

# SARCOIDOSIS

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**Abstract:** *The authors wish to present a case of sarcoidosis which is a systemic self-immune disease which is predominantly pulmonary. This case is associated with extrapulmonary symptoms that lead to a late diagnosis, subsequent to the installation of a moderate handicap.*

**Key words:** *sarcoidosis, lesions, respiratory system, self-immune disease, diagnosis.*

## 1. Introduction

Sarcoidosis is a predominantly pulmonary, systemic disease, which may produce virtually non-caseated epithelioid inflammatory granulomas in any organ [1], [3], [5]. It is affection with a great phenotypical diversity, with variable levels of activity, with different degrees of organic alteration. Minor inflammatory symptoms in an organ may have devastating consequences (ex. the heart) and other inflammatory lesions extended to other organs may be without consequences (ex. the skin) [1], [3], [9]. The variety of its location supports the hypothesis of several causes, each being responsible for the different pattern.

## 2. Epidemiology

Sarcoidosis appears to patients below 40 years of age, with a more frequent detection during winter and spring.

Prevalence was reported at 1 – 40/100.000 and the incidence at 10.9/100.000 for whites and 35.5/100.000 for blacks [1], [3], [5]. The etiology of sarcoidosis is unknown, but, there were studies which noted its increased association with chronic berylliosis, hypersensitivity pneumonias, fungal infections or mycobacteria, Chlamydia, tularemia, syphilis. Hills et al. reported an association between the nurses, the persons living in the vicinity of the hospital and sarcoidosis. Kern reported an increased frequency in firemen. Other studies associated sarcoidosis with exposure to metallic powder or antigens. Some self-immune diseases were associated with sarcoidosis (granulomatosis, primitive biliary cyrrhosis). Genetics may be important not only in the definition of the disease risk but also in the determination of the disease pattern, of its severity and of the prognosis (class I HLA-A1 and B8, class II HLD DR3 with whites) [3], [5].

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### 3. Case Report

We are going to show the case of a patient aged 25, hospitalized at the “Leon Daniello” Clinic of Pulmonology and Phthisiology, with whom the polymorphism of the lesions, with predominantly extra-pulmonary manifestations, led to the late diagnosis of the disease, subsequent to the installation of a moderate handicap. The patient, without significant hereditary collateral history, known with sugar diabetes of the I type, insulin dependent, smoker of 5 packs/year, employed as clerk, appeared in the clinic with dispnoea at medium, small efforts, dry cough, asteno-adyndamia, fatigue, transit troubles (diarrhea alternating with constipation), decrease of the muscular force, stepped walking, paraesthesia at the level of the inferior limbs; upon objective examination – slightly altered general status, walking troubles, dry pale tegument with areas of hypo-pigmentation of fingers, bilaterally; adenopathies: lateral cervical, left side axillary and inguinal; the examination of the respiratory system showed – vesicular murmur, bilaterally basal roughened; Blood pressure 115/75 mmHg; AV 76 beats; pain sensitivity in the right side iliac fossa, epigastrium, right and left hypochondrium; megalosplenia, positive Giordano on the right side, dysuria;

Blood tests: inflammatory syndrome with VSH 44 – 86 mm/h; slight anemia Hb = 11.3 g/dl; E = 4.04 mil/ $\mu$ L; Ht = 34.5%. It is highlighted a decompensation of the diabetes; Glycemia = 538 mg/dl; the investigation of the renal function shows: urea = 151 mg/dl, creatinine = 4.7 mg/dl.

The thoracic RX radiography shows multiple bilaterally symmetrical, polycyclic hilar and para-tracheal opacities. Bilaterally accentuated interstice. The suspicion of a lymphoma or of a sarcoidosis was raised. CT thorax supports the presence of mediastinal and abdominal superior adenopathies with the presence of splenomegaly as well as of bilateral renal lithiasis without hydronephrosis. Bronchoscopy is performed and it shows bilateral hyper-vascularization of the primitive bronchi; whitish nodules at the level of the intermediary and medium lobar bronchus – typical aspect of sarcoidosis (biopsies were taken).

Bronchial alveolar lavage – cytological examination; total number of cells =  $3.6 \times 1$  million. Differentiated cytology; Ma = 83%; LY = 13%; PMN = 2.4% Frequent epithelial bronchial cells

Anatomical-pathologic result: three of the multiple fragments of the bronchial mucous examined contain granulomas with giant multi nuclei epithelioid cells without necrosis. The aspect matches a sarcoidosis. Taking into consideration the phenotypical diversity with the potential alteration of numerous locations, a phase review was carried out, with the investigation of the most frequent pulmonary and extra-pulmonary locations.

Functional respiratory tests showed normal values.

Transfer factor through the alveolar capillary membranes; diffusion through the alveolar capillary membrane, moderately reduced through the inequality of the ventilation/perfusion report, which suggests pulmonary alteration even if with the CT are not shown but minimal interstitial modifications at the level of the

pulmonary parenchyma, thus framing the sarcoidosis within the stage II of the disease.

Abdominal ECO shows ganglionic masses of 1 – 1.8 cm diameter, sub-hepatic, retro-gastric and cranial from the pancreas located. Splenomegaly. Bilateral renal lithiasis without hydronephrosis.

Cardiac ECO; diastolic dysfunction of an altered relaxation type. Septalis hypokinesis. Degree I mitral insufficiency, tricuspid insufficiency of 2<sup>nd</sup> degree.

Ophthalmologic examination: suspicion of glaucoma.

Nephrology: diagnosis – diabetic nephropathy; bilateral renal lithiasis (more expressed at the level of the right side kidney), medium chronic renal insufficiency on the background of the diabetic nephropathy but possibly also on the background of the hyper-calcemia and hyper-calcaciuria from the sarcoidosis; Calcium = 12 mg/dl; Calciuria = 143.8 mg/24h.

Neurological evaluation: diminished rotulian bicipital tricipital ROT:

- abolished achylian, stylo-radial and cubital pronator ROT;
- exteroceptive hypo-esthesia, stepped walking, possibly with support.

Diagnosis – multiplex mono-neuritis, sarcoidosis, sugar diabetes type I.

Neurosurgical examination: Sylviana left side valley, arachnoidal cyst. Surgery is recommended in case of headaches, sight troubles, etc.

Rheumatology: diagnosis – sarcoidosis with pulmonary, ganglionic, muscular, SNC manifestations. Poly-neuropathy of axonal type, type I sugar diabetes, diabetic nephropathy, bilateral renal lithiasis, medium chronic renal insufficiency,

arachnoidal cyst, Sylviana left side valley, glaucoma. It is recommended the determination of: ANCA, C3, C4, AAN, CRP, AgHBs, Ac Anti-HGV, CPK and LDH. LDH = 190 U/L; CPK = 16 UI/L; Immunology: IgG = 456 UI/ml; IgA = 225 UI/ml; IgM = 298 UI/ml; C3 = 94 mg%; C4 = 33 mg%; CRP < 0.36 mg%; ANA = negative; ANCA = negative; CIC =  $155 \times 10^{-3}$  U.

Angiotensin convertasis 232 as a confirmation of the activity of the disease.

On the basis of the clinical and para-clinical extended review the established diagnosis was SARCOIDOSIS WITH PULMONARY, GANGLIONIC, MUSCULAR, SNC MANIFESTATIONS, POLY-NEUROPATHY OF AXONAL TYPE, TYPE I SUGAR DIABETES, BILATERAL RENAL LITHIASIS, MEDIUM CHRONIC RENAL INSUFFICIENCY, ARACHNOIDAL CYST, GLAUCOMA.

Taking into consideration the extension of the lesions and the disease severity it was decided to start the administration of cortico-therapy 1 mg/kg/body associated with 50 mg/day Imuran. The evolution under treatment was slow favorable with the attenuation of the respiratory symptoms, the diminution of the hilar adenopathies (without their disappearance) with the reduction of the angiotensin convertasis (22 UI). The motive recovery started also, with the improvement of walking, but with the persistence of the stepped walking.

#### 4. Discussions

The severity of sarcoidosis refers predominantly to the thoracic radiography (Scadding stage), to the evolution of the

disease and to the probability of spontaneous remission.

As sarcoidosis is fatal to a minority of patients, the calculation of the rate of survival as severity score may not be applied [9].

The most used severity score is related to the extension of the lesions seen on the radiography and the modification of the respiratory function tests. The extension of the lesions seen at CT examination does not correlate with the respiratory tests, nor does the extension of the inflammatory granulomas with the same tests.

The British Thoracic Society focused the degree of severity exclusively at the level of the lungs with the evolution under long term cortico-therapy [8], [9].

Muers found correlations between the dispnoea, reticular nodular aspect, fibrosis score and spirometry with TLCO. A higher score correlated decreased respiratory tests, radiological score as extended and deep with bad prognosis. Most of the surveys include the presence of symptoms, the radiological aspect, respiratory evaluations, Bronchial alveolar lavage, the life quality, severity and extension to other organs [9].

The neurological alteration is rare and only few surveys have long term follow-up with response to treatment. Most of the patients showed slight neurological symptoms months or years before medical consult (the average is 37 +/- 11 months) [7].

A percentage of 5-15 % of the cases with neurological lesions have an uncertain evolution. According to the evolution under treatment they fall into two categories:

1. full remission or amelioration but with sequelae after 12 months;
2. stable or aggravation.

MODIFIED OXFORD HANDICAP SCALE (MOHS) describes

Group 1:

- 0 no symptom
- 1 minor symptom without of the interferenceing quality of life
- 2 minor symptoms but with the restriction of the capacity of handling things by him/herself.

Group 2:

- 3 moderate handicap – incapacity of handling things by him/herself
- 4 moderate severe – need constant attention
- 5 severe handicap – total dependence day and night
- 6 – death.

The polymorphism of the lesions was not associated with the MOHS score or with the evolution of the disease. No correlations were found between MOHS and the extra-neurological manifestations and the systemic evolution was not a predictive factor for the evolution of the neuro-sarcoidosis [2], [4]. Over ½ of the patients with the SNC sarcoidosis had the progressive disease under treatment [10]. Those with limited lesions of chronic neuropathy or peripheral syndromes have a decreased risk of progression (except for optical neuropathy), those with meningitis have a decreased risk of retard and those with symptomatic intracranial disease have an accentuated risk of progression [4], [6-7]. Gedalia, on a survey on children made a global severity score on each of the 9 locations involved and the evolution under treatment [9].

## 5. Conclusions

1. The utility and the framing within a certain severity scale may demonstrate the necessity of other surveys with a genetic aim and the attempt of screening other risk factors.
2. The surveys carried out until now demonstrated as unfavorable factors: the duration of the disease, the smoker's status, the treatment with corticosteroids, the immunodepressant treatment, cardiac, neurological, tegument alteration.
3. The alteration of the extra-thoracic ganglions or the endocrine alteration do not influence the evolution of the disease.
4. The HLA-DRB1-15 and HLA DRB1-0602 forms are associated with the severe forms, with progressive chronicity and evolution of the disease.
5. The peculiarity of the case is the early age of a patient with late diagnosis to whom the moderate handicap is already installed, the total and complete recovery is less than probable, with reserved evolution under the terms in which almost all the unfavorable risk factors are present.
6. The use of new therapies (anti TNF alpha) at patients to whom classic therapy with corticosteroids or immunodepressants did not showed results may be a solution to such patients with bad prognosis.

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