Differential diagnosis of pulmonary Sarcoidosis in an elderly patient: case report

Diagnóstico diferencial de Sarcoidose pulmonar em um paciente idoso: relato de caso

DOI:10.34117/bjdv7n12-308

Recebimento dos originais: 12/11/2021
Aceitação para publicação: 09/12/2021

Reinaldo Leite de Morais Filho
Médico formado pela Universidade de Rio Verde – UNIRV
Avenida T-13, quadra S-06, setor Bela Vista. Cidade: Goiânia, Goiás.
reinaldo.morais97@hotmail.com

Bárbara Queiroz de Figueiredo
Discente do Curso de Medicina do Centro Universitário de Patos de Minas – UNIPAM
Rua Major Gote, 808 – Bairro: Caiçaras – Cidade: Patos de Minas, Minas Gerais
barbarafigueiredo@unipam.edu.br

Dalbert Samuel Dutra
Discente do Curso de Medicina do Centro Universitário de Patos de Minas – UNIPAM
Rua Major Gote, 808 – Bairro: Caiçaras – Cidade: Patos de Minas, Minas Gerais
dalbertdutra@unipam.edu.br

Janayna Fraga Teixeira
Discente do Curso de Medicina do Centro Universitário Goiatuba – UNICERRADO
Rodovia Go 320. s/n. Bairro: Jardim Santa Paula. Cidade: Goiatuba, Goiás.
janaynafragateixeira@gmail.com

Luanna Oliveira Gonçalves
Discente do Curso de Medicina do Instituto Master de Ensino Presidente Antônio Carlos – IMEPAC
Avenida Minas Gerais, 1889. Bairro: Centro. Cidade: Araguari, Minas Gerais.
luanna435@gmail.com

ABSTRACT

INTRODUCTION: Sarcoidosis is a worldwide disease with a lifetime incidence rate of 0.85–2.4%, generally affecting people between 25 and 40 years of age. The clinical phenotype of sarcoidosis can be extremely diverse in terms of presentation, involved organs, duration and severity, however, pulmonary involvement is present in 86–92% of cases according to chest radiography, alone or in association with locations extrapulmonary in about 50% of cases. PURPOSE: to demonstrate a clinical case, by differential diagnosis, of pulmonary sarcoidosis. METHODOLOGY: this is a clinical case study with a qualitative and descriptive perspective, which consists of research that, in general, takes place with direct data collection, whose researcher is the indispensable

instrument. CASE REPORT: elderly patient, who, after admission to the emergency room, had symptoms such as mental confusion, wasting syndrome, with previous imaging exams without alterations. The results of transbronchial biopsy showed foci of fibrosis in the lamina propria and non-caseating epithelioid granulomatous inflammation in the lung parenchyma, as well as negative Baar and fungus tests. From this perspective, the differential diagnosis was found, closing the clinical case for pulmonary sarcoidosis. DISCUSSION: The diversity of the sarcoidosis phenotype is often linked to epidemiological factors and, interestingly, as shown by recent studies, to the genotype. FINAL CONSIDERATIONS: sarcoidosis is a frequent but multifaceted disease that still poses diagnostic and therapeutic challenges.

keywords: Pulmonary sarcoidosis, Diagnosis, Transbronchial biopsy.

RESUMO

INTRODUÇÃO: A sarcoidose é uma doença mundial com uma taxa de incidência ao longo da vida de 0,85–2,4%, geralmente afetando pessoas entre 25 e 40 anos de idade. O fenótipo clínico da sarcoidose pode ser extremamente diverso em termos de apresentação, órgãos envolvidos, duração e gravidade, no entanto, o envolvimento pulmonar está presente em 86-92% dos casos de acordo com a radiografia de tórax, isoladamente ou em associação com localizações extrapulmonares em cerca de 50% de casos. OBJETIVO: demonstrar um caso clínico, por diagnóstico diferencial, de sarcoidose pulmonar. METODOLOGIA: trata-se de um estudo de caso clínico com perspectiva qualitativa e descritiva, que consiste em pesquisa que, em geral, ocorre com coleta direta de dados, cujo pesquisador é o instrumento indispensável. RELATO DO CASO: paciente idoso, que, após admissão no pronto-socorro, apresentou sintomas como confusão mental, síndrome debilitante, com exames de imagem prévios sem alterações. Os resultados da biópsia transbrônquica mostraram focos de fibrose na lâmina própria e inflamação granulomatosa epitelioide não caseosa no parênquima pulmonar, além de testes de Baar e fungos negativos. Nessa perspectiva, foi encontrado o diagnóstico diferencial, encerrando o caso clínico de sarcoidose pulmonar. DISCUSSÃO: A diversidade do fenótipo da sarcoidose está frequentemente ligada a fatores epidemiológicos e, curiosamente, como mostram estudos recentes, ao genótipo. CONSIDERAÇÕES FINAIS: a sarcoidose é uma doença frequente, mas multifacetada, que ainda apresenta desafios diagnósticos e terapêuticos.

Palavras-chave: Sarcoidose pulmonar, Diagnóstico, Biópsia transbrônquica.

1 INTRODUCTION

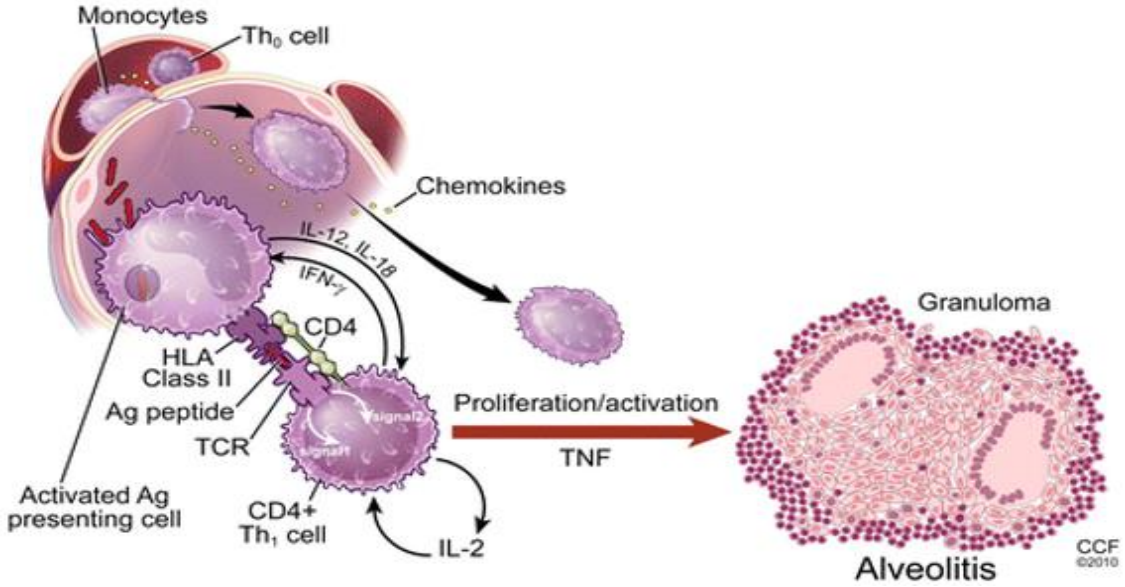
Sarcoidosis is a worldwide disease with a lifetime incidence rate of 0.85–2.4%, generally affecting people between 25 and 40 years (ZIEGENHAGEN et al., 2003). The clinical phenotype of sarcoidosis can be extremely diverse in terms of presentation, involved organs, duration and severity, however, pulmonary involvement is present in 86–92% of cases according to chest radiography, alone or in association with locations extrapulmonary in about 50% of cases. Furthermore, in at least half of the cases,

sarcoidosis follows a benign course with spontaneous resolution in less than 12 to 36 months (RICHTER et al., 2009).

The immunopathogenesis of sarcoidosis is not fully understood, but enormous progress has been made over the last decade, but most evidence suggests that the development of the disease is similar to other granulomatous diseases of known cause, such as chronic beryllium disease (MOLLER et al., 2007). That is, some antigens enter the host and are phagocytosed by antigen-presenting cells (APCs), predominantly macrophages or dendritic cells. APCs process the antigen and subsequently present it through human leukocyte antigen (HLA) class II molecules to a restricted set of T cell receptors on naive T lymphocytes, mainly CD4+class cells (MOLLER et al., 2002).

The pathogenesis of sarcoidosis appears to involve the interaction of antigens, class II HLA molecules and T cell receptors (EISHI et al., 2002). It is likely that specific combinations of these three facets are necessary for the development of sarcoidosis. If this scenario is correct, the pathophysiology of sarcoidosis depends on genetics that determine specific HLA polymorphisms, exposures in the form of putative antigens and T cell responses that can be genetically programmed, but can also involve memory of previous exposure to the antigen (BAUGHMAN et al. al., 2001; ZIEGENHAGEN et al., 2003). This scheme also suggests that there may be multiple causes of sarcoidosis, each requiring a specific arrangement of antigen, HLA molecule, and T cell receptor, as illustrated in Figure 1.

Figure 1: Inflammatory response of sarcoidosis with granuloma formation and subsequent resolution or persistence of the disease. HLA = human leukocyte antigen; IFN = interferon; TCR = T cell receptor; TNF = tumor necrosis factor.



Source: Ziegenhagen et al., 2003

The symptoms of sarcoidosis vary greatly depending on the location and extent of the disease, as well as the age and sex of the affected person, the most common being pain and redness in the eyes, fatigue, malaise, sweating, skin rash or red nodules, photosensitivity, blurred vision, dyspnoea, wheezing, weight loss, cough and lymph node enlargement. Furthermore, pulmonary fibrosis, extensive disease on high-resolution chest CT, impaired lung function, and pulmonary hypertension are well-established predictors of poor clinical outcomes (ZIEGENHAGEN et al., 2003).

From this perspective, the diagnosis of sarcoidosis is safe when there is a compatible clinical-radiological picture, appropriate histopathological support and absence of other known causes of granulomatous disease. Specimens for histopathological examination are usually obtained using fiberoptic bronchoscopy. Transbronchial biopsy has a diagnostic yield of around 75% and must always be performed. Bronchoalveolar lavage must be obtained before proceeding with the biopsy, and an increase in lymphocytes may be identified; in this specimen, the presence of a CD4/CD8 ratio > 3.5 has a specificity of 94-96% and a sensitivity of 52-59% (RICHTER et al., 2009). Thus, the aim of this study is to demonstrate a clinical case, by differential diagnosis, of pulmonary sarcoidosis.

2 METHODOLOGY

This article is a clinical case study with a qualitative and descriptive perspective, which consists of research that, in general, takes place with direct data collection, whose researcher is the indispensable instrument. The present study counted on the contribution of academic works between the years 2001 and 2021. Through access to the main databases, namely: National Library of Medicine data (PubMed MEDLINE), Scientific Electronic Library Online (Scielo), Cochrane Database of Systematic Reviews (CDSR), Google Scholar, Virtual Health Library (VHL) and EBSCO Information Services, from September to October 2021.

3 CASE REPORT

A 72-year-old female patient was admitted to the emergency department of a hospital in the interior of Minas Gerais on 09/14/2021, with the main complaint of mental confusion and weight loss (wasting syndrome). The history of the current illness reported generalized weakness without other symptoms, denying fever, recent travels and contact with animals. In the past pathological history, it was noted that the patient has arterial

hypertension (SAH), using pacemaker leads in the right heart chambers, and also reported previous seizures.

On physical examination, the patient was in good general condition (BEG), moist and pale mucosa, no skin changes and no lymph node enlargement. Upon symptomatic interrogation of the various devices and systems, she did not present other alterations. Thus, the following tests were requested: arterial blood gases, complete laboratory tests, thyroid ultrasonography followed by echocardiogram and chest computed tomography, which resulted, respectively, as shown in tables 1 and 2:

Table 1: Arterial blood gases

Parameteres	Dosed values	Reference values
PH	7,58	7,35-7,45
pCO2	22 mmHg	35-45 mmHg
pO2	174	80-100
HCO3	20,6 mEq/L	22-26 mEq/L
Saturation	100%	>95%

Source: Survey data, 2021

Table 2: Laboratory tests

Dosed elements	Dosed values	Reference values
Albumin	3,9 g/dL	3,5-4,7 g/dL
Total cholesterol	160 mg/dL	< 190 mg/dL
Total bilirrubin	0,6 mg/dL	Up to 1,2 mg/dL
Direct bilirrubin	0,2 mg/dL	Up to 0,4 mg/dL
Lipase	39,7 U/L	Up to 600 U/L
HDL cholesterol	42 mg/dL	>45 mg/dL (women)
LDL cholesterol	97 mg/dL	>115 mg/dL
Serum iron	94 ug/dL	50-170 ug/dL (women)
Creatine kinase	578 U/L	33-211 U/L (women)
D-dimer	750 ng/mL	Up to 500 ng/mL
TSH	1,22 mU/L	0,3-4,0 mU/L
Free T4	1,36 pg/mL	2,5-4 pg/mL
Procalcitonin	0,06 ng/mL	>0,5 ng/mL
Glucose	96 mg/dL	60-110 mg/dL
Urea	57 mg/dL	16-40 mg/dL
Hemoglobin	9,9 g/dL	12-16 g/dL (women)
VCM	92 fL	80-100 fL
HCM	31,5 g/dL	28-34 g/dL
CHCM	34,3 g/dL	31-36 g/dL
RDW	13%	11-14%
Total leukocytes	12400 u/L	4000-11000 u/L
Rod neutrophils	1 u/L	0-800 u/L
Eosinophils	4 u/L	0-500 u/L
Lymphocytes	1800 u/L	900-4000 u/L
Monocytes	4 u/L	100-1000 u/L
Platelets	25200 u/L	140000-450000 u/L
Magnesium	1,5 mg/dL	1,7-2,6 mg/dL
Calcium	14 mg/dL	8,5-10,2 mg/dL
Creatinine	1,1 mg/dL	0,6-1,2 mg/dL
Potassium	3,2 mmol/L	3,5-5,5 mmol/L
Sodium	132 mmol/L	135-145 mmol/L

TGO	30 u/L	5-40 u/L
TGP	12 u/L	7-56 u/L

Source: Survey data, 2021

Thyroid ultrasonography showed usual topography, with mild heterogeneity and volumetric reduction, which may have shown the relationship of thyroid sequelae, as well as the thyroid lobe measuring 3.4 x 1.1 x 0.8 cm, left 3 .5 x 1.1 x 0.7 cm, usual volume between 6.0 and 14 cm^3, showed no alterations in the parotid and submandibular glands, and no evidence of lymphomegaly in cervical chains.

In addition, echocardiography showed an ejection fraction of 62%, normal biventricular segmental and global systolic function at rest, mild left atrium dilation, anomalous movement of the interventricular septum, pulmonary hypertension (measurement of systolic pressure in the pulmonary artery: 35mmHg) and presence of cables of pacemaker. A computed tomography scan of the chest revealed the presence of bilateral micronodules.

Furthermore, the patient had recent previous exams of upper digestive endoscopy, myelogram, MRI of the total abdomen and cranial computed tomography, which helped in the process of differential diagnosis of the clinical case. Thus, by upper digestive endoscopy, hiatal hernia by small-volume slippage, grade A erosive distal esophagitis, endoscopically antral gastritis with medium-intensity flat erosions, mild enatematous duodenitis and positive urease test were noted. Also, unaltered myelogram.

Besides, magnetic resonance imaging of the abdomen showed no gallbladder surgery, dilatation of the intrahepatic bile ducts, accompanied by hepato-coledocal ectasia, multiple splenic nodules, hypocontrasts of an indeterminate nature, simple renal cyst, aortoiliac atheromatosis, small amount of fluid free in the pelvic cup, diffuse bone heterogeneity of the spine as well as the pelvis, in addition to multiple areas of enhancement by the intravenous contrast agent. Furthermore, the cranial computed tomography findings showed no alterations.

Later, on the second day after admission, the patient had improved agitation, awaiting transbronchial biopsy. The results showed foci of fibrosis in the lamina propria and non-caseating epithelioid granulomatous inflammation in the lung parenchyma, as well as negative Baar and fungus tests. From this perspective, the differential diagnosis was found, closing the clinical case for pulmonary sarcoidosis.

4 DISCUSSION

The diversity of the sarcoidosis phenotype is often linked to epidemiological factors and, interestingly, as shown by recent studies, to the genotype. Sarcoidosis can be considered mild or severe. Interestingly, mild and severe phenotypes do not seem to evolve from one to the other. Mild cases are usually characterized by absent or mild symptoms, stage I, erythema nodosum or acute uveitis, and rapid spontaneous resolution within 12 to 36 months. In contrast, severe cases are often characterized by prolonged evolution, evidence of stage III or IV, frankly impaired lung function and some extrathoracic locations such as heart, central nervous system, eyes, muscles, rhinosinusals, larynx or kidney (CHEN et al., 2010).

Furthermore, in patients who need systemic therapy to control their disease, corticosteroids comprise the most commonly used first-line treatment, with antimetabolites often representing an alternative for patients who do not respond to or cannot tolerate corticosteroids. In fact, corticosteroid therapy is associated with toxic effects that correlate with both the cumulative dose and the duration of treatment (GRUNEWALD et al., 2010). The scarcity of truly effective therapies and reliable predictors of unpredictable disease development in individual patients contribute enormously to making sarcoidosis such a difficult disease to control (FEHRENBACH et al., 2003).

5 FINAL CONSIDERATIONS

The severity of pulmonary sarcoidosis ranges from radiographic abnormalities discovered incidentally in asymptomatic patients to a chronic progressive disease that is refractory to treatment. Mortality from sarcoidosis appears to have increased in the last three decades, with respiratory failure being the most common cause of death related to sarcoidosis. In addition, pulmonary fibrosis, extensive disease on high-resolution chest CT, impaired lung function, and pulmonary hypertension are well-established predictors of poor clinical outcomes. In other words, sarcoidosis is a frequent but multifaceted disease that still poses diagnostic and therapeutic challenges.

REFERENCES

BAUGHMAN, R. P., et al. Grupo de pesquisa Case Control Etiologic Study of Sarcoidose (ACCESS). Características clínicas dos pacientes em um estudo caso-controle de sarcoidose. **Am J Respir Crit Care Med.,** v. 164, n. 4, p. 1885-1889, 2001.

CHEN, E. S., et al. A amiloide A sérica regula a inflamação granulomatosa na sarcoidose por meio do receptor 2 semelhante a Toll. **Am J Respir Crit Care Med**., v. 181, n. 5, p. 360-373, 2010.

EISHI, Y., et al. Análise quantitativa do DNA micobacteriano e propionibacteriano em linfonodos de pacientes japoneses e europeus com sarcoidose. **J Clin Microbiol.,** v. 40, n. 1, p. 198-204, 2002.

FEHRENBACH, H., et al. Os macrófagos alveolares são a principal fonte de fator de necrose tumoral alfa em pacientes com sarcoidose. **Eur Respir J.,** v. 21, n. 5, p. 421-228, 2003.

GRUNEWALD, J., et al. Distribuições de alelos HLA-DRB1 diferentes em subgrupos clínicos distintos de pacientes com sarcoidose. **Respir Res.,** p. 11, v. 25, p. 1-11, 2010.

MOLLER, D. R., et al. Base genética da sarcoidose remitente: triunfo do complexo trimolecular? **Am J Respir Cell Mol Biol.,** v. 27, n. 4, p. 391-395, 2002.

MOLLER, D. R., et al. Potenciais agentes etiológicos na sarcoidose. **Proc Am Soc Thorac.,** v. 4, n. 8, p. 465-468, 2007.

RICHTER, K. A. O., et al. As respostas celulares aos antígenos micobacterianos estão presentes no lavado broncoalveolar usado no diagnóstico da sarcoidose. **Infect Immun.,** v. 77, n. 5, p. 3740 -3748, 2009.

ZIEGENHAGEN, M. W., et al. A rede de citocinas na sarcoidose e sua relevância clínica. **J Intern Med.,** v. 253, n. 5, p. 18-30, 2003.