Case Report

Bilateral nodular lung opacities with a benign course in a young patient

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SUMMARY. Although multinodular disease of the lung is a common characteristic of metastatic lung disease, numerous, non-malignant diseases may also present with a similar radiological picture. This is a report of the first case of a young female patient with nodular sarcoidosis and concurrent bronchiolitis obliterans - organizing pneumonia (BOOP) presenting with multinodular lung disease and following a spontaneous benign course. *Pneumon 2013, 26(3):262-266.*

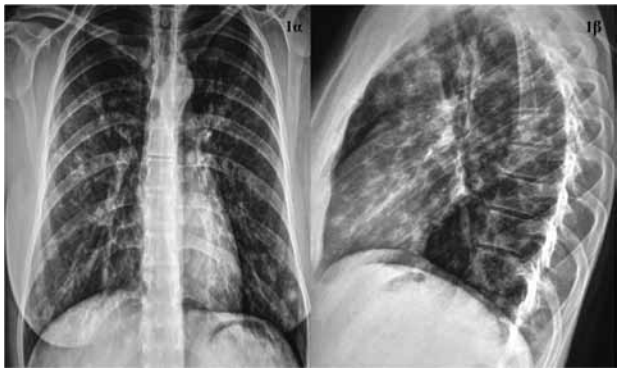
CASE PRESENTATION

A 35 year-old Caucasian female was referred to the outpatient clinic with right-sided pleuritic chest pain and a minor degree of dyspnoea on exertion. She reported no cough, chills, haemoptysis, night sweats or weight loss and had no history of muscle weakness, arthralgia or rash.

She reported previous good health, with the exception of a probable *Mycobacterium Tuberculosis* infection during infancy that was never documented microbiologically. She is a habitual smoker (less than 10 pack-years of smoking). She currently works as an insurance consultant and has no history of exposure to mineral dusts, fumes, mold, silica or asbestos, and denies drug abuse. The family medical history included death of her father from lung cancer.

Physical examination was unremarkable, revealing a healthy, well built young woman with normal BP of 110/70 mm Hg, pulse rate 95 bpm, respiratory rate 18breaths/min, and resting room air pulse oximetry saturation of 97%. The heart sounds were normal and no clubbing, cyanosis, palpable lymphadenopathy, skin lesions or oedema were detected.

Pulmonary function tests (spirometry, CO diffusion test and lung volumes) were within normal limits. Laboratory tests (including various serological tests) were also unremarkable. Chest X-ray (Figures 1a, 1b) revealed bilateral nodular interstitial infiltrates, with ill-defined parenchymal nodules in the middle and lower lung fields. High resolution computed tomography (HRCT) of the chest (Figures 2 a-d) revealed multiple, bilateral nodules, ranging from 3-17 mm in diameter. No lymphadenopathy, parenchymal infiltrates, ground glass opacities, bronchiectasis, or pleural fluid were observed.



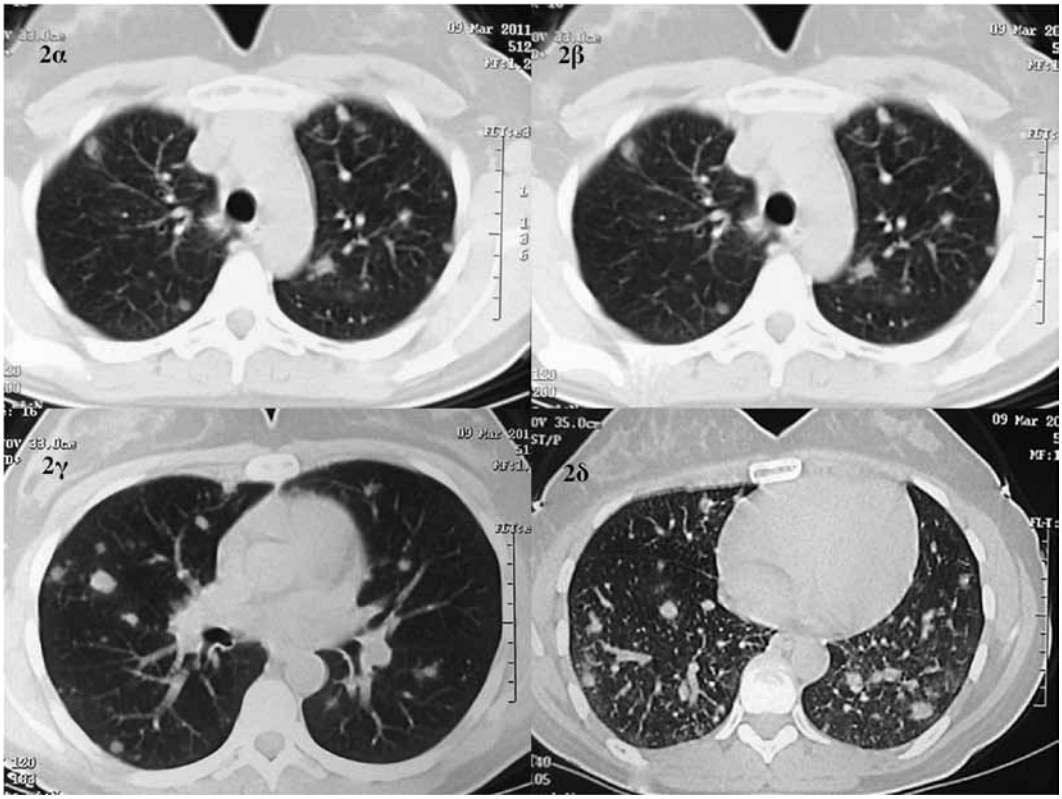
FIGURES 1A-B. Chest X-ray of 35 year-old female showing bilateral nodular interstitial lung infiltrates, with ill-defined parenchymal nodules in the middle and lower lung fields.

The patient underwent bronchoscopy, with bronchoalveolar lavage (BAL) and transbronchial biopsies. BAL cytology was negative for malignancy and cultures for common pathogens were sterile. Direct examination for acid fast bacilli (AFB) was also negative. The BAL cellular subpopulations were characterized by an elevated lymphocyte count (36.3%) and the CD4/CD8 ratio was 1.44. Transbronchial lung biopsy histology revealed non-specific fibrosing alveolitis. Because of these non diagnostic findings open lung biopsy was performed. The histopathological examination revealed well-formed non-caseous epithelioid granulomas of the sarcoid type, surrounded by scattered areas of bronchiolitis obliterans - organizing pneumonia (BOOP) (Figures 3a, 3b).

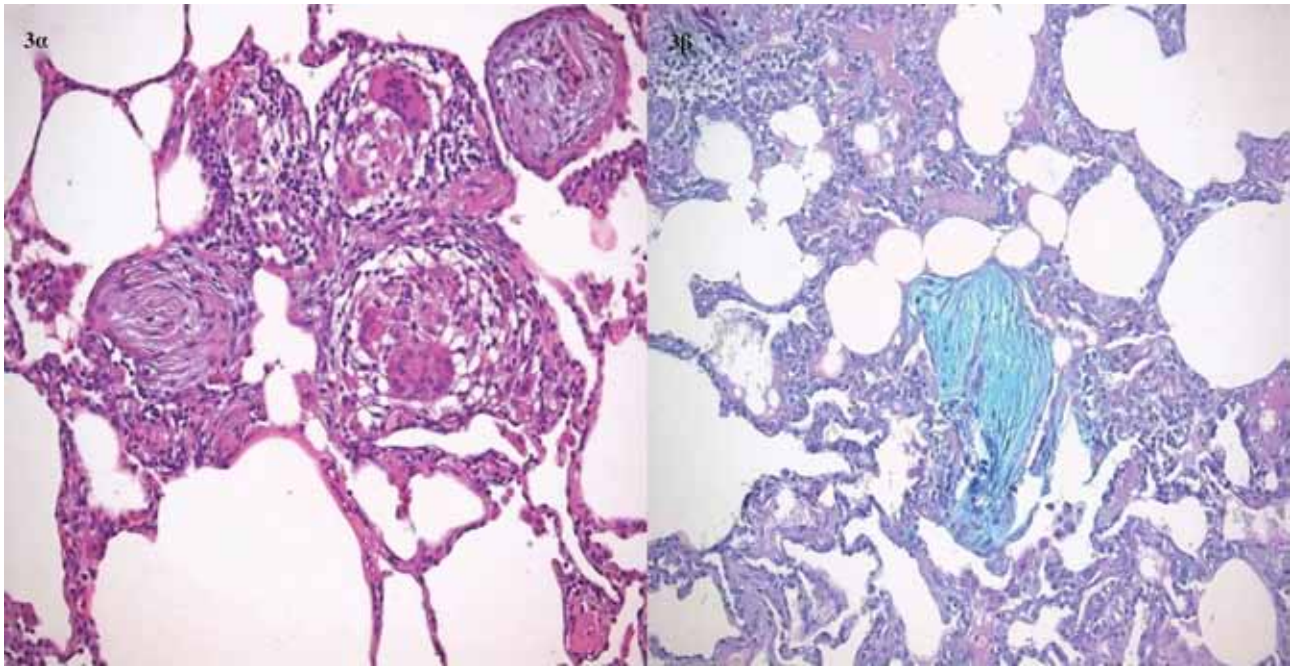
As the patient was completely asymptomatic she was given no treatment but was closely monitored for 6 months, during which period all cultures for tuberculous and non-tuberculous mycobacteria proved negative. Chest CT at 6 months revealed spontaneous remission of almost all the abnormal findings. (Figures 4 a-d).

CLINICAL AND RADIOLOGICAL DISCUSSION

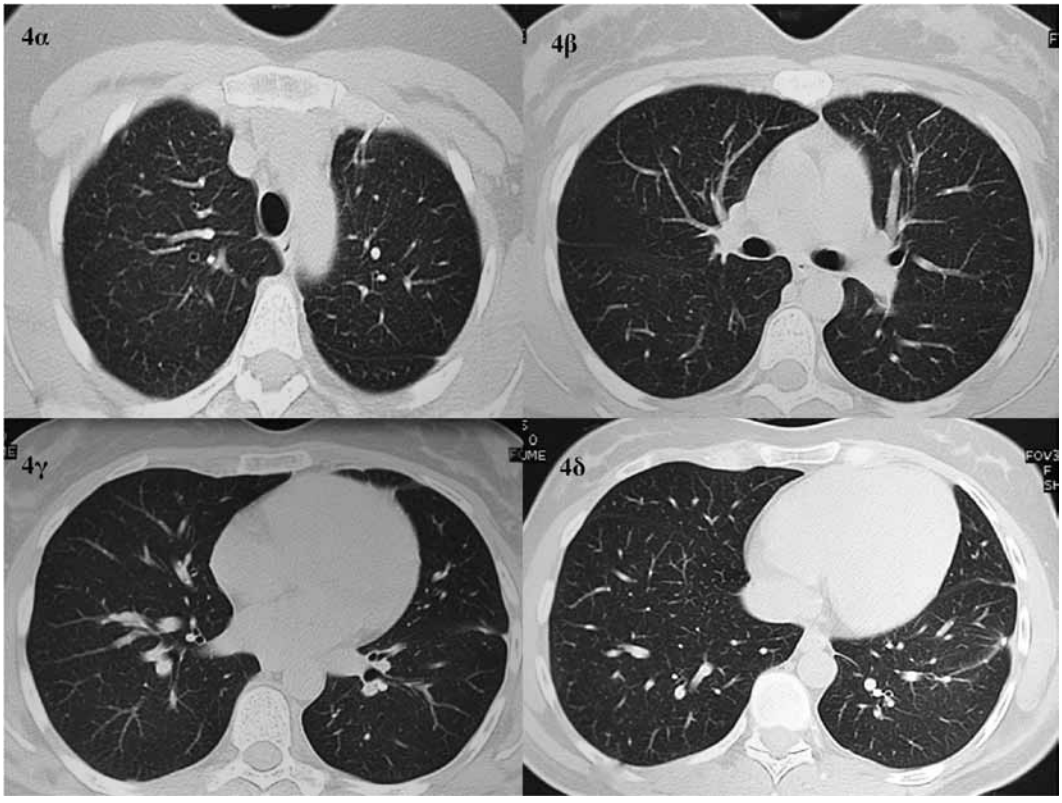
This case study reports a young female patient with multinodular lung disease. The patient presented with unremarkable clinical symptomatology and underwent spontaneous remission of both clinical and radiological findings. Histopathological examination of the lung



FIGURES 2A-D. Chest HRCT in 35 year-old female revealing multiple, bilateral nodules, ranging from 3-17 mm in diameter.



FIGURES 3A-B. Histopathological examination of open lung biopsy: **3a** Granulomas of sarcoid type with fibroblastic polyp (H-E x 200) **3b**. Fibroblastic polyp. (Alcian-Blue x 200).



FIGURES 4A-C. Chest HRCT of 35 year-old female 6 months after initial presentation, revealing spontaneous remission of almost all the abnormal findings shown in Figures 2a-d.

biopsy revealed well-formed non-caseous epithelioid granulomas of the sarcoid type, surrounded by scattered areas of BOOP.

Multinodular disease of the lung is a common characteristic of metastatic lung disease, associated in particular with renal, breast, thyroid and gastrointestinal tract (GI) malignancies[1]. Lymphoma of the lung may also present with bilateral pulmonary nodules.[2,3] Numerous, non-malignant diseases may also present with a similar radiological picture. Researchers have tried to reach a specific diagnosis based on a variety of algorithms[1] HRCT of the lung is a powerful tool, providing detailed depiction of lung nodules[4]. The morphological characteristics and anatomic localization of the nodules are highly suggestive, but not conclusive, of their nature. Nodules that predominate in the lung periphery and lung interstitium are usually associated with sarcoidosis, whereas nodules located at the base of the lung, within the secondary lobule, are associated with diseases of haematogeneous spread[1].

As none of the nodule features studied on CT can reliably differentiate benign from malignant lesions, histopathological examination remains the gold standard for diagnosis.[5] In the present case histopathological examination significantly narrowed the differential diagnosis by excluding malignant disease of the lung, both primary and metastatic. The finding of non-caseous epithelioid granulomas, in association with the sterile cultures for AFB, along with the benign and self limited course of the disease in a young patient was suggestive of sarcoidosis of the nodular type.[6,7] The presence of areas of BOOP in the lung biopsies made the exclusion of granulomatous infections mandatory. BOOP is characterized by intra-alveolar buds of granulation tissue, consisting of intermixed myofibroblasts and connective tissue.[8] Organizing pneumonia (OP) may be cryptogenic or may develop in a secondary form on a background of autoimmune rheumatic processes or drug toxicity, or as a response to infectious agents during the resolving phase of pneumonia. Nodular opacities constitute a common radiological pattern in almost 40% of patients with OP and they frequently undergo spontaneous remission[9-11].

This patient reported no drug abuse and search for infection, including staining for fungi and AFB was negative. Several recent reports have linked *Mycobacterium Avium Complex* (MAC) lung infection from exposure to water containing MAC with the development of a disorder called "hot tub lung"[7,12]. The presenting symptoms of hot tub lung include dyspnoea, cough, low grade fever and hypoxaemia, with diffuse centrilobular nodules and/or ground glass opacities on chest X-ray. The characteristic histopathological findings include a combination of well formed non-necrotizing granulomas and OP. This patient, however, had no history of exposure to hot water aerosols from indoor swimming pools, hot tubs or spas, and culture for MAC was negative.

Based on the above findings the diagnosis of nodular sarcoidosis with concurrent BOOP was made. A few cases of BOOP associated with sarcoidosis have been described in patients who have undergone lung transplantation for end-stage pulmonary disease[13], or in association with alveolar sarcoidosis[14] and in patients with atopy and asthma.[15,16]

CONCLUSION

The radiological pattern of multinodular lung disease embraces a wide range of malignant and benign clinical entities. Sarcoidosis of the nodular type often presents with vague symptomatology and may mimic metastatic disease. Histopathological examination remains the gold standard for diagnosis, since there is no other specific diagnostic feature that excludes malignancy. Hypersensitivity reactions to infectious and non infectious agents should be excluded and appropriate treatment should be initiated accordingly. To the knowledge of the authors, this is the first case of concurrent BOOP and sarcoidosis with spontaneous remission.

"Conflict of Interest: None"

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