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## A 49-Year-Old Man with Fever and Chronic Cough

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### WHAT IS YOUR DIAGNOSIS?

A 49 year-old non smoker man from an Iranian rural region residing in Tehran, presented with chronic non-productive cough since 7 months ago. He worked in a dairy farm located in Tehran and had a 7-year history of contact with chemical agents. He had fever and night sweats since 3 months ago with episodes of myalgia and arthralgia and a 10 kg weight loss. He did not give any history of hemoptysis or dyspnea. During this period he was treated with multiple courses of antibiotics including ceftriaxone and azithromycin without any improvement. He was also under a regimen of clonazepam and amitriptyline for a major depressive disorder. On physical examination, his vital signs were stable with no respiratory distress. All physical findings were normal, except for an oral temperature of 38.2°C and end inspiratory crackles in lower lobes of both lungs. Complete blood count revealed a PMN dominant leukocytosis. Blood biochemistry, liver function tests and urinalysis were normal. Erythrocyte sedimentation rate (ESR) for the first hour was 125mm. PPD test was nonreactive. Three consecutive sputum smears and cultures plus sputum polymerase chain reaction (PCR) were all negative for mycobacterium tuberculosis. Severe restrictive pattern was observed in pulmonary function test. Transthoracic echocardiography was reported to be normal. Chest x-ray (Figure 1) and thoracic spiral CT scan (Figure 2) were performed. Ground glass opacity and infiltration in lingula, right middle lobe and both lower lobes with mild cardiomegaly and small sized mediastinal adenopathy were revealed on CT scan. (*Tanaffos 2010; 9(1): 67-69*)



Figure 1. Chest x-ray of the patient.

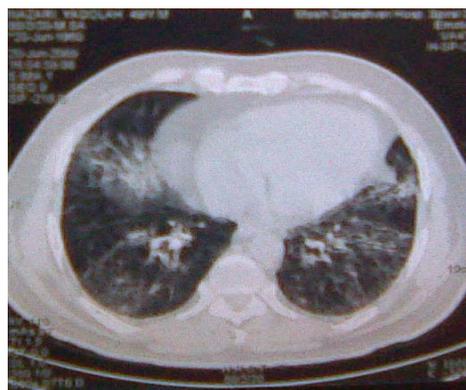


Figure 2. Lung CT-Scan of the patient.

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### Diagnosis: Non Specific Interstitial Pneumonia (NSIP) with organizing pneumonia

Bronchoscopy was performed which revealed normal airways with no endobronchial lesion, and a mixture of macrophages and ciliated columnar cells and PMNs on a hemorrhagic background was seen in the bronchial washing with no evidence of malignancy. Histopathological study of the specimen obtained by transbronchial lung biopsy demonstrated mild focal interstitial thickening and inflammatory cells plus few Masson body formations with no evidence of granuloma which was compatible with organizing pneumonia and interstitial pneumonitis. All rheumatologic tests were normal except for an elevated anti-nuclear antibody (ANA) and anti SS-A (Ro-1) antibody titer. Due to uncertainty of the definite diagnosis, an open lung biopsy was performed and non-specific interstitial pneumonia pattern associated with nodular ossifications and a vaguely formed intra-alveolar granuloma were reported on pathologic examination of the lung tissue (Figure 3).

Considering the existence of myalgia and arthralgia with positive ANA and anti SS-A antibody, a diagnosis of NSIP plus organizing pneumonia in the setting of a probable collagen vascular disease was confirmed.

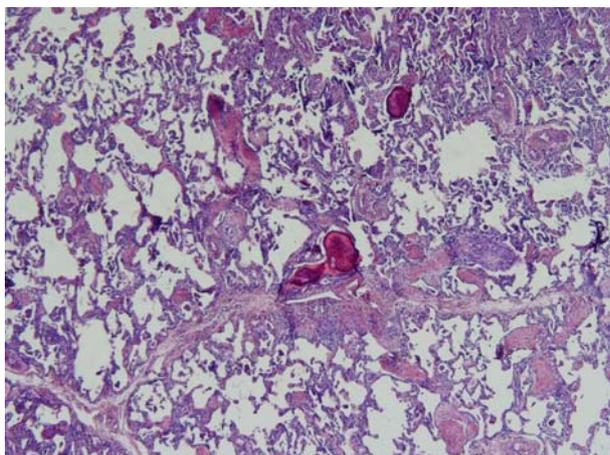


Figure 3. Pathologic examination of the lung tissue.

Nonspecific interstitial pneumonia (NSIP) is a type of idiopathic interstitial pneumonia (IIP). The term NSIP has been associated with many medical conditions, although a causal link has not been identified. An association with AIDS (1) and different medications is reported in several studies (no association with clonazepam or amitriptyline was found in the literature). Exposure to airborne organic antigens (e.g. barns, birds, hot tubs, humidifiers, mold and plastic manufacturing) can also be a probable cause (2). Several connective tissue disorders including polymyositis, dermatomyositis, rheumatoid arthritis, Sjogren's syndrome, and systemic sclerosis have also been associated with NSIP (3-6).

Epithelial injury and disregulated repair likely play a role in the pathogenesis of NSIP. Numerous cytokines (7) along with attenuation of dendritic cells, fibroblasts (8) and lymphocytes in the alveolar septa and bronchoalveolar lavage play an important role in NSIP pathogenesis (9).

The most common symptoms of NSIP are dyspnea and cough that develop subacutely over weeks to months. About one-third of patients have fever or flu-like symptoms. Depending on whether an underlying collagen vascular disease is present, patients may also report dry mouth or eyes, joint or muscle pain, muscle weakness, Raynaud's phenomenon, rash, or other skin changes. The majority of patients have bibasilar crackles, but only 10 to 35 percent have clubbing. Careful attention should be paid to identifying stigmata of collagen vascular disease. Nail bed capillaroscopy may also be helpful if systemic sclerosis is suspected (9).

Chest radiographs typically show increased interstitial markings with a basilar predominance.

The most frequent HRCT findings in NSIP include increased reticular markings, traction bronchiectasis, lobar volume loss, and ground glass opacification (10).

The patient was treated with prednisolone (0.5 mg/kg/day) which resulted in significant clinical amelioration and normalization of the elevated ESR after one week. He is supposed to continue this regimen with gradual tapering for further months.

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