Distant Cutaneous Granulomas after Bacille Calmette-Guérin Immunotherapy for Malignant Melanoma: Case for Direct Infection

Bacille Calmette-Guérin (BCG) immunotherapy has been used for many years for various neoplasms. From intravesicular instillation for transitional cell carcinoma of the bladder to intralesional injections for cutaneous malignant melanoma [1], the goal of this therapy is to stimulate host immunity and to induce tumor regression. Unfortunately, because of the large inoculum size used, this treatment is not without complications. In addition to disseminated infection, [2] cutaneous complications from BCG administration include reactions such as erythema nodosum, pustular dermatitis, and disseminated cutaneous granulomas [3]. Importantly, the inability to isolate BCG from specimens from any of the cutaneous sites in immunocompetent patients has raised the question whether the granulomatous response with BCG administration is a true infection or a hypersensitivity reaction [4]. We describe a patient with recurrent melanoma treated with BCG immunotherapy which resulted in granulomatous dermatitis distant from the site of BCG inoculation; cultures of specimens from near the injection site were positive for BCG, a finding that may help settle this question.

An 81-year-old man had malignant melanoma on his right heel that was diagnosed in 1971. He underwent localized surgery with excision and skin grafting. The patient did well for 2 years but subsequently developed recurrent melanoma at the original grafting site. Over the following 17 years, he underwent 15 more excisions of recurrent melanomas on his right leg and received 7 immunizations that included both irradiated melanoma tumor cells and live BCG.

In 1998, the patient received BCG immunotherapy with local injections into his right heel. Both injections contained 0.2 mL of BCG (Tice BCG, Organon Teknika, Durham, NC; concentration, 5 × 10⁷ cfu/mL) administered intradermally at the periphery of the melanoma. After the second injection, the patient had shaking chills and subsequently developed an extensive, local inflammatory reaction with ulceration at the injection site. One week later, he began having low-grade fevers and occasional night sweats. Despite prolonged antibiotic therapy, the patient had worsening pain, erythema, and swelling of the right leg. Two months after the last BCG injection, he was admitted to the hospital for further evaluation.

At admission to the hospital, the patient was afebrile. A 5 × 5-cm oval, moist, boggy lesion with rim of induration, surrounding erythema, and skin desquamation were shown. B. Photomicrograph of skin biopsy specimen from 30 cm proximal to BCG injection site that displays caseating granuloma with Langhans' giant cells (stain, hematoxylin-eosin; original magnification, ×100).

5 × 5-cm oval, moist, boggy lesion was present on the dorsum of the right foot with a mild rim of induration surrounding the BCG injection site. Erythema, desquamation, and ulcerations were noted on the foot, with inflammation extending proximally to the right knee (figure 1A). Culture of a biopsy specimen from near the injection site yielded acid-fast bacilli that were identified as BCG vaccine organisms by HPLC. In addition, evaluation of 2 skin biopsy specimens from 30 cm proximal to the BCG injection site revealed caseating granulomas, consistent with BCG infection (figure 1B). A 6-month course of therapy with isoniazid and rifampin was initiated. At the conclusion of the 6-month regimen, the patient’s fever and night sweats had...
resolved. The dorsum of his right foot had only small, red macules, and erythema in the pretibial region had resolved.

BCG vaccine has been used for decades for the prevention of tuberculosis. More recently, BCG has been used as immunotherapy for various tumors. Importantly, the dosing of BCG is much higher when given as cancer immunotherapy [5]. As a result, BCG immunotherapy is often complicated by systemic side effects. Although BCG has been recovered from blood immediately after subcutaneous injection [6], attempts at isolating the organism from skin specimens from patients with chronic cutaneous changes have been futile [7]. Therefore, the cause of the cutaneous granulomatous lesions has remained controversial. Even though some investigators have postulated a hypersensitivity reaction to BCG as the underlying etiology, others have pointed to the rapid response of patients to antituberculosis treatment as evidence for direct invasion [5].

To our knowledge, we report the first case of culture-proven BCG infection of a chronic cutaneous lesion. When combined with the granulomatous changes seen during pathological evaluation and an excellent clinical response to antituberculosis therapy, it appears that direct BCG infection is the etiology of at least some of the postimmunization cutaneous abnormalities in our patient.

*Klebsiella pneumoniae* Liver Abscess, Endophthalmitis, and Meningitis in a Man with Newly Recognized Diabetes Mellitus

In the United States, culture of material from pyogenic liver abscesses most often yields polymicrobial bowel flora [1]. In Taiwan, however, monomicrobial *Klebsiella pneumoniae* infection causes most pyogenic liver abscesses, particularly among diabetics [2]. Endogenous (hematogenous) endophthalmitis is a recognized complication in this population [3–5]. To my knowledge, this is the first report from the United States to describe a patient with *K. pneumoniae* liver abscess, endophthalmitis, and meningitis.

A 38-year-old black man with no known medical problems was well until 4 days before admission, when he developed a headache and fever. Photophobia, neck stiffness, anorexia, and abdominal pain followed. On examination, the patient appeared uncomfortable, and his temperature was 40°C. Ophthalmologic examination findings were normal. Nuchal rigidity and right-upper-quadrant tenderness were present.

Lumbar puncture yielded cloudy CSF with the following characteristics: WBC count, $372 \times 10^6$/$L$, with a predominance of polymorphonuclear leukocytes; total protein, 2.78 g/L; and glucose, 7.8 mmol/L (140 mg/dL). Gram staining revealed large, encapsulated gram-negative bacilli. The serum glucose concentration was 18.7 mmol/L (337 mg/dL). Hepatic aminotransferase and $\gamma$-glutamyltransferase levels were each elevated to $\sim5$ times the upper limit of normal.

Ceftriaxone and metronidazole were given intravenously. *K. pneumoniae* grew in a culture of the CSF. A CT scan of the abdomen showed a 6-cm multicystic mass in the right hepatic lobe. Percutaneous aspiration provided green pus that yielded, in pure culture, *K. pneumoniae* with an antibiogram identical to that of the CSF isolate. A drainage catheter was left in place until output ceased.

On hospital day 3, the patient reported left-eye pain and blurry vision. Periorbital edema, chemosis, and conjunctival hyperemia were present (figure 1). Further ophthalmologic findings included visual acuity of 20/400 in the left eye, hypopyon, and vitreal haze suggestive of endophthalmitis. Vitreous humor was aspirated, and ceftazidime and vancomycin were injected intravitreally. Vitreous cultures were negative.

Ciprofloxacin, cefazolin, and corticosteroid eye drops were administered every 1–2 h. The patient was discharged after receiving ceftriaxone for 21 days and metronidazole for 17 days. Thereafter, he completed a 30-day regimen of oral levofloxacin and metronidazole. A subsequent CT scan showed no reaccumulation of fluid in the liver. At his most recent follow-up

References