Case report

A diagnostic challenge: PCP in a non-HIV patient

S. ELIAS1, O. ALMOGI-HAZAN2, M. AKER3, A. BEN-YEHUDA1, A. BAYYA1* and Y. TAL1*

From the 1Department of Medicine, Hebrew University-Hadassah Medical Center, POB 12000, Jerusalem 91120, 2Department of Bone Marrow Transplantation, Hebrew University-Hadassah Medical Center, POB 12000, Jerusalem 91120 and 3Department of Pediatric Hematology-Oncology and Bone Marrow Transplantation, Hebrew University-Hadassah Medical Center, POB 12000, Jerusalem 91120, Israel

Address correspondence to S. Elias, Department of Medicine, Hebrew University-Hadassah Medical Center, POB 12000, Jerusalem 91120, Israel. email: selias@hadassah.org.il

*These authors contribute equally to this work.

Case report

A 58-year-old Ashkenazi Jew presented with fever and dyspnea. Over the 2-month period prior to his admission, he suffered from flu-like symptoms including fever and sore throat. His medical background only included hypertension for which he was treated. On admission his oxygen saturation was 91% on nasal cannula. He had a papular rash on his chest and back as well as enlarged sub-mandibular lymph nodes which were considered to be reactive lymph nodes by sonography. The rest of his physical examination was normal, including his lungs which were clear to auscultation. His laboratory tests indicated an elevated LDH (1773 U/l), cholestatic dysfunction with elevated alkaline phosphatase (191 U/l) and GGTP (316 U/l). He also had leukocytosis (white cell count of 12.2 × 10^9 cells/l) and an increased C-reactive protein (18.4 mg/dl, normal <1). His chest X-ray and high-resolution CT (HRCT) scan revealed diffuse interstitial disease (Figure 1). He was treated initially for a community acquired pneumonia. Six days after admission, his respiratory condition deteriorated, necessitating intubation and transfer to the medical intensive care unit (MICU).

Due to the patient’s rapid respiratory deterioration, we conducted a bronchoscopy with bronchoalveolar lavage (BAL) and a trans-bronchial biopsy which demonstrated infection with *Pneumocystis jiroveci* (Pneumocystis pneumonia, PCP) (Figure 2). The patient developed severe acute respiratory distress syndrome (ARDS) due to PCP and was treated with inhaled nitric oxide (iNO), pressure-control ventilation, antibiotics (trimethoprim-sulfamethoxazole which was changed to pentamidine) and corticosteroids. Twenty-four days after his admission to the ICU, the patient was successfully extubated.

We initiated a work-up to identify an underlying disease which would explain the occurrence of PCP in this patient. Multiple tests for HIV were negative and he had a normal CD4 count. The patient had never been treated previously with corticosteroids or chemotherapy. Imaging studies revealed only mild lymph node enlargement, and specifically there was no evidence of thymoma for the possibility of Good’s syndrome.1 The patient’s immunologic serology (antinuclear antibody and anticytoplasmatic antibody) was negative. His bone marrow and blood smear were interpreted as normal.

Immunological tests revealed hypogamaglobulinemia (for which he received intravenous immunoglobulin, IVIG) and a low response to T-cell mitogens. We used flow cytometry to better define the T-cell dysfunction which showed a lack of surface expression of CD3 in most CD4-positive cells, which is unusual for T-cells (Figure 3A). We searched the English literature for descriptions of PCP in non-HIV patients with a similar immunophenotype. We found a report on two patients with PCP and smoldering adult T-cell leukemia due to a human T-cell lymphotrophic virus (HTLV) infection.2
Similar to our case, the fraction of CD3 cells did not sum up to the combined fraction of CD4 and CD8 cells. Based on this report we sent a serology test for HTLV infection which returned positive and was confirmed subsequently by western blot. Revision of the patient’s blood smear revealed few (<5%) flower-cells, which are typical of HTLV infection (Figure 3B). Three weeks after his discharge from the ICU, a marked cervical lymph node enlargement was noted. His blood tests indicated severe cholestasis which had worsened since his initial admission. Biopsies from a cervical lymph node and from the liver were positive for T-cell lymphoma. The patient was transferred to the Department of Hematology where he was treated with chemotherapy. The patient subsequently died from complications of his hematologic disease.
Discussion

According to two American series most (90–100%) non-HIV patients with PCP have been previously treated with corticosteroids or chemotherapy. Therefore encountering PCP in a non-HIV patient without any known risk factors poses a diagnostic challenge. The patient described above was eventually diagnosed with adult T-cell leukemia–lymphoma (lymphoma type) due to the HTLV infection. Infection with HTLV, which is endemic mainly in Japan, is rare in our region as well in the United States and Europe. The unique immunophenotype described in relation to HTLV infection led finally to this surprising diagnosis. Although HTLV-infected patients are prone to opportunistic infections, especially PCP, it is not a recognized cause of PCP in non-HIV patients in Western series. Moreover, our case demonstrates for the first time the role of the specific immunophenotype in the diagnosis of HTLV.

Conflict of interest: None declared.

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References