Pulmonary nocardiosis in a patient with idiopathic CD4 T-lymphocytopenia

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Keywords
Idiopathic CD4 T-lymphocytopenia, immunodeficiency, pulmonary nocardiosis.

Abstract
Idiopathic CD4 T-lymphocytopenia (ICL) is a rare immunodeficiency characterized by low CD4 T-lymphocyte count, which usually manifests with opportunistic infections. Nocardia as an opportunistic pathogen infecting patients with this condition has rarely been reported. Here, we describe the case of a 46-year-old male who presented with lung mass and respiratory and systemic symptoms and was eventually diagnosed with pulmonary nocardiosis. A workup for predisposing immunodeficiencies suggested a picture of ICL. This case illustrates the importance of considering ICL as a possible predisposing condition when an otherwise healthy individual presents with pulmonary nocardiosis.

Introduction
Idiopathic CD4 T-lymphocytopenia (ICL) is an extremely rare form of immunodeficiency. It was first defined in 1992 by the US Centers for Disease Control and Prevention (CDC) as “an absolute CD4 T-lymphocyte count <300/mm³ or <20% of total T cells on more than 1 cell count at least 6 weeks apart; no evidence of infection with human immunodeficiency virus (HIV)-1/2 or human T-cell lymphotropic 1/2 (HTLV-1/2); and lack of a defined immunodeficiency disease or therapy that are associated with depressed levels of CD4 T cells.” Patients with ICL typically present with opportunistic infections, malignancies, or autoimmune disorders. The opportunistic infections commonly associated with ICL include cryptococcal, mycobacterial, candidial, and viral infections [1]. So far, there have only been three reported cases of nocardial infection in ICL [2,3]. We present a case of pulmonary nocardiosis in a patient with ICL.

Case Report
A 46-year-old male with no significant medical history was referred to the pulmonology office for evaluation of a lung mass. The patient’s history was notable for 30 pack-years smoking, although he had quit 5 years prior to presentation (Tables 1–2). He also reported some exposure to dust and smoke as he worked in the automotive industry. He had a pet dog at home and had no significant travel history. Family history was significant for Hodgkin’s lymphoma in one first-degree relative and two second-degree relatives. The lung mass was first noted on a chest computed tomography (CT) done after he presented to another hospital with productive cough, haemoptysis, fevers, chills, and an 18-lb weight loss over the course of 1 month (Fig. 1). On reviewing the CT, a 6.2 × 5.7-cm² mass was seen in the left lower lobe’s superior segment with some cavitation and air bronchograms. Our patient underwent bronchoscopic evaluation of the mass with washings, needle aspiration, and transbronchial biopsy. Two days after the procedure, he was hospitalized with acute hypoxic respiratory failure. He was initially managed with clindamycin as inpatient without significant improvement. Four days into the hospital stay, fungal culture from the bronchial washings done in the pulmonology office resulted as positive for partially acid-fast, branching Gram-positive bacilli, later identified as Nocardia abscessus. After the preliminary culture results came back, the patient was started on intravenous

imipenem (later switched to meropenem due to intolerance) and trimethoprim–sulfamethoxazole (Fig. 2). A magnetic resonance imaging of the brain showed no sign of disseminated infection. Following the diagnosis, an extensive workup was done to look for possible immunosuppression. Workup was negative except for a low CD4/CD8 ratio (0.1) and low CD4 T-cell count (70), which may be seen with acute infectious processes. However, repeat labs done with the patient asymptomatic and back to his baseline (after completing 6 months of antibiotics) revealed persistently low CD4/CD8 ratio and low CD4 T-cell count. Workup for the causes of low CD4 count including Human T-Cell Lymphotropic Virus, Human Immunodeficiency Virus, cytomegalovirus, Epstein-Barr virus, tuberculosis, fungal aetiologies, autoimmune aetiologies, and so on was negative, making ICL the most probable diagnosis.

**Discussion**

Nocardia is a partially acid-fast, Gram-positive bacterium that usually causes opportunistic infections in immuno-

### Table 1. Lab values at the time of admission and 6 months after admission.

| Tests                  | At the time of admission | 6 Months after admission |
|------------------------|--------------------------|--------------------------|
| WBC                    | 20.7                     | 3.2                      |
| Haemoglobin            | 13.0                     | 15.5                     |
| Platelets              | 338                      | 143                      |
| Neutrophils            | 19.7                     | 1.9                      |
| Lymphocytes            | 0.6                      | 0.7                      |
| Monocytes              | 0.3                      | 0.5                      |
| Sodium                 | 138                      | 134                      |
| Potassium              | 4.1                      | 4.4                      |
| Chloride               | 102                      | 99                       |
| Bicarbonate            | 24                       | 27                       |
| BUN                    | 15                       | 14                       |
| Creatinine             | 0.92                     | 0.94                     |
| Sodium                 | 8.9                      | 9.3                      |
| Albumin                | 3.7                      | 4.7                      |
| Alkaline phosphatase   | 85                       | 64                       |
| Aspartate aminotransferase | 26                      | 28                       |
| Alanine aminotransferase | 21                      | 53                       |
| Bilirubin total        | 1.0                      | 0.4                      |
| ESR                    | 124                      | —                        |
| HIV-1 p24 antigen, HIV-1/HIV-2 antibodies | Non-reactive | —  |
| ANA screen             | Negative                 | —                        |
| IgG                    | 960 (normal range 564–1765 mg/dL) | —  |
| IgA                    | 156 (normal range 85–385 mg/dL) | —  |
| IgM                    | 97 (normal range 45–250 mg/dL) | —  |

**ANA, antinuclear antibody; BUN, blood urea nitrogen; ESR, erythrocyte sedimentation rate; Ig, immunoglobulin; WBC, white blood cells.**

### Table 2. Comparison of immunology parameters at the time of admission and 6 months after admission.

| Tests                               | At the time of admission | 6 months after admission |
|-------------------------------------|--------------------------|--------------------------|
| CD4/CD8 ratio                       | 0.1 (normal range 0.6–6.2) | 0.1                      |
| Absolute lymphocyte count           | 1000 mil/L               | 800 mil/L                |
| Absolute CD3 total T-cells          | 710 mil/L (normal range 730–2460) | 568                      |
| Absolute CD4 T-helper cells         | 70 mil/L (normal range 433–1722) | 64                       |
| Absolute CD8 T-suppressor cells     | 560 mil/L (normal range 143–921) | 440                      |
| Absolute CD56 natural killer cells  | 80 mil/L (normal range 42–352) | —                        |
| Absolute CD19 B-cells               | 180 mil/L (normal range 44–683) | —                        |
compromised patients, particularly those with cell-mediated immunodeficiency. Immunodeficient states that predispose to nocardial infections include solid organ or haematopoietic stem cell transplantation, glucocorticoid and other immunosuppressant therapy, HIV infection, malignancy, and diabetes mellitus [4,5]. The occurrence of nocardiosis in patients who are immunodeficient on account of ICL has only been reported previously in a few case reports [2,3].

A review by Ahmad et al. discussed various opportunistic infections, autoimmune diseases, and malignancies reported from 258 diagnosed cases of ICL described in 143 published papers [3]. Only two cases of nocardiosis were reported in this review.

During our literature review, we came across one more reported case of nocardiosis in ICL, in addition to the ones included in the review by Ahmed et al. However, in this case, the authors admit that the nadir CD4 count was greater than 300/mm³ and hence the diagnosis of ICL was not in strict adherence with the CDC definition [2]. In two of the three previously reported cases, ICL-associated nocardial infection manifested as *Nocardia farcinica* brain abscesses with no evidence of pulmonary nocardiosis. The third case presented with disseminated *Nocardia asteroides* infection. The nadir CD4 count for our patient was 70/mm³, a much lower CD4 count than the two cases of nocardial brain abscesses. The case involving disseminated nocardiosis had a nadir CD4 count of 10 ± 5/mm³. Similar to most cases of ICL, our patient had no previous clinical evidence of immunodeficiency until he developed an opportunistic infection. Much like cell-mediated immunodeficiencies, chronic granulomatous disease (CGD), which impairs the function of phagocytes, can predispose patients to nocardiosis. Since our patient did not have hypergammaglobulinaemia, low B-cells, or persistent hypoalbuminaemia—lab features commonly associated with CGD, he was not tested for it.

We present, to our knowledge, the first reported case of isolated pulmonary nocardiosis in a patient with ICL. As far as we know, this is also the fourth reported case of nocardiosis in a patient with ICL. Although not as common as cryptococcal, mycobacterial, or viral infection, nocardiosis should be considered in the differential diagnoses for patients known to have ICL, who present with suggestive symptoms. Likewise, if nocardiosis develops in an otherwise healthy individual, the CD4 count should be monitored over 6 weeks period or longer, so as not to miss a diagnosis of ICL.

**Disclosure Statement**

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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