Sarcoidosis is a disease of unknown aetiology where non-caseating granulomas form in one or more organs and tissues. The lung and lymphatic systems are most frequently involved, but sarcoidosis may affect any organ. Necrotising sarcoid granuloma (NSG) is an uncommon condition that primarily involves the lung. It is estimated that between 1.6% and 4% of pulmonary sarcoidosis cases present as NSG, which is generally limited to the lung with extrapulmonary involvement being very rare.1

The characteristic pathological features of NSG are confluent granulomas, granulomatous angitis and necrosis within granulomas, varying from tiny foci to large foci of infarct-like necrosis. Granulomatous infection, especially tuberculosis, should be excluded before making a diagnosis of NSG. We describe one of the very few reported cases of NSG with pulmonary and extrapulmonary involvement.

CASE PRESENTATION
A 58-year-old Iranian female was referred to the outpatient clinic with a 5-month history of worsening non-productive cough, night sweats, low-grade fever and a 6-kg weight loss. Her medical history revealed diabetes mellitus, which was controlled with glybenclamid. There was no family history of lung disease. The patient was a housewife, who did not smoke and did not have a household pet. On physical examination, she appeared in relatively good physical condition, with mild fever (38°C) but no abnormal clinical symptoms. Blood pressure was 140/85 mm Hg. A normal breathing rhythm was observed. Abdominal examination showed mild hepatosplenomegaly. The extremities did not reveal cyanosis or clubbing and there were no skin lesions. Neurological examination was also normal.

INVESTIGATIONS
Laboratory findings showed serum glutamic oxaloacetic transaminase 85 mg/dl, serum glutamate pyruvate transaminase 90 mg/dl, alkaline phosphatase 500, and erythrocyte sedimentation rate 85 mm/h. White blood cell count was 6.4×10^9/L, haemoglobin 10 mmol/l and platelet count 300×10^9/L. Eosinophilia was not found. Serum calcium was 10 and ACE concentration was normal. Serum protein electrophoresis was within normal limits. Antineutrophil cytoplasmic antibodies (ANCA) and anti-DNA antibodies were not detected. Chest radiography and thorax CT scan showed diffuse bilateral pulmonary nodules, especially around bronchovascular bundles, and small mediastinal lymphadenopathies (figure 1). Pulmonary function tests showed a mild restrictive pattern. Abdominal sonography revealed mild hepatosplenomegaly. A purified protein derivative test was negative. Fibrotic bronchoscopy with bronchoalveolar lavage (BAL) and a transbronchial lung biopsy showed no endobronchial abnormality. Acid fast bacilli were not found in the BAL fluid but a specimen was sent for mycobacterial culture. Histopathological analysis of the biopsies revealed mild chronic non-specific inflammation. The patient then underwent liver biopsy. Histopathological evaluation of the liver specimen showed liver tissue with chronic granulomatous inflammation containing multi-nuclear giant cells of the Langerhans and foreign body type. No acid fast bacilli were found.
bacilli or necrosis were observed. At this point, the differential diagnosis included tuberculosis, sarcoidosis or other granulomatous diseases and Hodgkin’s lymphoma. The result of the mycobacterial culture was negative and as the patient had a normal ACE level, splenectomy was carried out in order to obtain a definite diagnosis and especially to rule out Hodgkin’s lymphoma. On gross examination, small and large series of confluent whitish nodules extensively replacing the splenic parenchyma were observed. Routinely processed sections revealed splenic tissue heavily affected with multiple granulomas. Large multi-nucleated giant cells were distributed in the immediate vicinity of these granulomatous areas. There was extensive central necrosis, which was infarct-like and in some areas looked caseous (figure 2). In view of the clinicoradiological features, the patient’s ethnic background and the presence of chronic necrotising granulomatous inflammation in the splenectomy material, a diagnosis of tuberculosis was made.

DIFFERENTIAL DIAGNOSIS
Granuloma formation is a non-specific immunological response, which can be triggered by a wide range of infections, chemicals, enzyme defects, neoplasms, allergens and other conditions.

TREATMENT
The patient was treated with 300 mg isoniazide, 600 mg rifampicin, 1500 mg pyrazinamide and 800 mg ethambutol daily for 6 months. During this period the patient was carefully followed, but as no significant changes were observed, mycobacterial infection was ruled out. After the patient’s history, chest x-ray, liver and spleen specimens were reviewed, the diagnosis was changed to sarcoidosis with necrosis of the granulomas. The patient was treated with prednisone 30 mg/day for 6 weeks, and a remarkable improvement was achieved. The rapid clinical response led to the final diagnosis of NSG.

OUTCOME AND FOLLOW-UP
After 1-year follow-up the patient is in good condition, her erythrocyte sedimentation rate is 25 mm/h and her thorax CT scan shows no evidence of residual disease (figure 3).

DISCUSSION
Sarcoidosis is a variable multi-system disorder characterised histologically by the presence of non-caseating granulomas in affected tissues. The aetiology of sarcoidosis remains unclear. Sarcoidosis has an uneven distribution, with high prevalence rates in European countries. Pathological diagnosis of sarcoidosis relies heavily on the exclusion of other causes of non-necrotising granulomas. Granuloma formation is a non-specific immunological response which can be triggered by a wide range of infections, chemicals, enzyme defects, neoplasms, allergens and other conditions. 2 NSG is a rare and still poorly understood variant of sarcoidosis. 3 A survey of the literature shows that this disorder is uncommon. 4 – 7 In 1973, Liebow 4 made the first reference to a disease characterised by sarcoid-like granulomas with vasculitis and necrosis when describing his classification of pulmonary angitis and granulomatosis not caused by known infectious agents or associated with rheumatoid disease. He called this disease ‘necrotising sarcoid granulomatosis’ and initiated the debate as to whether the disease represented necrotising angitis with a sarcoid reaction or sarcoidosis with necrosis of the granulomas and vessels. NSG is diagnosed on the basis of pathological features and shares common histological and clinical patterns with sarcoidosis. Clinical features include a subacute onset of fever, night sweats, cough, pleuretic chest pain, dyspnoea and malaise. The disease usually occurs in the fourth to sixth decades of life and mostly affects women. As previously noted, most patients experience pulmonary symptoms with a small percentage of cases being described with extra-pulmonary involvement, which most commonly affects the eyes and central nervous system. 1 Our patient was a 58-year-old Iranian woman with a non-productive cough, night sweats, low-grade fever and weight loss. In addition, she had hepatosplenomegaly and abnormal liver function tests. Multiple pulmonary nodules, with or without hilar node enlargement, are a prominent radiographical feature in NSG. In the present case, chest radiography and thorax CT scan showed diffuse bilateral pulmonary nodules, especially around bronchovascular bundles, and small mediastinal lymphadenopathies.
logical symptoms that mimic tuberculosis. A diagnosis of NSG should be considered in patients with necrotising granulomatous inflammation when bacteriological proof of tuberculosis is lacking. In addition, in contrast to many previous reports, extra-pulmonary manifestations can be found in NSG.

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REFERENCES

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