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A CASE OF PULMONARY NOCARDIOSIS

İlkay KESKİNEL*
Müzeyyen ERK*
Tunçalp DEMİR*
Benan MÜSELLİM*
Ayhan YÜCEL**

SUMMARY

A 55-year-old female patient was first admitted to the Rheumatology Department of Cerrahpaşa Faculty of Medicine, where she got the diagnosis of Familial Mediterranean Fever (FMF) and was prescribed oral colchicine in 1984. She was admitted to the hospital with chronic coughing and fever, and Nocardia was detected in bronchial lavage fluid. The patient, who discontinued follow-up, was admitted to our clinic with dyspnea on exertion and fever. Sputum culture revealed *Nocardia asteroides*. Therapy was started, but the patient did not contiue regular treatment and follow-up. Her last CAT scan showed progression of the lesions. Nocardiosis is mentioned to occur concomitantly with diseases like bronchiectasis, chronic granulomatous disease, Cushing's syndrome, systemic lupus erythematosus, Goodpasture's syndrome, however our case is the first in literature to occur concurrently with FMF. and long-term colchicine treatment.

ÖZET

1984 yılında ailevi Akdeniz ateşi tanısı konan ve o dönemden beri sürekli kolşisin tedavisi alan hasta, 1992 yılında inatçı irritatif öksürük ve ateş nedeniyle tetkik edilerek bronş lavajında Nocardia saptanmış. Tedavi önerilen ancak takibe gelmeyen ve ateş, öksürük, balgam yakınmalarının tekrarlaması üzerine kliniğimize başvuran hastanın balgam kültüründe *Nocardia asteroides* üredi. Tedaviye başlanan ancak bir kaç kez tedavi rejimi değiştirilmek zorunda kalınan ve zaman zaman takipten kaybolan hastanın son yapılan toraks BT kontrolünde progresyon saptandı. Bronşektazi, kronik granülomatöz hastalık, Cushing Sendromu, sistemik lupus eritematosus, Goodpasture Sendromu gibi hastalıklarla beraber görüldüğü bildirilen Nokardiyozun ailevi Akdeniz ateşi ve kronik kolşisin kullanımı ile birlikte olduğu bizim olgumuz literatürde ilktir.

INTRODUCTION

Nocardiosis, which has a worldwide distribution, is an infectious process caused by *Nocardia asteroides*, or less frequently by other Nocardia species (1). Members of the genus Nocardia form a complex group of organisms (2). Nine Nocardia species have been listed, but only three are well-documented pathogens of humans: *N. asteroides, N. brasiliensis,* and *N. otitidis-caviarum* (formerly *N. caviae*) (1, 2).

Nocardiae are gram-positive, partially acid-fast, crooked, nonmotile, aerobic rods (1, 3).

Nocardia species are ubiquitous in the environment and may be found in the soil, where they contribute to decay of organic matter (1, 4). These organisms are generally responsible for sporadic pulmonary diseases acquired by inhalation of spores, with secondary localizations in the central nervous system and subcutaneous tissues (1, 4). There is not an absolute evidence of person to person transmission (4). Lungs are considered to be the portal of entry in the majority of cases (5). Although depressed host resistance favors nocardial infection, cases may occur in persons with no known underlying disease (6, 7). Groups at the highest risk include patients with transplantation, immunosuppressive therapy, malignancies, cellular immunity impairment and AIDS (1, 5, 8, 9). Nocardiosis has also been associated with pulmonary alveolar proteinosis, tuberculosis, and chronic granulomatous disease (1, 10, 11).

Lungs are the primary cites of involvement in 65-85% of the cases (12). *N. asteroides* pneumonia infection typically presents as a subacute pneumonia, with symptoms being present for one to several weeks (1). Cough, sputum production (typically thick and purulent), fever, anorexia, weight loss, and malaise are common symptoms, while dyspnea, pleuritic pain, and hemoptysis are less common (1, 12).

One half of cases with pulmonary nocardiosis, has also disease outside the lungs (1). Central nervous system

* Cerrahpaşa Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı, İSTANBUL
** Cerrahpaşa Tıp Fakültesi, Mikrobiyoloji Anabilim Dalı, İSTANBUL

Yazışma Adresi:
Dr. İlkay Keskinel Cerrahpaşa Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı İSTANBUL

involvement is the most common manifestation of disseminated disease (one fourth of all cases with pulmonary nocardiosis) (1).

CASE REPORT

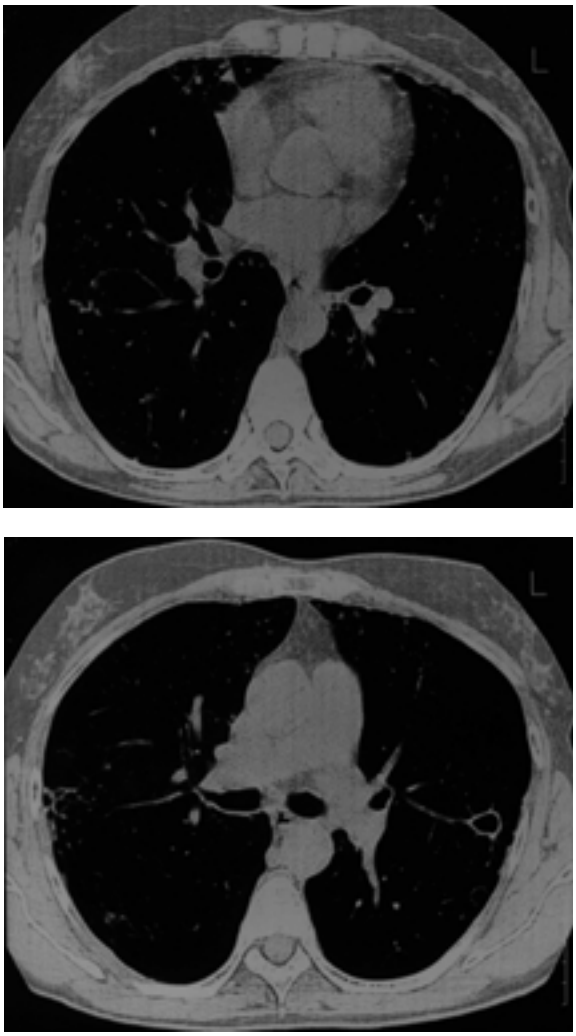
A 55-year-old female patient was first admitted to the Rheumatology Department of Cerrahpaşa Faculty of Medicine, where she got the diagnosis of Familial Mediterranean Fever (FMF) and was prescribed oral colchicine in 1984. She continued colchicine treatment until she presented with chronic, irritative cough and fever in 1992. Nocardia infection was detected then by bronchial lavage and trimethoprim-sulfamethoxazole (TMP-SMX) was given. The patient, who discontinued follow-up, was admitted to our clinic with dyspnea on exertion and fever in 1997. Being diagnosed as bronchial asthma and given bronchodilator therapy, the patient again refused further investigation on nocardiosis, and did not come to the hospital for the controls. The patient who had recurrent symptoms that are mentioned above was admitted to another hospital in March 1999, where she did not accept to be hospitalized and was given aminoglycosides.

In June 1999, the patient presented with coughing, sputum production, malaise, dyspnea, arthralgies, and fever and was hospitalized in our clinic for further investigations.

Her previous history included pulmonary tuberculosis being treated for 6 months when she was 14 years old; FMF diagnosis in 1986; cholecystectomy in 1997 and an operation of the right mamma because of an cystic lesion which was not malignant.

Her family history did not reveal any pathology other than her brother's ischemic heart disease. The patient had a smoking history of 15 pack-years (not smoking for 8 months). She did not drink alcohol, and did not use any other drugs than colchicine 1 mg/day.

Physical examination showed prolonged expiration and rare ronchi upon pulmonary auscultation and apical 2/6 systolic murmur upon cardiovascular auscultation. The hemogram revealed a normal cell count. The sedimentation rate was elevated (61 mm/hr). Biochemical analyses were within normal limits. Pulmonary function tests were as follows: FVC: 2520 mL (%89), FEV_1: 1740 mL (%72), FEV_1/FVC: %79, MMFR: 1,19 L/sn (%38), PEF: 5,71 L/sn (%93). Chest X-rays and the computerized axial tomogram (CT) scans revealed bilateral apical sequelas; cavitary lesions with thin walls having diameters of 11 and 12 millimeters in the apicoposterior segment of the left upper lobe; infected bullae; a nodulary lesion with a diameter of 5 millimeters in the posterior segment of the right upper lobe (granuloma) and mild panaciner emphysema (Pictures 1 and 2). The ECG of the patient showed left bundle block, findings suggesting past anterior myocardial infarction and left ventricular hypertrophy. The echocardiographic findings included mild hypertrophy of the left ventricle, hypokinesia of the interventricular septum; mild mitral regurgitation and diastolic dysfunction of the left ventricle.



Picture 1, 2: CT scan of the patient

As the patient refused bronchoscopic intervention, sputum microbiological examination was performed, and it revealed the presence of *Nocardia asteroides* complex and erythromycin 4x500 mg/day was prescribed, but had to be discontinued because of severe gastrointestinal side effects at the end of the

10th day of treatment. Gentamycin 2x80 mg/day was given instead. The antibiogram revealed that Nocardia was susceptible to gentamycin, amikacin, TMP-SMX, and ceftriaxone, but no significant clinical progression was observed at the end of two months. Following consultation with Department of Infectious Diseases, gentamycin was replaced with amikacin 2x500 mg/day, via intramuscular route. Significant clinical progression was obtained in one week, and amikacin was continued for two months, the patient being externated and, followed closely on renal and hepatic functions. Although the patient was better clinically, the CT scan did not show any regression of the lesions compared to the initiation of treatment. Meanwhile, the patient refused further injections, and was hospitalized for planning new treatment. A combination treatment was chosen this time, consisting of TMP-SMX and grepofloxacine. As the patient described allergic reaction to TMP-SMX, all clinical precautions were taken before the administration of this drug, but no important adverse effects was observed. After one and a half months later, grepofloxacine was stopped being sold, because of serious side effects. Grepofloxacine was replaced with ciprofloxacine 2x500 mg/day. The patient again did not continue outpatient follow-up and it was learned that she did not go on with her treatment. She was readmitted with clinical recurrence in March 2000. As she did not accept to go under bronchoscopic evaluation and could not produce any sputum, levofloxacine 500 mg/day was prescribed empirically. At the end of 6 months, radiological analysis showed progression of the lesions. The patient then started to produce sputum, and her sputum culture is currently been evaluated.

DISCUSSION

Nocardia, a resistant microorganism, used to be classified as a fungal agent, but has recently been regarded as bacteria. It can cause both pulmonary, and extrapulmonary disease (1). Skin involvement and mycetomas are generally seen in normal persons, but bronchopulmonary disease and systemic hematogenous dissemination are observed in immunosuppressed patients with cellular immunity impairment (13).

Our patient has been taking colchicine everyday for 16 years. Colchicine is known to inhibit leukocyte chemotaxis, block lysosomal enzymes, DNA synthesis and cellular proliferation. We propose that, long-term use of colchicine might contribute to recurrent nocardiosis in our patient.

Nocardiosis is mentioned to occur concomitantly with diseases like bronchiectasis, chronic granulomatous disease, Cushing's syndrome, systemic lupus erythematosus, Goodpasture's syndrome (11, 14, 15, 16, 17), however, our case is the first in literature to occur concurrently with FMF.

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