Case report

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Nocardia infection presenting with papulopustular lesions in a patient with pediatric leukemia

Papülopüstüler lezyonlarla başvuran pediatrik lösemi hastasında nokardiya enfeksiyonu

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Abstract

Nocardia is an anaerobic gram-positive bacterium and it is transmitted through inhalation of spores or by direct injection. Nocardia generally does not cause infections in healthy individuals, the agent may become pathogenic in the presence of malignant diseases that impair cellular immunity, and in individuals who are treated with steroids or immunosuppressives. Case reports related to *Nocardia farcinica* infections generally describe older patients. Herein; we report a patient, who were receiving maintance chemotheraphy for acute lympholastic leukemia (ALL), admitted with papulopustular lesions otherwise normal physical findings but later diagnosed pulmonary and cutaneous *Nocardia farcinica* infection. The initiation of empirical therapy before the appearance of clinical signs in these patients can potentially cure Nocardia infections, which are otherwise associated with a high rate of mortality.

Key words: *children, leukemia, nocardia farcinica, papulopustular lesion*

Özet

Nocardia anareobik gram pozitif bir bakteri olup sporların inhalasyonu ya da direk inokulasyonu ile bulaşır. Nocardia enfeksiyonu genellikle sağlıklı kişilerde değil, hücresel immunitenin bozulduğu malign hastalıklarda, steroid ve immunsupresif tedavi alanlarda görülmektedir. Nocardia enfeksiyonları sık görülmemesi nedeni ile daha çok olgu sunumları yada olgu serileri şeklinde rapor edilmektedir. Rapor edilen olgular da daha çok yetişkin olgulardır. Biz burada akut lenfoblastik lösemi tanısı ile idame kemoterapisi almakta iken papülopüstüler lezyonlar ile başvuran, başlangıçta klinik bulguları normal olup, takibinde pulmoner ve kutanöz *Nocardia farcinica* enfeksiyonu tanısı koyulan çocuk hastayı rapor ettik. İmmunsupresif hastalarda Nocardia enfeksiyonunun klinik bulgularının başlangıçta belirgin olmaması nedeni ile bu hastalarda çok dikkatli olunmalıdır. Klinik bulguların tam ortaya çıkması beklenmeden ampirik olarak tedaviye başlanması mortalitesi yüksek olan Nocardia enfeksiyonlarının tedavisini mümkün kılabilmektedir.

Anahtar kelimeler: *çocuk, lösemi, nocardia farcinica, papülopüstüler lezyon*

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Introduction

Nocardia is an anaerobic gram-positive bacterium that belongs to the Actinomycetales group. Soil is the main source of Nocardia, and it is transmitted through inhalation of spores or by direct injection. While Nocardia generally does not cause infections in healthy individuals, the agent may become pathogenic in the presence of malignant diseases that impair cellular immunity, diabetes mellitus, acquired immune deficiency syndrome and in individuals who are treated with steroids or immunosuppressives. As Nocardia infections are uncommon, their coverage in the literature is mostly in the form of case reports or case series, and previously reported cases mostly describe adult patients.[1-3]

In this study, we present a report on a pediatric patient who referred with cutaneous and oral mucosal lesions with abdominal pain who had normal initial clinical findings but was diagnosed with *Nocardia farcinica* infection during the follow-up period while undergoing maintenance chemotherapy following a diagnosis of ALL.

Case report

The 15-year-old male patient, who had been followed-up with a diagnosis of high-risk pre B-cell ALL, referred to our clinic with left-side abdominal pain four days after receiving of maintenance chemotherapy.[4] The patient's white blood cell count was 950/mm^3, and his absolute neutrophil count was 550. His body temperature was 36.6°C, and his respiratory rate was 19/minute. A physical examination revealed a well-demarcated impetiginized crusted ulcer promptly evolved from papulopustular lesions at the philtrum and mucosal erosions (Fig.1), while respiratory sounds were bilaterally equal on lung auscultation, and other system examinations were normal. Due to neutropenia, the patient was started on piperacillin tazobactam (100 mg/kg/dose in three doses) therapy and was re-evaluated 12 hours later when a lung X-ray showed left paracardiac infiltration. Vancomycin (40 mg/kg/day, in four doses) was added to the treatment regimen. His body temperature started to increase thereafter and reached its highest level of

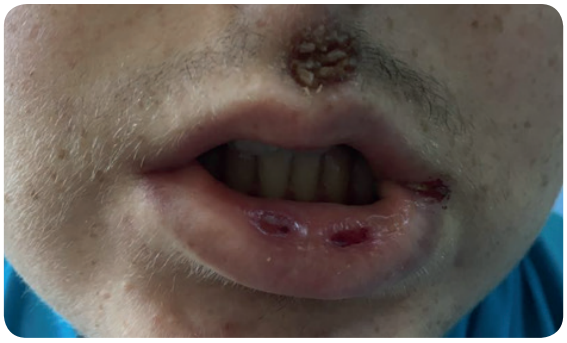

Fig. 1. A well-demarcated impetiginized crusted ulcer promptly evolved from papulopustular lesions at the philtrum and mucosal erosions

39.4°C 24 hours after admission. Throat swab cultures turned out negative for Influenza A,B, Parainfluenza, *Hemophilus influenza, Bordetella Pertussis*, Adenovirus, Mycoplasma IgM, Galactomannan and Legionella antigens. Thoracic ultrasonography (USG) was performed of fluid was identified in the left costodiaphragmatic sinus. A thoracentesis was performed to obtain a sample of the fluid. Due to the persistently elevated fever and the increased pleural effusion on the second day of hospitalization, clarithromycin (20 mg/kg/d) and amikacin (15 mg/kg/d) were added to the treatment regimen, and tazocin therapy was switched with meropenem (90 mg/kg/d). On the fifth day of hospitalization, a *Nocardia farcinica* growth was detected in the culture of the thoracentesis fluid, and intravenous trimethoprim/sulfamethoxazole (TSM) therapy was initiated at a dose of 20 mg/kg/day. Vancomycin and clarithromycin therapies were stopped on the 10th day, and amikacin was stopped on the 15th day. A thoracic CT obtained on the seventh day of hospitalization revealed a cavitary nodular lesion measuring 13x10 mm in the apicoposterior segment of the left lung upper lobe, a left-sided massive pleural effusion and almost total atelectasis of the left lung lower lobe (Fig. 2). The patient's cranial MRI was normal. His body temperature returned to normal levels on the 13th day of hospitalization. Pleural fluid culture was negative on the 24th day of the treatment. The thorax tube was removed on the 37th day of hospitalization. A check-up thoracic CT obtained by the 6th mouth was normal. As his overall status was good during the fol-

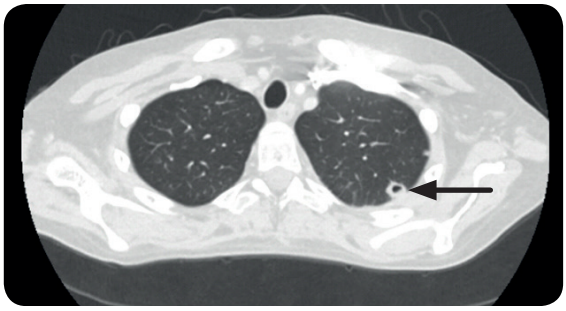

Fig. 2. A thoracic CT, a cavitary nodular lesion measuring 13x10 mm in the apicoposterior segment of the left lung upper lobe

low-up, meropenem treatment was stopped on the 80th day. Thus, TSM treatment was stopped after almost the sixth month of therapy.

Discussion

Nocardia causes pulmonary, cutaneous and disseminated infections, and *Nocardia farcinica* is highly pathogenic and resistant to several antibiotics and could become life-threatening in the presence of systemic involvement. Nocardia can be isolated in microbiological cultures of sputum, bronchoalveolar lavage fluid, or abscess or blood samples, or can be identified by genotypic studies. Although it has specific treatment, it is an infection with high mortality due to difficulties in diagnosis .[3,5-7]

Cough, fever and dyspnea are the most common symptoms in pulmonary nocardiasis. At the same time, alveolary concolidation, cavitation and pleural fluid are common in radiological findings.[1,5]

Wang et al.[5] reported 132 cancer patients who had Nocardia infections. The mean age of the patient group was 59 years, and of these patients, 35% had undergone stem-cell transplants. The most common finding in their patient group was pulmonary infiltrates. In addition, 20% of the patients experienced rapid respiration, coughing and fever, 12% had deep and soft tissue infections, and 3.7% developed brain abscesses. *Nocardia farcinica* species were isolated in 19 patients.[5]

Cutaneous and subcutaneous nocardia infections can be developed as primer inoculation or seconder dissemination. Primary cutaneous nocardiosis present as one of three clinical patterns; lymphocutaneous, mycetoma, and superficial skin infection. Superficial cutaneous lesions include ulcers, papules, pustules, plaques, nodules, diffuse erythema, and cellulitis leading abscess formation. Secondary cutaneous involvement in disseminated Nocardia infection seen as abscess, nodules and cellulitis.[7,8] In our patient, there were skin and pulmonary involvement. The patient had a well-demarcated impetiginized crusted ulcer promptly evolved from papulopustular lesions at the philtrum and mucosal erosions. We thought that *Nocardia farcinica* infection may have spread by inhalation through the skin and cause pulmonary involvement.

Nocardia farcinica is resistant to many beta-lactam antibiotics and amikacin, and is generally treated with a combination of TSM, imipenem-cilastatin, moxifloxacin, amikacin, linezolid or ciprofloxacin. The duration of treatment varies from 6 to 12 months, depending on the presence of cranial involvement.[1] Our patient was treated initially with a triple combination of TSM, carbapenem and amikacin, and then, the amikacin was stopped and treatment was continued with the double combination.

Case reports related to *Nocardia farcinica* infections generally describe older patients. In the present report, we describe a case of pulmonary and cutaneous *Nocardia farcinica* infection in a 15-year-old ALL patient. As Nocardia infections initially have nonspecific clinical signs, attention must be paid to rule out this infection, particularly in immunosuppressed patients. The initiation of empirical therapy before the appearance of clinical signs in these patients can potentially cure Nocardia infections, which are otherwise associated with a high rate of mortality.

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