Case report

A 27 year old woman was admitted to our hospital with a history of a nonproductive cough and breathing-dependent chest pain. The symptoms were manifested after a common cold a few weeks earlier. No fever or loss of body weight was noted. The patient’s medical history was remarkable for insulin-dependent diabetes mellitus of 6 yrs duration. She had never smoked.

On physical examination, the patient had a normal heart rate and blood pressure. Chest examination revealed normal breathing sounds, and findings on cardiac examination were normal. In fact, no abnormalities were found.

Laboratory evaluation, including kidney function and different serological tests, was within normal limits: angiotensin-converting enzyme (ACE) 11.6 nmol·min⁻¹ (normal level 7–20 nmol·min⁻¹), rheumatoid arthritis haemagglutination (RAHA) <40 (0–40), L-antistreptolysine titre (AST) 40 IE·ml⁻¹ (normal level 0–299 IE·ml⁻¹), negative values of antinuclear factors (ANF), anti-double-stranded deoxyribonucleic acid (anti-dsDNA), antineutrophil cytoplasmic antibodies (ANCA) and treponema pallidum haemagglutination (TPHA). Tuberculin reaction was negative. Blood gas analysis revealed normoxaemia and normocapnia. An electrocardiogram was unremarkable. The chest radiograph and computed tomograph (CT), are shown in figures 1 and 2, respectively.

In the differential diagnosis, a disseminated malignant process was considered. Extensive evaluation including; thyroid scan, skeletal scan and mammography, revealed no abnormalities.

However, CT scan of the abdomen showed an enlarged uterus and irregular thickening of the uterosacral ligaments. A subsequent endometrial curettage showed no histological abnormalities. On laparoscopy, biopsies were taken of tiny white tumours present on the right ligamentum latum and liver surface (fig. 3a). CT guided biopsy of two peripheral pulmonary nodules was not diagnostic. A videothoracoscopic lung biopsy was performed (fig. 3b and c).
BEFORE TURNING THE PAGE: INTERPRET THE CHEST RADIOGRAPH, COMPUTED TOMOGRAPHY AND BIOPSY SPECIMENS. SUGGEST A DIAGNOSIS AND TREATMENT.
**Interpretation of chest radiograph**

The chest radiograph (fig. 1) shows multiple bilateral well-defined pulmonary nodules, especially in the lower lung zones. There is no hilar or mediastinal lymphadenopathy, or pleural effusion.

**Interpretation of the computed tomography**

The CT section through the base of the lungs (fig. 2) shows multiple pulmonary nodules of various sizes.

**Interpretation of the biopsies**

The laparoscopic biopsy specimen of the right ligamentum latum (fig. 3a) shows a granulomatous infiltrate, with central necrosis and peripheral palisading of epithelioid nuclei. The videothoracoscopic lung biopsy (fig. 3b) reveals a necrotizing granulomatous process; and (fig. 3c) obliteration of the lumen of small muscular arteries by a mononuclear infiltrate.

Immunohistochemical staining was negative for ACE, and CD4/CD8 ratio in the lung tissue was within the normal range.

In the differential diagnosis of the present case, granulomatous lung disorders or necrotizing sarcoid granulomatosis, Wegener's disease and necrobiotic granulomas were considered. Because of the absence of kidney function disturbances, synovitis and negative immunological laboratory results, a diagnosis of necrotizing sarcoid granulomatosis was made.

**DIAGNOSIS: "necrotizing sarcoid granulomatosis"**

**Clinical course**

Treatment was initiated with oral prednisone, 60 mg-day⁻¹. Within 6 months all pulmonary nodules decreased in size or resolved.

**Discussion**

Necrotizing sarcoid granulomatosis (NSG) is a rare disease, with rather aspecific clinical symptoms of fatigue, dry cough and chest pain [1]. Most patients are middle-aged, with a varying female predominance [2–4]. The exact aetiology of the disease is unknown, although a hypersensitivity reaction to aspergillus [3], or an (unidentified) micro-organism [4], is suggested.

On radiographic examination of the chest, a solitary nodule suggesting a carcinoma may be found, but more often multiple nodular lesions are present, sometimes associated with pleural effusion [3]; hilar lymph node involvement is uncommon. Other granulomatous lung disorders, such as the classical and limited Wegener's granulomatosis, lymphomatoid granulomatosis, Churg-Strauss syndrome, and bronchocentric granulomatosis have to be excluded. The diagnosis is made by thorough histological examination of lung tissue. When histological confirmation cannot be obtained in the case of a solitary nodule, surgical excision should be considered.

Microscopic hallmarks of NSG are necrotizing angiocentrically confluent granulomas, with epithelioid and giant cells and a focal destructive vasculitis of veins and arteries of small-to-medium size [4]. Whether NSG is a sarcoid reaction with vasculitis and necrosis, or a vasculitis with sarcoid reaction, remains unclear [1, 5, 6].

NSG is a quite distinct clinical entity from sarcoidosis. T-cell hypoactivity, B-cell hyperactivity, cutaneous anergy, impaired cellular defence, elevated levels of immunoglobulins G, M and A (IgG, IgM and IgA) and, sometimes, presence of circulating immune complexes during active disease and elevated ACE levels can be found in sarcoidosis [7–9]. In NSG there is a normal T- and B-cell activity and a normal level of ACE in serum and tissue [6, 10]. Cutaneous anergy and elevated immunoglobulin levels in the absence of circulating immune complexes can be found in NSG. Furthermore, massive necrosis and vasculitis, which are typical findings in NSG, are very uncommon in sarcoidosis.

Histologically proven extrapulmonary localization of NSG, as found in our patient in the pelvic area, has been reported only once in previous studies [10]. It is possible that extrapulmonary disease activity has until now been underestimated. The prognosis of the disease is usually favourable, with almost always complete response to corticosteroids [3], although spontaneous regression of the abnormalities has been described [4].

**Keywords:** Chest pain, necrotizing sarcoid granulomatosis, pulmonary nodules.

**References**