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Case study

Peripheral blood eosinophilia as a clue to the diagnosis of an occult *Coccidioides* infection

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Summary A marked peripheral blood eosinophilia is an uncommon finding in a complete blood count (CBC). According to Wardlaw and Kay (Eosinophils and Their Disorders. In: Beutler E, Lichtman MA, Coller BS, Kipps TJ, Seligsohn U, editors. *Williams Hematology*. 6th ed. New York: McGraw-Hill, 2001. p. 790-93), the most common causes are infection by helminthic parasites, atopic disease, and, less commonly, primary hypereosinophilic syndromes. Therefore, when eosinophilia is seen in a CBC, it can provide an important clue to the correct diagnosis. We present a case of a patient with a finding of pulmonary nodules in the setting of cancer and a CBC finding of profound peripheral blood eosinophilia. As a result of the high level of clinical suspicion for *Coccidioides* infection due in part to the eosinophilia, adequate steps were taken in the clinical laboratory not only to correctly diagnosis the patient, but also to protect the laboratory staff from work-related exposure to this easily aerosolizable infectious agent.

1. Introduction

Pulmonary nodules in a cancer patient present a clinical quandary. The appropriate classification of these nodules as malignant or otherwise is imperative, as treatment and prognosis depend upon it. However, this task is not always easy. Aside from primary lung tumors and metastases, an infectious cause is in the differential diagnosis. The appropriate use and interpretation of a wide variety of diagnostic modalities is often needed to ascertain the etiology of these lesions. Occasionally, important information that is readily available is overlooked. The following case report illustrates this point, as this patient had marked peripheral blood eosinophilia. This finding helped guide the diagnostic approach that, ultimately, led to the correct characterization of the pulmonary nodules and the subsequent treatment. In addition, the high level of suspicion raised by the clinical history and peripheral blood eosinophilia allowed the laboratory to take adequate precautions to protect the staff from infection.

2. Case report

A 70-year-old immunocompetent man from Arizona presented to Vanderbilt University Medical Center as a potential candidate for robotically assisted radical prostatectomy. His medical history was significant for prostate cancer, coronary artery disease, and a 2-year history of cough that had been previously diagnosed in Arizona as new-onset asthma. An initial complete blood count (CBC) laboratory value demonstrated macrocytic anemia. Further examination of the peripheral blood smear demonstrated profound

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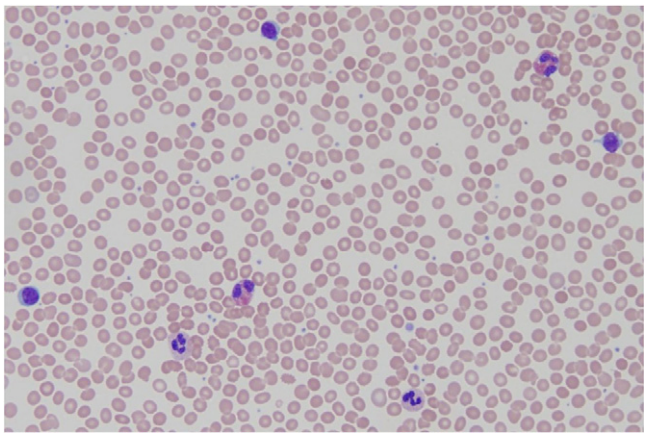

Fig. 1 Peripheral blood smear with an increased number of eosinophils (Wright-Giemsa stain, original magnification ×20).

eosinophilia, which, upon differential, was found to be 1070 per μL or 16.5% (reference range 0.4%-7.5%) of total leukocytes (Fig. 1). A subsequent routine abdominal computed tomography (CT) scan done as part of the workup to exclude the metastatic spread of prostate cancer revealed multiple, bilateral pulmonary nodules in the lung bases. As a result, a chest CT was ordered and additional nodules were identified throughout the lungs bilaterally (Fig. 2A). They ranged in size from 1-2 to 9 mm, with concomitant bulky mediastinal and hilar lymphadenopathy. A bronchoscopy with fine-needle aspiration of the pulmonary nodules plus a paratracheal lymph node was performed. The fine-needle aspirates were negative for organisms on initial Gram and acid-fast stains and were cytologically negative for any neoplastic process. However, after 7 days, a nonpigmented mold grew on Sabouraud agar (Fig. 3A). The mycelial form demonstrated true septa along its length (Fig. 3B) with the classic alternation of live and dead barrel-shaped arthroconidia. Based upon the suggestive appearance of the mycelium, a gene probe was done at a reference laboratory, which confirmed the identity of the fungus as *Coccidioides immitis*. Serology demonstrated the presence of *Coccidioides* immunoglobulin G (IgG) antibody and was negative for immunoglobulin M (IgM) antibody.

The patient was started upon fluconazole 400 mg once daily and at a 1-month follow-up CT scan, there was already some observable decrease in the size of the nodules with marked symptomatic improvement (Fig. 2B). The patient subsequently underwent an uncomplicated prostatectomy, and a 6-month follow-up CT scan revealed complete resolution of the pulmonary nodules with the exception of one small calcified nodule.

3. Discussion

Coccidioides species are found in the soil of the southwest United States, spanning from southern California to west

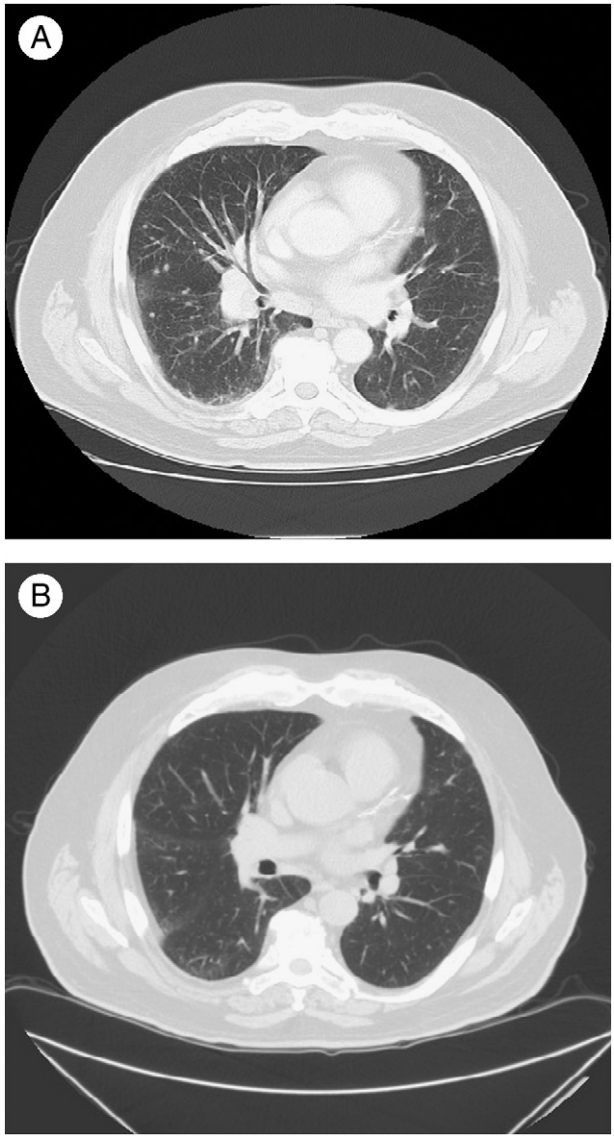

Fig. 2 A, Initial chest CT scan showing scattered, bilateral pulmonary nodules. B, Chest CT scan, 1 month later, demonstrating marked reduction in the number and size of the bilateral pulmonary nodules.

Texas. *Coccidioides* species cause a spectrum of disease that ranges from a subclinical respiratory infection, in as many as 60% of cases, to the uncommon widespread systemic infection, coccidioidomycosis [1]. Systemic sites include the skin, bones, and cerebrospinal fluid. Pulmonary nodules are a rare, but well-known, complication that occurs in about 4% of patients with a respiratory infection. Treatment for symptomatic disease includes antifungal medications such as fluconazole, 400 mg by mouth once daily, for 3 to 6 months [2].

The diagnosis, as in this case, is typically made with the use of fungal culture and serology, although fungal culture alone is the diagnostic criterion standard [2]. *Coccidioides* species are dimorphic, with a mycelial form found in culture at room temperature and a spherule form that can be seen histologically in infected tissues. Either of these