

Case Report

Rheumatoid pneumoconiosis (Caplan's syndrome) with a classical presentation*

Pneumoconiose reumatoide (síndrome de Caplan)
com apresentação clássica

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Abstract

Although rare, rheumatoid pneumoconiosis, also known as Caplan's syndrome, can occur in workers exposed to silica, as well as in patients with silicosis, coal workers' pneumoconiosis or asbestosis. Prevalence is higher among patients with silicosis, despite the fact that it was originally described in coal workers with pneumoconiosis. The classical finding that defines this syndrome is that of rheumatoid nodules in the lungs, regardless of whether there are small rounded opacities suggestive of pneumoconiosis or large opacities consistent with massive pulmonary fibrosis, with or without clinical rheumatoid arthritis. We describe the case of a female patient with rheumatoid arthritis, diagnosed 34 years after 7 years of occupational exposure to silica at a porcelain plant. A chest X-ray showed circular opacities of 1-5 cm in diameter, bilaterally distributed at the periphery of the lungs. A CT-guided thoracic punch biopsy of one of those nodules revealed that it was rheumatoid nodule surrounded by a palisade of macrophages, which is typical of Caplan's syndrome. Aspects of diagnosis, classification and occurrence of this syndrome are discussed, emphasizing the importance of the occupational anamnesis of patients with rheumatoid arthritis and lung opacities on chest X-rays.

Keywords: Pneumoconiosis; Arthritis, rheumatoid; Caplan's syndrome; Silicosis.

Resumo

Apesar de rara, a pneumoconiose reumatoide, também chamada de síndrome de Caplan, pode ser diagnosticada entre trabalhadores expostos à sílica e entre pacientes com silicose, pneumoconiose dos mineiros de carvão e asbestose. A maior prevalência ocorre entre os silicóticos, apesar de ter sido descrita inicialmente em mineiros de carvão com pneumoconiose. O achado que define o tipo clássico da síndrome é a presença de nódulos reumatoides nos pulmões, independente da presença ou não de pequenas opacidades pneumoconióticas, ou de grandes opacidades de fibrose pulmonar maciça, associada ou não a um quadro de artrite reumatoide em atividade. Relatamos o caso de uma mulher com quadro de artrite reumatoide, diagnosticada 34 anos após exposição à sílica livre em uma indústria de porcelana por 7 anos, apresentando radiograma de tórax com opacidades arredondadas de 1 a 5 cm de diâmetro, distribuídas na periferia de ambos os pulmões. A biópsia transtorácica guiada por TC de um dos nódulos revelou tratar-se de nódulo reumatoide com macrófagos em paliçada, típico da síndrome de Caplan. São discutidos aspectos de diagnóstico da síndrome, classificação e ocorrência, ressaltando a importância da anamnese ocupacional em casos de artrite reumatoide com opacidades radiológicas pulmonares.

Descritores: Pneumoconiose; Artrite reumatoide; Síndrome de Caplan; Silicose.

Introduction

In 1953, Caplan defined rheumatoid pneumoconiosis as characterized by rounded, peripheral pulmonary radiological images, 0.5-5.0 cm in diameter, with or without small opacities consistent with pneumoconiosis or massive pulmonary fibrosis, in patients with

rheumatoid arthritis (RA) and exposed to mineral coal or silica dust.⁽¹⁾ The prevalence of this entity among patients with pneumoconiosis is low. Caplan⁽¹⁾ found a prevalence of 0.4% and, more recently, Honma and Vallyathan showed that the incidence was 0.75% in Japan and 1.5% in the

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USA.⁽²⁾ In Brazil, data regarding this syndrome are restricted to two published clinical cases.^(3,4) Here we describe one clinical case with a typical pulmonary presentation and rheumatoid nodules in the lungs, as confirmed through tomographic and histopathological studies.

Case report

A 55-year-old female patient was referred to our facility suspected of having metastatic neoplasm in the lung, without weight loss, cough, or hemoptysis. She complained of dyspnea on exertion for four months. The patient reported a five-year history of polyarthritis in the hands, feet, and knees, accompanied by morning stiffness for more than one hour. On physical examination, she presented slightly increased hand joint volume and ulnar deviation at the wrist, which is consistent with a diagnosis of RA. She had been using chloroquine, prednisone, meloxicam, and ranitidine. She was an active smoker (25 pack-years) but had no history of lung disease. The patient presented an occupational history of a 7-year exposure to silica at a porcelain plant, where she worked as an enameller from 1966 to 1972, when collective protection measures were not taken at these types of companies. She was diagnosed with RA 34 years later.

Upon physical examination, she presented good overall health status, without symptoms of RA. Her breathing was normal, with a respiratory rate of 12 breaths/min, her heart rate was rhythmic (72 bpm), pulmonary auscultation revealed no alterations, and her SpO₂ was 94% on room air. Spirometry revealed an FVC of 2.44 L (87% of predicted), an FEV₁ of 1.49 L (66% of predicted), an FEV₁/FVC ratio of 0.61, and an FEV_{25-75%} of 0.86 L/s (38% of predicted). The rheumatoid factor was 277 IU/mL, the test result for antinuclear factor was negative, and the erythrocyte sedimentation rate was 13 mm in the first hour.

Hand and wrist X-rays showed a symmetric decrease in joint spaces, marginal bone erosion, and periarticular osteoporosis in the proximal metacarpophalangeal and interphalangeal joints (Figure 1a).

Chest X-rays revealed rounded, well-delimited nodules of various sizes (1-5 cm in diameter), bilaterally distributed at the periphery of the lungs, affecting the upper and lower halves of

both lungs, together with larger, also peripheral, masses in both apices (Figure 1b).

An HRCT scan of the chest revealed bilateral, round, well-delimited nodules with peripheral distribution, together with nodules \leq 5 cm, with the same characteristics, in the apices. Many of the opacities showed point calcifications. Small centrilobular nodules, with slight ground-glass attenuation, were observed in the upper regions of both lungs. There was adenopathy with mediastinal calcification (Figure 2).

A CT-guided thoracic punch biopsy of a 5-cm peripheral nodule located in the posterior region of the left lung revealed, in the histopathological analysis, that it was a rheumatoid nodule of loose collagen in concentric layers surrounded by fibrocytes and a palisade of macrophages, interspersed with refracting particles (Figure 3).

Discussion

Between 1950 and 1952, Caplan studied approximately 14,000 claimants for pneumoconiosis disablement benefits.⁽¹⁾ The author found that the prevalence of images consistent with massive fibrosis was higher among those with coal worker's pneumoconiosis (CWP, also known as black lung) accompanied by RA (90% of the cases), than among those with pneumoconiosis who did not present with RA (massive fibrosis observed in 90% and 30%, respectively). The prevalence of RA among the 14,000 studied cases of CWP was 0.4% (51 cases), which was not higher than expected.⁽¹⁾ In addition, in 25% of the cases with CWP and RA, Caplan observed, and described in detail, a characteristic radiolog-

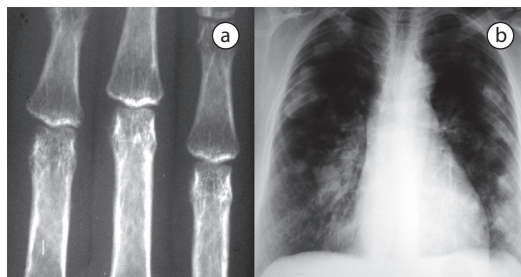


Figure 1 - In a), hand X-rays showing a symmetric decrease in joint spaces, marginal bone erosion, and periarticular osteoporosis in the proximal metacarpophalangeal and interphalangeal joints. In b), chest X-rays showing nodules of various sizes, 1-5 cm in diameter, rounded, well delimited, distributed at the periphery of both lungs.

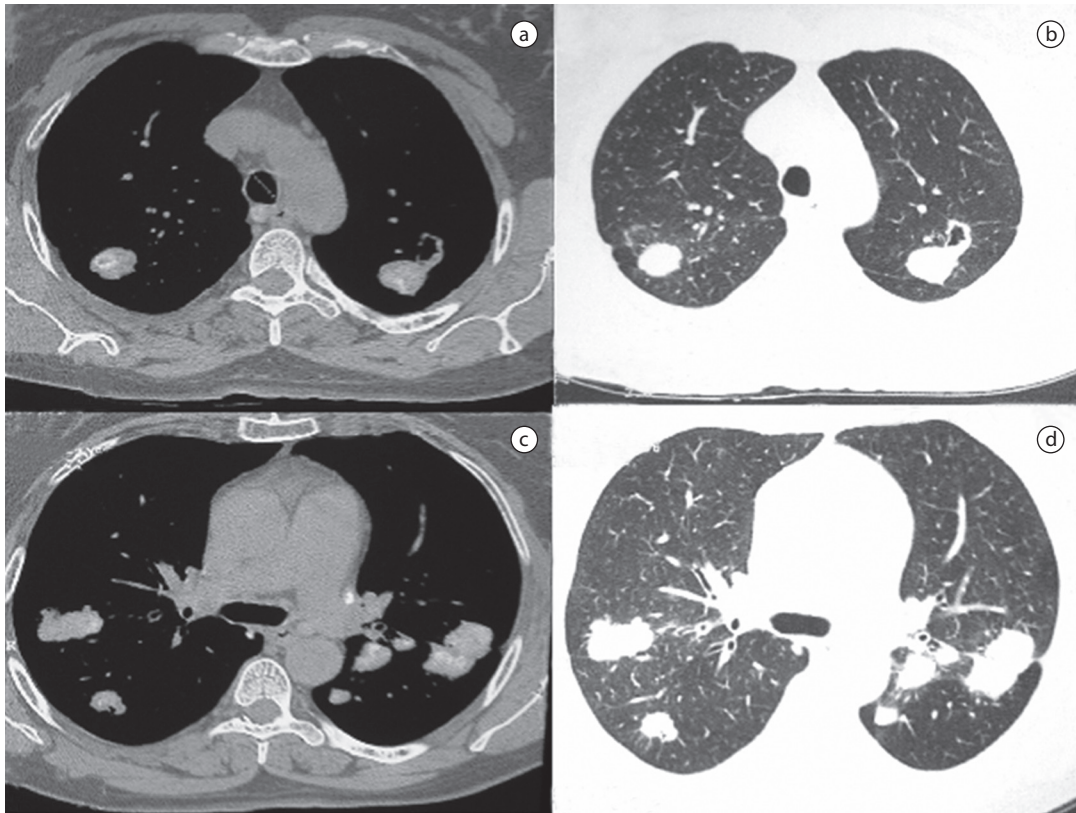


Figure 2 - HRCT images showing nodules of various sizes, 1-5 cm in diameter, rounded, well delimited, distributed at the periphery of both lungs, affecting the upper and lower halves of the lungs, and larger, also peripheral, masses in both apices. Several opacities show point calcifications.

ical profile that was different from the images typically seen in coal miners with CWP.⁽¹⁾ The profile consisted of well-defined, rounded opacities (0.5-5.0 cm in diameter and therefore much larger than the typical opacities found in pneumoconiosis and in the limit to be considered as part of the massive fibrosis profile), distributed bilaterally throughout the lungs, especially at their peripheries. Caplan highlighted that "(...) an important finding in these cases is that the background of simple pneumoconiosis is often slight or absent (category 1 or 0)."⁽¹⁾ Therefore, the presence of small rounded opacities, typical of pneumoconiosis, is not a necessary condition for a diagnosis of Caplan's syndrome. In his original study, Caplan showed the presence of small opacities, category 1 or lower (according to the International Labour Organization classification at the time), in 45% of the cases.⁽¹⁾ He also suggested that the non-occupational exposure to coal or silica dust could explain the presence of rheumatoid nodules in the lungs of patients with RA without images of pneumo-

coniosis.⁽⁵⁾ On the other hand, the syndrome's characteristic lesions would be those presented by the 0.5-5.0 cm, peripheral, rounded nodules, regardless of the presence of opacities typical of pneumoconiosis. In another study, conducted in 1965, Caplan expanded upon this definition of the "syndrome".⁽⁵⁾

Studies in the French literature have proposed that this syndrome be called Colinet-Caplan's syndrome, due to the description of cases with the clinical and radiological characteristics described by Caplan in three patients with silicosis and RA, diagnosed in 1948 and 1950.^(6,7)

In 1955, Gough⁽⁸⁾ described the histopathological alterations of the syndrome, showing that the nodules described by Caplan in simple X-rays were rheumatoid nodules, with central area of necrotic collagen, surrounded by an inflammatory process involving macrophages and leucocytes, with varying degrees of dust deposition. In 1992, Gardner corroborated Gough's findings, stating that the presence of a rheumatoid nodule in the lung was necessary in

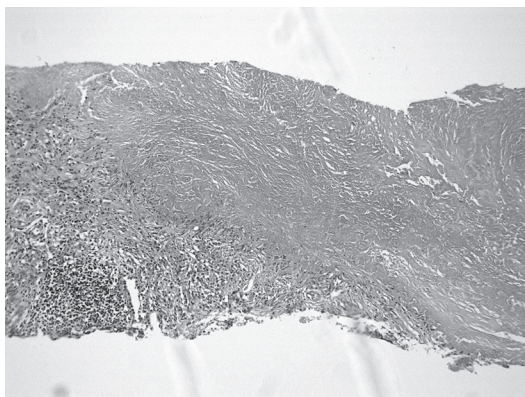


Figure 3 – Histopathological analysis of a sample collected through CT-guided thoracic punch biopsy, showing a rheumatoid nodule of loose collagen in concentric layers surrounded by fibrocytes and a palisade of macrophages.

order to diagnose rheumatoid pneumoconiosis, regardless of the presence of nodules characteristic of pneumoconiosis. Perhaps the most sensible view regarding nomenclature and classification of this entity was that put forth by Honma and Vallyathan,⁽²⁾ who classified rheumatoid pneumoconiosis as two types: classic (Caplan's syndrome), as described by Caplan in 1953/1959^(1,9) and by Gough in 1955⁽⁸⁾; and silicotic, without rheumatoid nodules in the lungs, although with small silicotic nodules, or pneumoconiosis as a consequence of mixed dust, accompanied by RA.

Although the syndrome was originally described in coal miners, several cases have since been diagnosed in individuals exposed to free silica or asbestos.^(2,10-12) However, such cases are much rarer than those occurring in individuals exposed to mineral coal dust.

The relationship between pneumoconiosis, especially silicosis, and the triggering of autoimmune diseases has been recognized since the 1950s, and numerous cases of pneumoconiosis accompanied by scleroderma (Erasmus's syndrome), systemic lupus erythematosus, and connective tissue mixed disease, etc., as well as by the abnormal presence of autoantibodies, have been reported.⁽¹³⁻¹⁶⁾ The joint inflammatory process of RA is triggered by cytokines produced by activated macrophages. These cytokines, which are clearly implied in RA development and maintenance of inflammatory process, such as IL-1 and TNF, are detected in high concentrations in the synovial membrane, synovial liquid,

and patient serum, a finding that is likely related to the extra-articular manifestations of RA.⁽¹⁷⁾

The immunological mechanisms involved in the immune hyperactivity triggered by the presence of free silica in the human body have yet to be completely elucidated. Experimental studies clearly show that silica triggers an important adjuvant effect in animal immune response, stimulating monocytes and macrophages, with consequent release of cytokines, such as IL-1, granulocyte-macrophage colony-stimulating factor and TNF- α .⁽¹⁸⁾ Additionally, silica stimulates the macrophages to produce reactive oxygen species and release lysosomal proteases. Regarding lymphocytes, there is strong evidence that silica does not stimulate these cells directly, but through the macrophage stimulus, connecting the innate immune system (phylogenetically older than the adaptive one, based on the initial macrophage response) with the adaptive branches of the immune system (responsible for humoral and cellular specific responses to antigens), including the activation of dendritic cells, which present antigens to CD4 T lymphocytes.⁽¹⁸⁾ Through this connection, the exposure to silica could probably trigger autoimmune responses in genetically predisposed individuals, as clinically occurs in RA, scleroderma, systemic lupus erythematosus, and other collagen-related mixed diseases.

We also emphasize the significantly higher frequency of TB in cases of rheumatoid pneumoconiosis when compared with cases of pneumoconiosis without rheumatoid nodules.⁽²⁾

In reviewing the specialized literature of Brazil, we found no case reports describing the typical radiological and histopathological characteristics of the syndrome, such as those described in this case. One study, carried out in 1981, reported the case of a 61-year-old male patient, a stone cutter, with joint lesions typical of RA and nodular opacities in the middle and upper thirds of both lungs, although without a detailed description of these radiological findings and without histopathological testing.⁽³⁾ Subsequently, another group of authors described a case of subacute silicosis and RA in a 59-year-old male rock driller, although without the chest X-ray characteristics that are typical of the syndrome. A lung biopsy showed nonspecific fibrosis without silicotic or rheumatoid

nodules, and the rheumatoid nodule described was subcutaneous.⁽⁴⁾

From the radiological, histopathological, and exposure history points of view, the clinical case we present here meets all of the criteria established for the diagnosis of Caplan's syndrome. We emphasize the importance of the occupational anamnesis in RA cases with radiological opacities different from the pulmonary alterations that are the most typical of the disease. This case also illustrates the potential of free silica and other mineral dusts to trigger autoimmune diseases.

References

1. Caplan A. Certain unusual radiological appearances in the chest of coal-miners suffering from rheumatoid arthritis. *Thorax*. 1953;8(1):29-37.
2. Honma K, Vallyathan V. Rheumatoid Pneumoconiosis: A comparative study of autopsy cases between Japan and North America. *Ann Occup Hyg*. 2002;46(Suppl 1):265-7.
3. Samara AM, Napoli MD. Síndrome de Caplan e po de pedra. *Rev Bras Reumatol*. 1981;21(6):193-5.
4. Franco CA, Suzuki I, Madi K, Bethlem NM. Síndrome de Caplan: relato de caso. *J Pneumol*. 1986;12(1):31-5.
5. Caplan A. Rheumatoid pneumoconiosis syndrome. *Med Lav*. 1965;56(6):494-9.
6. Colinet E. Evolutive chronic polyarthritis and pulmonary silicosis [Article in Undetermined Language]. *Acta Physiother Rheumatol Belg*. 1953;8(2):37-41.
7. Clerens J. Silicose pulmonaire et rhumatisme ou syndrome de Colinet-Caplan. *Arch Belg Med Soc*. 1953;11(10):336-42.
8. Gough J, Rivers D, Seal RM. Pathological studies of modified pneumoconiosis in coal-miners with rheumatoid arthritis; Caplan's syndrome. *Thorax*. 1955;10(1):9-18.
9. Caplan A. Rheumatoid disease and pneumoconiosis (Caplan's syndrome). *Proc R Soc Med*. 1959;52:1111-3.
10. Rickards AG, Barrett GM. Rheumatoid lung changes associated with asbestosis. *Thorax*. 1958;13(3):185-93.
11. Morgan WK. Rheumatoid pneumoconiosis in association with asbestosis. *Thorax*. 1964;19:433-5.
12. Caplan A, Cowen ED, Gough J. Rheumatoid pneumoconiosis in a foundry worker. *Thorax*. 1958;13(3):181-4.
13. Erasmus LD. Scleroderma in goldminers on the Witwatersrand with particular reference to pulmonary manifestations. *S Afr J Lab Clin Med*. 1957;3(3):209-31.
14. Innocencio RM, Sampaio-Barros PD, Capitani EM, Souza ML, Marques-Neto JF. Esclerose sistêmica associada à silicose pulmonar: relato de caso. *Rev Bras Reumatol*. 1998;38(4):249-52.
15. Costallat LT, De Capitani EM, Zambon L. Pulmonary silicosis and systemic lupus erythematosus in men: a report of two cases. *Joint Bone Spine*. 2002;69(1):68-71.
16. Sanchez-Roman J, Wichmann I, Salaberri J, Varela JM, Nuñez-Roldan A. Multiple clinical and biological autoimmune manifestations in 50 workers after occupational exposure to silica. *Ann Rheum Dis*. 1993;52(7):534-8.
17. Arend WP. Physiology of cytokine pathways in rheumatoid arthritis. *Arthritis Rheum*. 2001;45(1):101-6.
18. Pernis B. Silica and the immune system. *Acta Biomed*. 2005;76 Suppl 2:38-44.

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