Clinical picture

Cellulitis in a post-kidney transplant patient—more than meets the eye

A 47-year-old woman was hospitalized due to fever, shortness of breath and anterior thoracic chest pain. She had undergone an uneventful cadaveric kidney transplantation 2 months prior to her referral to hospital.

The patient’s past medical history was significant for several years of hemodialysis for an undiagnosed end-stage renal disease, hypertension and hyperlipidemia. Her medications included tacrolimus, prednisone, mycophenolate mofetil, valgancyclovir, sulfamethoxazole/trimethoprim, amlodipine, doxazocin, metoprolol, simvastatin, papaverine and lansoprazole.

On physical examination she had decreased airflow over her left lower lung. Chest radiography demonstrated a consolidation in the left lower lung field and the right upper lobe (Figure 1A). A computer tomography scan showed multiple lesions in both lungs, some of them with cavitary centers. The patient had no productive cough and did not produce sputum for analysis and cultures. Echocardiography was normal. The patient was treated with oral azithromycin and intravenous cefuroxime antibiotics. Within 2 days, the fever and shortness of breath abated and the patient was discharged. Given the severity of the imaging findings, a 3-week course of intravenous ceftriaxone antibiotics was recommended. However, the patient stopped this treatment and follow-up after 10 days.

Three weeks later, the patient returned because of pain, edema and erythema of her old arterio-venous shunt in the right arm that started shortly after stopping the antibiotics. Her left arm was swollen, painful and erythematosus (Figure 1B). The radial pulse was palpated and there was no arthritis. Laboratory results showed mild leukocytosis. The erythrocyte sedimentation rate was 100 mm/h and the C-reactive protein was 7.87 mg/dl (normal range <1 mg/dl). A venous duplex study of her right arm did not demonstrate a deep vein thrombosis. The patient was admitted with the diagnosis of cellulitis and started on cefazolin antibiotic therapy.

On repeat physical examination several additional findings were noticed. There were two furuncles, one on her right cheek, near her upper lip and the other on the lateral aspect of her left wrist (Figure 1C and D). Additionally, a 7 cm subcutaneous mass was found on the medial aspect of her left breast. The chest radiograph was identical to the previous one performed several weeks previously. However, computer tomography of the thorax revealed a slight enlargement of the previous pulmonary nodules and new a subcutaneous mass in the left breast (Figure 1E). Mammography also demonstrated a hyper-dense mass suspected of being either a malignancy, an organized hematoma or an abscess.

Needle aspirations were performed from the furuncle on the left wrist and from the left breast mass. From both, Nocardia asteroides complex was cultured (Figure 1F).

The nocardiaceae were originally discovered by a veterinarian named Edmond Nocard in 1888, who isolated the organism from cattle suffering from lymphadenitis (farcy). In 1889, the bacteria was named Nocardia farcinica. The original strains from this discovery, kept and later shipped to the USA, were found to include two different organisms. Subsequent typing discovered that one was actually Mycobacteria, while the other was Nocardia. Indeed, culturing and identification have always posed a challenge to microbiological laboratories. Over the years, there have been taxonomic changes and controversies with regard to the species’ nomenclature. For example, a wide range of antibiotic resistance profiles demonstrated great variability within the strain N. asteroides leading it to be considered a complex of several species, rather than a single one.
Most often, the nocardia cause syndromes which are dependent on the patient’s immune status. Systemic disease is predominantly pulmonary, usually subacute in nature or indolent, progressing over weeks, with thick purulent cough being the predominant feature. Constitutional symptoms may also exist (fever, malaise and weight loss). Of note, 50% of pulmonary Nocardiosis will also have extra-pulmonary manifestations, by either local or hematogenous spread (skin, subcutaneous tissue and central nervous system). Immunocompetent patients present with a predominantly soft tissue skin infection, either a lymphocutaneous infection, a superficial cellulitis or an abscess. The infection can affect the face (most often in children) and lower extremities (adults). Most cases described in the literature are chronic, misdiagnosed/undiagnosed cases with development of drainage sinuses and lymphatic insufficiency.

The treatment of Nocardia infections have dramatically changed since the antibiotic era began. The disease was associated with 100% mortality before antibiotics were available. Sulfonamides decreased mortality rates to 50% among patients with central nervous system involvement.

Cure rates were very high among patients with soft tissue infections or solitary lung infections. Still this treatment is far from satisfactory. For example, a report of patients with acquired immune-deficiency syndrome diagnosed with nocardia infection found that of 20 patients treated with sulfamethoxazole-trimethoprim, 18 died from the infection. Studies assessing sulfamethoxazole/trimethoprim prophylaxis to prevent Pneumocystis jiroveci (carinii) pneumonia found no beneficial effect on the incidence of nocardia infection. The use of sulfamethoxazole/trimethoprim is the result of it being the most common available sulfonamide compound. The trimethoprim has no additional effect. Therefore, additional antibiotic therapy is recommended and antibiotic susceptibility testing required for all laboratory Nocardia isolates. A prudent empirical approach will include sulfamethoxazole, amikacin and a β-lactam.

Our patient was immediately begun on sulfamethoxazole/trimethoprim treatment with immediate improvement in her arm pain and a prominent decrease in the size of the left breast abscess. She was additionally given minocycline treatment. She was continued on both medications for 12 months. During that period she experienced no relapses. Chest imaging after cessation of medication demonstrated almost complete disappearance of the lung findings.

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**Figure 1.** Chest radiography with a right upper lung lesion and left lung consolidation (A). Right arm cellulitis (B) and two subcutaneous lesions near here right upper lip (C) and in the left arm (D). Computer tomography revealed multiple pulmonary lesions and a breast mass (arrow), which was palpable (E). Needle aspiration from the left arm and breast lesions yielded pus with Gram positive, filamentous bacteria (F) identified as *N. asteroides* complex.