Granulomatous *Pneumocystis carinii* Pneumonia in Patients with Low-Grade Lymphoid Malignancies: A Diagnostic Dilemma

Most cases of *Pneumocystis carinii* pneumonia (PCP) not associated with HIV infection have occurred in patients with acute leukemia who were treated with chemotherapy [1]. PCP that is associated with low-grade lymphoid malignancies (LGLM) is uncommon [2]. Granulomatous response to pneumocystis infection is unusual and is presumably related to immune deficits; such a response may suggest another process, such as mycobacterial infection, with different therapeutic implications. We report two cases of granulomatous PCP in patients with LGLM who were previously treated with chemotherapy. Both cases underscore the diagnostic dilemmas these patients can pose.

**Patient 1.** A 74-year-old man with Rai stage I chronic lymphocytic leukemia was treated with cyclophosphamide, vincristine, and prednisone after prolymphocytic transformation occurred. Following the third cycle of chemotherapy, he presented with fever and pancytopenia. A chest radiograph revealed new pulmonary nodules, which increased in size despite hematopoietic recovery. Examination of specimens obtained by bronchoalveolar lavage (BAL) and transthoracic needle biopsy was nondiagnostic. An open lung biopsy was performed, and examination of specimens revealed necrotizing granulomas (figure 1) with intragranulomatous *P. carinii*. The results of all other microbiological studies were negative. Serology for HIV-1 was negative. Quantification of T-lymphocyte subsets was not performed. Oral trimethoprim-sulfamethoxazole (TMP-SMZ) therapy (six double-strength tablets per day) was poorly tolerated; the patient had nausea and anorexia and developed progressive pulmonary disease while receiving therapy. The results of open lung biopsy again showed intragranulomatous *P. carinii*. Therapy was changed to oral dapsone/trimethoprim; the patient subsequently received a 21-day course of atovaquone, during which his condition improved clinically.

**Patient 2.** A 57-year-old man with progressive small lymphocytic lymphoma was treated with fludarabine. Three courses of therapy were well tolerated, with the exception of an episode of presumed fludarabine-associated pneumonitis that resolved when the patient was treated with corticosteroids. Therapy was changed to that with cyclophosphamide, doxorubicin, vincristine, and prednisone because the disease continued to progress. Soon after this regimen was begun, the patient developed diffuse interstitial and alveolar infiltrates. Examination of specimens obtained by BAL and transbronchial biopsy revealed only chronic interstitial pneumonitis.

**Figure 1.** Lung biopsy section showing a granuloma with central necrosis in a patient with chronic lymphocytic leukemia who had granulomatous *Pneumocystis carinii* pneumonia (stain, hematoxylin-eosin; original magnification, ×25).

All other microbiological studies were negative. In spite of treatment with intravenous erythromycin, TMP-SMZ, and imipenem, the symptoms abated only after steroids were added to the regimen. The patient developed progressive pulmonary disease 1 month after steroid therapy was discontinued. Examination of an open lung biopsy specimen revealed extensive caseating granulomas with intragranulomatous *P. carinii*. Serology for HIV-1 was negative. The peripheral CD4⁺ lymphocyte count was zero. He was treated with intravenous TMP-SMZ and later with oral dapsone/trimethoprim; the radiographic findings and clinical symptoms resolved.

PCP is an uncommon complication of LGLM, with yearly attack rates for patients with chronic lymphocytic leukemia estimated at 0.05% [2]. Fewer than 25 cases of granulomatous PCP have been described in the literature; only two of these cases occurred in patients with LGLM [3, 4]. Both of these patients, unlike ours, had prolonged pulmonary syndromes related to PCP before a definitive diagnosis was made by means of open lung biopsy. In one case, the granulomas were described as noncaseating [3], while in the other, they were described as necrotizing [4].

While corticosteroid therapy appears to be a major risk factor in the development of PCP in patients with cancer, other chemotherapeutic agents have also been implicated [1, 5]. Therapy with fludarabine causes prolonged T-cell dysfunction and likely contributes to higher rates of PCP in patients with LGLM [5]. PCP may be more likely to occur in patients such as ours when agents with known pulmonary toxicity, such as cyclophosphamide or fludarabine, are administered [5, 6]. Fludarabine therapy has also been associated with noninfectious granulomatous lung disease [5].

Owing to the relatively high organism burden seen in HIV-infected patients, the diagnosis of PCP can usually be made via BAL [7]. Patients with hematologic malignancies who develop PCP have a lower organism burden, which makes diagnosis by BAL problematic [8]. In both cases presented herein, serial attempts at diagnosis by means of BAL and transbronchial biopsy were unsuccessful; these failures underscore the poor sensitivity of these procedures in evaluating patients with granulomatous PCP and highlight the need for an expeditious open lung biopsy for a
definitive diagnosis in suspected cases. With the advent of aggressive chemotherapeutic regimens for the treatment of LGLM, it is likely that additional cases of atypical PCP may be seen. PCP must be considered in the differential diagnosis of pneumonic syndromes in chemotherapy-treated patients with LGLM, even when bronchoscopy is nondiagnostic. Open lung biopsy remains an important diagnostic procedure for these patients.

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References


Recurrent Cellulitis and Bacteremia Caused by Flavobacterium odoratum

Flavobacterium odoratum is an aerobic gram-negative bacterium that is common in environmental freshwater sources but is rarely isolated from clinical specimens [1, 2]. We describe a case of recurrent cellulitis and bacteremia due to F. odoratum.

A 63-year-old man with severe chronic obstructive pulmonary disease who had been receiving maintenance therapy with prednisone (30 mg/d) for 3 years was admitted to the hospital with bilateral upper extremity cellulitis that had developed during the previous week. There was no history of trauma, use of antibiotics, swimming, or contact with animals within the previous year. Water for drinking and bathing at his home was obtained from a well.

On admission, the patient’s temperature was 37.4°C, and he remained afebrile throughout his hospitalizations. Physical examination revealed a cushingoid appearance; fragile, parchment-like skin on the extremities, with multiple superficial ecchymoses and excoriations; erythema, tenderness, warmth, and edema of most of the right arm from wrist to mid-biceps; and warmth and edema of the entire left forearm. Axillary adenopathy was not detected. The patient’s WBC count was 19,000/mm³ with 85% neutrophils, 8% band forms, 4% monocytes, and 3% lymphocytes; toxic granulation was present.

Intravenous cefazolin therapy was begun. On the second hospital day, the cellulitis was unchanged; blood cultures (Bectec Becton Dickinson Instrument Systems, Sparks, MD) were positive and yielded an organism that was eventually identified as F. odoratum [1]. In both disk diffusion and broth microdilution assays [3, 4], the isolate proved to be resistant to vancomycin, gentamicin, amikacin, cefazolin, and ceftazidime and was immediately susceptible to ceftriaxone. It was susceptible to trimethoprim-sulfamethoxazole, piperacillin, and imipenem. When these results became available, the patient’s therapy was switched to intravenous imipenem/cilastatin (500 mg q6h). The cellulitis abated within 24 hours of this change in therapy, and it continued to diminish. Following 10 days of intravenous therapy, the patient was discharged and instructed to continue treatment with oral trimethoprim-sulfamethoxazole (160 mg/800 mg b.i.d.) for an additional 2 weeks.

Four days after completing antimicrobial therapy, the patient returned to the hospital with recurrent cellulitis of his left upper extremity. Once again, he was afebrile and did not appear toxic. However, blood cultures were again positive for F. odoratum, with an identical antibiotic susceptibility pattern. Following 10 days of intravenous piperacillin therapy (5 g q6h), the patient was discharged with instructions to take trimethoprim-sulfamethoxazole (160 mg/800 mg b.i.d.) for an additional month. When the patient was seen for a follow-up examination a few months later, his cellulitis had resolved. A sample of the patient’s home tap water, which was obtained during the second hospitalization, failed to yield F. odoratum.

As of 1979, only 24 cases involving isolation of F. odoratum from clinical specimens had been reported; infection was suspected in five of these cases [2]. Urinary tract infection was present in three cases, and cutaneous infection was present in two. Both skin infections affected immunologically compromised sites—an amputation stump of a patient with peripheral vascular disease and a gangrenous frostbitten foot of the other patient. Only one other report mentions isolation of F. odoratum from cutaneous sites—a single case in which the organism was described as a colonizer of a gangrenous amputation stump [5].

In our patient’s case, F. odoratum infection also involved a cutaneous site with impaired defenses. The portal of entry was likely the area of cutaneous breakdown on the upper extremities, and chronic corticosteroid therapy was the predisposing factor. The findings in our case further illustrate the invasive potential of this opportunistic pathogen, which spread from the cutaneous site of origin to the bloodstream on two occasions. Although tap water from the patient’s...