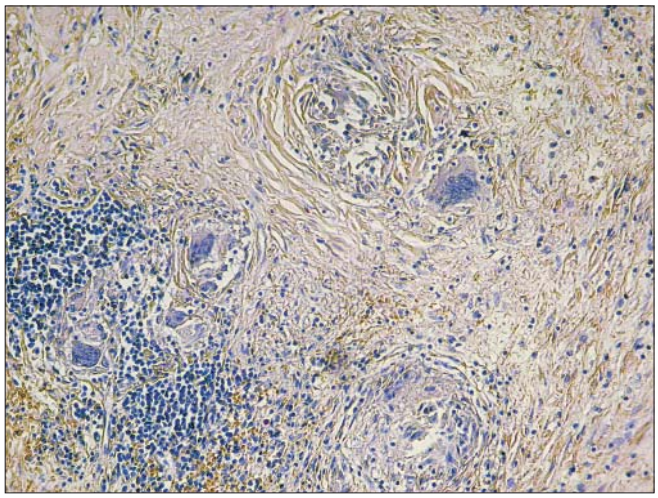


Figure 6. *Granulomas with fibrosis (advanced lesion) and residual white pulp. HE staining, Ob 10 x 20*

macrophages, mast cells, killer cells) perpetuates the inflammatory response, by release of cytokines, monocyte chemotactic factor, macrophage migration inhibitory factor, leukocyte inhibitory factor, adhesion molecules (CD 49, CD 54, CD 102) and growth factors. As a result of these various and multiple interactions, an acute inflammatory cascade, or more commonly chronic, occurs. The disease is characterized by changes in tissue permeability, cellular influx, local cell proliferation, which will generate a granuloma. Persistent antigenic stimulus is considered to maintain the disease process (1). Were observed and other immune abnormalities in patients with sarcoidosis, such as circulating immune complexes, hipereactivity of B cell, immunoglobulin secretion in focus, decreasing of delayed cutaneous hypersensitivity reaction.

Although the most common affecting is the lung disease, it can be located anywhere: lymph nodes, eyes, skin, liver, spleen, kidney, bone, nervous system, heart, joints.

Granulomas produce due to compression of tissue, the growth of cytokines secretion attract inflammatory cells, which may cause local tissue damage and symptoms, and ultimately develop factors that cause fibrosis. This response occurs in severe and often irreversible forms of disease, affecting organs and causing visceral malfunctions.

Disease incidence varies in relation to several factors from 1-40 cases/100.000 inhabitants. In Europe the frequency of diagnosis ranges from 3-50 cases/100.000 inhabitants, most commonly interested segment being the one between 30-40 years. Sweden is the country with the highest incidence of the disease in Europe, 64 cases / 100,000 inhabitants. However, necroptic studies have shown, an incidence of 641 cases per 100,000 deaths autopsy. This is because many patients are asymptomatic and remain undiagnosed.

Estimated risk of sarcoidosis in the U.S. is 2.4 % in blackpopulation and 0.85 % in whites. It is noted that the black population has a 10-17 times higher risk.

In Spain, Portugal, India, South America, Saudi Arabia incidence of sarcoidosis is low (1).

The sarcoidosis symptoms are not specific, and therefore, the most common manifestations (fever, fatigue, weight loss) are difficult to be interpreted. Pulmonary location often generate dyspnea, dry cough, and rarely chest pain and fever. Pulmonary radiography may reveal bilateral hilar lymphadenopathy (74%), nodular peribronhovasculare lesions or well-defined small nodules. Imaging differential diagnosis must be done with histoplasmosis, a fungal infection, and most of all with lymphoma or tuberculosis (1).

The disease can have multiple locations (multisystemic) or can occur isolated, limited to one organ or system, as we have seen.

A palpable superficial lymphadenopathy, hepatomegaly or splenomegaly are less common manifestations.

Eye localization is manifested by uveitis, which occurs in 25-50% of adult cases.

In 25% of cases of sarcoidosis skin lesions appear, which may take different aspects:

Erythema nodosum - reddish sensitive nodules to the legs

Lupus pernio - purple indurated lesions (nose, lips, ears).

Lofgren syndrome, described in acute forms of sarcoidosis, occurs mostly in women and is manifested by fever, bilateral hilar lymphadenopathy, erythema nodosum and arthralgia (shoulder, knee).

Renal and endocrine sarcoidosis, seen in 5-10% of adults, is characterized by hypercalcaemia, hypercalciuria, proteinuria, leucocyturia, hematuria, hypertension, renal failure.

Cardiac sarcoidosis consists on conduction abnormalities and arrhythmias due to granulomatous infiltration of the myocardium. The disease can progress to infiltrative cardiomyopathy, congestive heart failure, pericardial effusion, whole valve or only papillary muscle dysfunction with a mortality of 60% to untreated ones.

In 5% of cases, sarcoidosis can affect any part of the nervous system. More common lesions affects optic nerve, acoustic nerve, facial nerve and also the leptomeninges causing hydrocephalus, hypopituitarism, diabetes insipidus, cerebellar ataxia, peripheral neuritis (1,2).

Rarely sarcoidosis affects skeletal muscle (1.4%).

Heerfordt syndrome, characterized by fever, increase in volume of the parathyroid glands, anterior uveitis, cranial nerve paralysis, meets often in adults.

The bone marrow granuloma, directly or indirectly through the action of secreted cytokines at this level, may explain the installation of a hematopoietic syndrome: anemia (4-20%), leukopenia (40%), thrombocytopenia, eosinophilia, hemolytic autoimmune anemia, leukemoid reaction.

Digestive localizations of the disease are very rare (less than 1%), most often interesting the stomach and being communicated sporadically esophageal, intestinal, appendiceal, rectal or pancreatic lesions.

There may be non-specific manifestations of sarcoidosis in E.N.T.: there are communicated several locations of laryngeal sarcoidosis (3,4).

It was reported an isolate case of breast sarcoidosis (5).

Discussing etiology, various and heterogeneous causes were incriminated: a number of infectious agents, chemicals, drugs, autoimmune disorders, genetic factors. It is suspected that the disease occurs to genetically susceptible hosts exposed to environmental agents that trigger the excessive cellular immune response, leading to granuloma formation.

From this point of view Mycobacteria, including Mycobacterium tuberculosis and other atypical species have been incriminated as potential infectious agents, because has been detected fragments of mycobacterial DNA and RNA in sarcoidosis lesions, wich may demonstrate that presence of this bacterial cell wall components could be a trigger of desease. There were vehement objections to these results, thus the role of mycobacteria in sarcoidosis remains controversial. Other microbial antigens have been incriminated in sarcoidosis etiogy: Propionibacterium acnes, Streptococcus species, Borrelia burgdorferi, Nocardia species. Epstein-Barr virus, herpes virus, Coxsakie B virus, cytomegalovirus, retroviruses. Also, elevated levels of certain chemicals in the environment (Berilium, Aluminium, Zirconium, Titanium), pine pollen, peanut dust or ingestion of clays have been incriminated to play a role in disease etiology.

Racial variation in the incidence of sarcoidosis has suggested a genetic predisposition to disease etiology. A wealth of genetic factors like human leukocyte antigen (HLA), immunoregulatory cytokines, growth factors, angiotensin converting enzyme (ACE) were considered to have a role in the etiology of sarcoidosis (1).

The differential diagnosis of sarcoidosis must be made primarily with tuberculosis infection and fungal or mycobacterial pulmonary infection. Hilar adenopathy raises problems of differential diagnosis with lung cancer or lymphoma. Hypercalcemia of sarcoidosis may be confused with primary hyperparathyroidism.

The haematopoietic marrow affect must exclude the existence of neoplasia. Remember that there is no specific laboratory test for sarcoidosis. Clinical diagnosis is made by exclusion and is determined only after histopathological examination. Incraesing of ESR test value, a anemic syndrome, leucopenia, eosinophilia, hypergammaglobulinemia are found in 75% of patients. Hypercalcemia and/or hypercalciuria are found in 30% of patients. Angiotensin converting enzyme, produced by epithelial cells of the granuloma, increase in the serum of patients with sarcoidosis (60%). Scintigraphy with Gallium (Ga67), which concentrate in viscera affected by sarcoidosis, is not recommended being nonspecific, expensive and producing significant radiation (1).

Biopsy is recommended as the only way to establish the diagnosis. It will be done from palpable lymph nodes, skin lesions, conjunctivitis, lacrimal gland, parotid or lung tissue (transbronchial biopsy). Biopsy of the liver, bone marrow puncture and cytological examination of bronchoalveolar lavage may be, in some cases, other ways to obtain cytological material for histological examination.

The pathologic diagnose of sarcoidosis is made by highlighting the typical noncaseating granuloma. Sarcoid granuloma is composed of round cells, epithelioid cells and multinucleated giant cells surrounded by lymphocytes and macrophages in combination with varying degrees of fibrosis, but without cazeum. This type of granuloma was first described by Schaumann (6). Active disease may also have an fibrinoid necrosis. The histopathologic characteristics of the granulomatous exclude other infections (histoplasmosis, blastomycosis, tuberculosis).

The disease develops spontaneously to disappear in 50% of cases.

In case of unfavorable evolution of the disease treatment is necessary but only after histopathologic exam. The goal of therapy follows preventing or reducing inflammation and also granuloma formation, processes that are responsible for organic dysfunction that may progress to the development of hyaline fibrosis and in the end to visceral parenchyma destruction.

The most recommended therapy is using glucocorticoids (prednisone 1-2 mg per kg body weigh per day for 4-8 weeks as induction therapy followed by a dose of 10-15 mg per kg body weigh per day for at least 6 months. In case of relapse, therapy should be resumed. Eventually will associate

immunosuppressive therapy, as Methotrexate 1 to 1.5 g / day for 6 months to 2 years. Azathioprine, Cyclofosfamid, Chlorambucil, Cyclosporin were used, but with questionable efficacy (1).

Because sarcoidosis can affect any system or organ, various complications can occur. The most common complication encountered is severe ventilatory restriction. The eye affect includes conjunctival synechiae, glaucoma, blindness. Hypercalcemia and hypercalciuria leading to reduced glomerular filtrate, impaired ability to concentrate urine, nephrocalcinosis, nephrolithiasis, obstructive uropathy (7). Disease often produces cranial nerve paralysis, heart failure, vasculitis, which particularly interested in the aortic arch. Mortality in sarcoidosis varies at around 3%.

Asymptomatic disease generally has a favorable outcome in many patients meeting the spontaneous regression.

Cases with persistent symptoms and multisystem determinations generate disabilities in 20%, especially the lung and eye desease.

Clinical observations of splenic sarcodosis are reported very rarely. Indication for splenectomy in these cases is based on the existence of splenomegaly, its possible mechanical effects of compression, on the existence of haematological hypersplenism (sometimes severely), splenic rupture prophylaxis and exclusion of malignancy.

There are reported laparoscopic splenectomies performed for sarcoidosis (8).

Conclusions

1. Sarcoidosis is a diagnosis established only after histopathological examination by evidentiating non-caseating granulomas.
2. Clinical diagnosis of sarcoidosis is made by excluding other deseses.
3. The most common location of sarcoidosis is in the lungs (90%). Other posible locations are: eye, skin, lymph nodes, liver, nervous system, bones, muscles, joints.
4. Location of isolated splenic sarcoidosis is extremely rare.
5. The etiology of sarcoidosis is still unclear.
6. Splenectomy is indicated for the treatment of splenic sarcoidosis and was followed by a good result.
7. Sarcoidosis, once diagnosed, requires the patient to benefit dispensarization for any complications or recurrences that may arise.

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