Cushing’s Syndrome Presenting as Disseminated Cutaneous Mycobacterium chelonae Infection

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Mycobacterium chelonae infection has not to our knowledge been reported as a complication of endogenous Cushing’s syndrome. We describe a patient who presented with sporotrichoid M. chelonae infection and olecranon bursitis whose symptoms did not completely resolve until after bilateral adrenalectomy.

Mycobacterium chelonae infection typically causes localized skin lesions, often following penetrating trauma or injections. Disseminated disease usually occurs in patients with significant immune compromise that is most commonly attributable to exogenous steroid use. We describe an unusual case in which the finding of disseminated mycobacteriosis led to the diagnosis of endogenous Cushing’s disease.

Case report. In March 1998, a 66-year-old woman presented to a dermatologist’s office with a 3-month history of violaceous subcutaneous nodules on her left forearm. Three weeks prior to presentation, the nodules had become more prominent and new lesions were noted on the right forearm. A punch biopsy of a nodule was performed and histopathological examination of the specimen revealed acid-fast bacilli (AFB). The patient was referred to our clinic.

The patient denied experiencing fever, chills, or Night sweats but reported having lost 25 pounds during the previous 5 months. The patient reported skin darkening, loss of scalp hair, and hirsutism. She also noted generalized weakness during the previous year. She reported no trauma or puncture wounds to her extremities and denied having travelled recently, having worked in the garden, and having any known tuberculosis exposure or risk factors for HIV infection. She had discarded a fish tank 3 years before presentation.

During the previous 4 months, the patient had been participating in physical therapy for rheumatoid arthritis, which included whirlpool and swimming pool treatments at a local rehabilitation center. Arthritis symptoms had been well controlled with nonsteroid analgesics. She had not received oral steroids or other immunosuppressive agents, but had received 2 intra-articular cortisone injections into her left knee (2 weeks and 1 month prior to the initial visit). She was also taking medication for hypercholesterolemia and for recently diagnosed depression, hypertension, and diabetes mellitus.

Physical examination revealed a woman with a cushingoid appearance, a ruddy face, and dark facial hair. No lymphadenopathy or thyromegaly was found. Prominent supraclavicular fat pads and truncal obesity were noted; however, there were no pink or purple striae on her skin. There were >20 firm, moveable nodules on both forearms, measuring 5–15 mm in diameter. A patient with similar nodules is shown in figure 1. Ballottable fluid and erythema were detected at the left olecranon process. Results of laboratory studies were as follows: WBC count, 13,600 cells/μL (81% neutrophils, 1% band forms, 13% lymphocytes, 1% basophils, 1% metamyelocytes, and 2% myelocytes); platelet count, 405,000 cells/μL; erythrocyte sedimentation rate, 35 mm/h; and serum glucose level, 178 mg/dL. The CD4 cell count was 659 cells/μL (49% of T cells). An afternoon cortisol level determined at a random time was 36.2 μg/dL (normal range, 3–15 μg/dL). Examination of fluid from...
the left olecranon bursa revealed a WBC count of 16,140 cells/μL (81% neutrophils, 11% lymphocytes, and 8% monocytes). Results of routine stains and cultures were negative for fungal pathogens. Modified Kinyoun staining of a second biopsy specimen from a nodule showed AFB (Figure 2).

Because of the temporal association of the symptoms with use of swimming pools, the patient was treated empirically with oral trimethoprim-sulfamethoxazole, 160/800 mg b.i.d., for presumptive Mycobacterium marinum infection. However, cultures of the skin biopsy specimen and of a sample of the bursa fluid yielded growth in <7 days. The isolate was sent to the National Jewish Medical and Research Center (Denver), where it was identified as M. chelonae; the strain was resistant to trimethoprim-sulfamethoxazole, cefoxitin, imipenem, gentamicin, streptomycin, and minocycline, but it was susceptible to azithromycin, clarithromycin, erythromycin, kanamycin, amikacin, tobramycin, ciprofloxacin, and levofloxacin.

The patient’s therapy was changed to oral clarithromycin, 500 mg b.i.d. However, this therapy was poorly tolerated and the patient returned to the clinic with worsening subcutaneous nodules and new right olecranon bursitis. She also had developed Candida esophagitis, which was subsequently treated with fluconazole. Therapy was changed to ciprofloxacin, 500 mg b.i.d., and azithromycin, 500 mg q.d. Moderate improvement was noted within 2 weeks. After 3 months, bursal inflammation had resolved and only 2 nodules remained.

In view of the elevated afternoon cortisol level, an endocrinologic evaluation was conducted. A dexamethasone suppression test revealed a morning cortisol level of 70 μg/dL (normal value, <5 μg/dL). Results of further tests were suggestive of Cushing’s syndrome, yet inconclusive. However, the patient had severe symptomatic steroid myopathy, uncontrolled diabetes, massive mediastinal lipomatosis, and hypertension; therefore, ablative therapy was started with aminoglutethimide and supplemental low-dose hydrocortisone. The patient’s symptoms improved, but she had difficulty tolerating aminoglutethimide and it was discontinued. An additional 24-h urine free-cortisol test demonstrated an elevated cortisol level of 68 μg/24h (normal range, 3–51 μg/24h), a finding consistent with Cushing’s syndrome. Testing of blood samples from the inferior petrosal sinuses revealed elevated levels of adrenocorticotropic hormone (ACTH; 79–89 pg/mL; normal range, 9–52 pg/mL), but despite extensive laboratory testing and radiologic imaging, an ACTH-producing tumor could not be found.

One year after the initial office visit the patient underwent bilateral adrenalectomy. Pathological examination revealed bilateral adrenal hyperplasia. The patient received azithromycin and ciprofloxacin for 2 months after the operation and the subcutaneous nodules and olecranon bursitis resolved completely. The clinical manifestations of Cushing’s syndrome gradually resolved within several months after the adrenalectomy.

Figure 2. Modified Kinyoun stain of a biopsy specimen of a skin nodule showing multiple intracellular acid-fast bacilli and aggregates of mycobacteria within extracellular vacuoles (original magnification, ×400).

One year after treatment with azithromycin and ciprofloxacin was discontinued, there was no evidence of recurrent mycobacterial infection.

Discussion. Mycobacterium chelonae is a rapidly growing acid-fast bacillus that is found in soil and fresh water throughout the world [1]. Infections of the skin can occur by way of accidental penetrating trauma, injections, or surgical procedures [2–4] and generally cause a localized abscess or cellulitis. Disseminated cutaneous disease (defined as >5 nodular subcutaneous lesions) also occurs and is more common in the immunocompromised host [2, 5]. Lesions predominate on the distal surface of a single extremity. However, scattered lesions may be detected on the opposite extremity. A source of infection, such as a visible site of entry or long-term percutaneous catheter, is usually not evident. The infection spreads by the hematogenous route but rarely spreads to the viscera, lungs, bones, or other organs [5, 6].

In a 1992 study, Wallace et al. [2] identified 53 patients with disseminated cutaneous M. chelonae. The most common underlying disorders in this group were organ transplantation, rheumatoid arthritis, and miscellaneous autoimmune disorders. Of note, 49 of the 53 patients in this study received oral corticosteroids, with or without other immunosuppressive drugs. Interestingly, our patient had not received oral corticosteroids for her arthritis. Instead, her immunosuppression was caused by endogenous release of excess cortisol secondary to Cushing’s syndrome.

 Opportunistic infections are rarer in patients with endogenous Cushing’s syndrome than they are in patients treated with pharmacologic corticosteroids [7–9]. In 1984, Graham and Tucker [7] compiled a series of 23 such patients who had been described in the literature. The 4 most frequent opportunistic infections were cryptococcosis, aspergillosis, nocardiosis, and Pneumocystis carinii pneumonia. No cases of atypical mycobacterial infection were reported. The extent of immunologic
impairment and risk of infection correlated with the degree of hypercortisolism. Pneumocystosis predominated in patients with severe hypercortisolism (morning cortisol level >121 μg/dL), whereas cryptococcosis occurred in patients with morning cortisol levels that ranged from slightly above normal to 70 μg/dL.

In a more recent 1998 review by Bakker and colleagues [10], only 36 patients were described during a 40-year period who had had opportunistic infections secondary to endogenous Cushing’s syndrome. Fungi were the most commonly isolated pathogens: Aspergillus fumigatus, Pneumocystis carinii, and Cryptococcus neoformans predominated [10]. These authors also concluded that patients who died had significantly higher plasma cortisol concentrations than did survivors.

Pituitary Cushing’s disease ordinarily accounts for 70% of all cases of endogenous Cushing’s syndrome. However, patients with pituitary Cushing’s disease usually have plasma cortisol levels in the range of 15–35 μg/dL. Those with higher levels of cortisol (due to adrenal tumors or ectopic ACTH syndrome) are more likely to have an opportunistic infection [7, 10]. Our patient’s morning cortisol level was 70 μg/dL even after overnight dexamethasone suppression. This is a unique case, because, to our knowledge, there are no reported cases of infection with M. chelonae or other atypical mycobacteria in patients with endogenous Cushing’s syndrome. Our patient’s clinical manifestations of M. chelonae and Cushing’s syndrome resolved only after treatment with azithromycin and ciprofloxacin was combined with normalization of the elevated cortisol level.

References