Majocchi's Granuloma After Kidney Transplantation

Michael Burg,[1] Dagmar Jaekel,[1] Eva Kiss,[2] Volker Kliem[1]

Mycosis may follow an atypical course in an individual undergoing immunosuppressive therapy. We describe a patient with a fungal infection that was manifested as a bilateral inguinal granuloma. Owing to suspected inguinal lymphadenopathy characterized by distinct subcutaneous swellings in the groin, a 39-year-old man who had undergone kidney transplantation 14 years earlier was admitted to the Nephrologisches Zentrum in Hann. Muenden, Germany. The results of a clinical examination revealed bilateral, soft, partly fluctuant, indolent swellings in the groin as well as onychomycosis of the right great toe. An ultrasonographic scan showed bilateral hypoechogenic lesions (≤ 1.5 cm) in the groin. The lesions were surgically removed, and the results of histologic examination revealed severe granulating pseudocystic inflammation with a distinct foreign body reaction. Dermatophytes of the species *Trichophyton rubrum* were detected microbiologically. After the lesions had been resected, the wound healed without complications. Immunosuppressive treatment with tacrolimus 8 mg/d and steroids 7.5 mg/d was not changed. Local antimycotic treatment of the onychomycosis with ciclopirox cream was initiated. At the patient's 2-year follow-up examination, there was no evidence of recurrence. In transplant recipients, local fungal infections should be treated as a matter of course, because dermatophytosis is present in almost every other such patient. In patients with a suspicious inguinal lesion, an atypical form of dermatophytosis must be considered. *T rubrum*, the most frequently occurring dermatophyte, causes 80% of the dermatophytosis that develops in immunosuppressed patients.

Key words: *Dermatophytosis, Renal transplantation, Lymph node*

Case Report

A 39-year-old man was admitted to the Nephrologisches Zentrum in Hann. Muenden, Germany, because of painless bilateral swellings in his groin that had increased in size during the prior 6 months. There were no other complaints. No B symptoms were present. The patient had undergone kidney transplantation with limited graft function 14 years earlier and since that time had received combined immunosuppressive treatment with tacrolimus 8 mg/d and prednisolone 7.5 mg/d.

The patient was in good general health. His cardiopulmonary function was within normal limits, and his blood pressure value was approximately 140/100 mm Hg. The lymph nodes in the upper thoracic region were not enlarged; on palpation, the liver and spleen were not enlarged. Distinct, indolent, partly fluctuant inguinal tumors could be felt. The skin and external genitals were not irritated, and the results of pathologic testing were unremarkable. Mycosis of the nail of the right great toe and dysmelia of the left lower leg were also noted.

The patient's erythrocyte sedimentation rate was 62 mm/h. His C-reactive protein level was within the normal range. A complete blood count revealed macrocytic anemia with a hemoglobin level of 10.7 g/dL and a leukocyte count of 9500 cells/μL. All other values were within the normal range. The patient's T-cell status was within normal limits, and electrophoresis and immunoelectrophoresis revealed nothing irregular. His whole-blood trough level of tacrolimus was 6 ng/mL, which is within the target therapeutic range. His serum creatinine and blood urea nitrogen levels were significantly increased (450 μmol/L and 17.2 mmol/L, respectively). His liver

[1]*Department of Internal Medicine and Nephrology, Nephrologisches Zentrum Niedersachsen, Hann. Muenden, Germany,* [2]*Department of Cellular and Molecular Pathology, Deutsches Krebsforschungsinstitut, Heidelberg, Germany*

Address reprint requests to: *Michael Burg, MD, Abt. Innere Medizin/Nephrologie, Nephrologisches Zentrum Niedersachsen, Vogelsang 105, 34346 Hann. Muenden, Germany*

***Phone**: 00 49 5541 99 60 **Fax:** 00 49 5541 99 63 15 **E-mail:** m.burg@awogsd.de*

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enzyme levels and coagulation parameters were within the normal range.

Abdominal ultrasonographic and computed tomographic scans revealed no additional abnormalities (eg, there were no indications of lymphoma). Histologic testing of the tissue sample showed a severe, granulating, focal, xanthogranulomatous, pseudocystic inflammation with a distinct foreign body reaction but without lymph node involvement (Figure 1). Intracellular and extracellular fungal hyphae were confirmed by Grocott-Gomori methenamine-silver nitrate stain (Figure 2). Given the preceding data, we identified the fungus as *Trichophyton rubrum*.

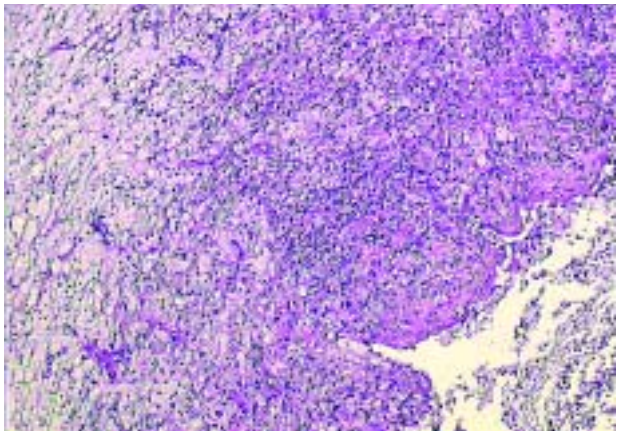

Figure 1. Histologic analysis of the tissue sample shows a severe, granulating, focal, xanthogranulomatous, pseudocystic inflammation with a distinct foreign body reaction but without lymph node involvement (hematoxylin-eosin, original magnification x200).

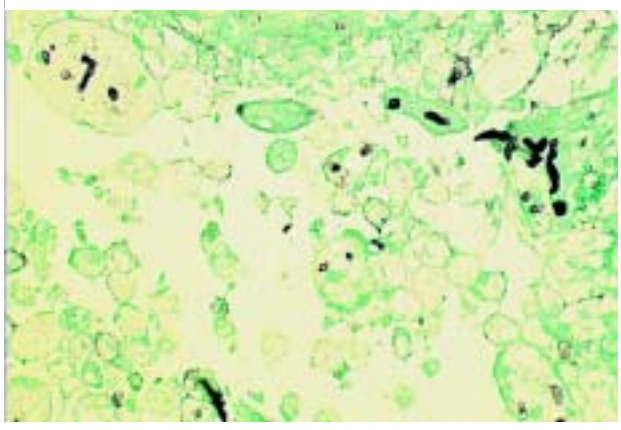

Figure 2. Grocott-Gomori methenamine-silver nitrate stain confirms the presence of intracellular and extracellular fungal hyphae (Grocott-Gomori methenamine-silver nitrate stain, original magnification x400).

The lesions in the right groin, which were characteristic of inguinal lymphoma, were removed. Because no pathogens were found, the granulomas in the left groin were removed as well. The results of microbiologic examination showed dermatophytes of *T rubrum*. Because the patient had no systemic symptoms (eg, fever, night sweats, weight loss) and no granulomatous skin changes were noted, systemic antimycotic treatment was discontinued and local antimycotic treatment with ciclopirox cream twice daily was initiated. At the time of this writing (ie, at the 2-year follow-up examination), the patient remains disease free and exhibits no signs of recurrent disease.

Discussion

Lymphoproliferative disease (ie, malignant neoplasia) and other infectious causes must be considered in immunosuppressed patients presenting with slowly enlarging swellings in the inguinal region. Because of the long-term immunosuppression and the lack of inflammatory indications in our patient, we initially considered the diagnosis of a malignant disease, despite the lack of B symptoms.

Extirpation of the lymph nodes was performed. During surgery, no typical definitive lymph node structures were found. Histologic examination revealed a severe granulating inflammation with a distinct foreign body reaction but without lymph node involvement. Microbiologic evidence of bacteria was found, and the results of fungal cultures confirmed the presence of *T rubrum*, which was identified as the cause of the inflammation. The staining of specific fungal cultures provided histologic evidence of fungal hyphae.

The appearance of a granuloma with concomitant dermatophytes has been described frequently in the literature [1-5]. In our patient, the primary site of the granulomatous inflammation was the groin; this seemed to be consistent with a diagnosis of Majocchi's granuloma. In 1883, Majocchi first described a granulomatous infection caused by dermatophytes [6]. To date, the spectrum of Majocchi's granuloma has not been sufficiently defined, and neither the etiologic organism nor the affected population has been isolated [4]. However, 17 different cases of Majocchi's granuloma have been reported by Smith and colleagues [4].

Majocchi's granuloma may occur in healthy individuals with chronic dermatophytosis and in immunodeficient individuals. Initially, there is physical trauma with irritation of a hair follicle and fungal dermal invasion [4, 5]. In most cases, the cause of the infection can be found in the patient's skin (for example, our patient's onychomycosis of the right great toe). Normally, Majocchi's granuloma is manifested as chronic dermatophytosis characterized by purplish papules and nodules [1]. Histologically, the dermatophytes are surrounded by granulomatous and inflammatory infiltrates of neutrophils. The skin often shows interstitial edema and fibrosis; fungal hyphae

can be identified in the stratum corneum [4]. In addition to *T rubrum*, other pathogens (eg, *Trichophyton mentagrophytes, Trichophyton epilans*, or *Microsporum canis*) can cause granuloma. However, there are no typical histologic features of the granuloma caused by each of those infectious organisms, nor have any typical effects on the patient's immune functioning been elucidated [4]. In our patient, although no skin alterations in the area of the granuloma were seen, Majocchi's disease associated with *T rubrum* could be added to this symptom complex.

Approximately 40% of renal transplant recipients are predisposed to the development of dermatophytosis [1, 3]. As a rule, infection with the most frequently isolated pathogen, *T rubrum*, is noted in addition to tinea or onychomycosis [1, 3, 7]; however, our patient demonstrated an atypical presentation of granuloma.

An increased risk of infection exists in all patients undergoing immunosuppressive treatment (which leads to a reduction of cellular immunity). This appears to be one cause of Majocchi's granuloma [4]. In some patients, therapy for Majocchi's disease has consisted of a reduction in the patient's existing immunosuppressive regimen and in systemic antifungal treatment. However, patients treated in this manner have shown signs of systemic infection and/or malignant disease [1, 5]. In our patient, there were no indications of a malignant disease. Therefore, we decided to maintain his immunosuppressive regimen on strict follow-up, and we refrained from prescribing systemic antifungal treatment.

Conclusions

Local fungal infections in transplant recipients should be treated. In patients with a suspicious inguinal lesion, an atypical form of dermatophytosis must be considered. *T rubrum*, the most frequently occurring dermatophyte, is responsible for 80% of the dermatophytosis seen in immunosuppressed patients.

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