Case Report

Sarcoidosis-like Reaction Related to *Propionibacterium acnes* and Immune Restoration Syndrome in HIV Infection

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ABSTRACT. *Propionibacterium acnes* is thought to be a potential triggering agent of sarcoidosis. We describe a woman who developed chronic meningitis with sarcoid-like multisystemic involvement under treatment for human immunodeficiency virus infection. *P. acnes* was isolated from cerebrospinal fluid. We assume that *P. acnes* might have triggered this sarcoid-like reaction with meningitis, as a consequence of an immune reconstitution. (J Rheumatol 2007;34:2495–6)

Key Indexing Terms:
SARCOIDOSIS AIDS PROPIONIBACTERIUM ACNES

The causes of sarcoidosis remain unknown, but many reports have suggested potential infective triggering agents. Propionibacteria may contribute to the formation of granulomatous lesions[1,2], and have emerged as a putative candidate. In the course of HIV infection, immune reconstitution inflammatory syndrome (IRIS) occurring under highly active antiretroviral therapy (HAART) can exacerbate coinfections or autoimmunity, with sarcoidosis and thyroiditis being most common[3].

We describe a woman who developed chronic meningitis with sarcoid-like multisystemic involvement under treatment for human immunodeficiency virus (HIV) infection.

CASE REPORT

A 43-year-old woman with transfusional HIV infection (stage IV C of the CDC classification), diagnosed 10 years earlier, presented with headache and photophobia in October 2005. She had received a 10-day course of amoxicillin-clavulanate, followed by an 8-day course of cefpodoxime for cough, without clinical improvement. She had been treated with HAART for 10 years. The lowest level of CD4 lymphocyte count was 112/μl (9%). Her history revealed aseptic lymphocytic meningitis noted in 1999 when CD4 lymphocytes were 713/μl (29%).

The day she was admitted, plasma HIV viral load was 41,900 RNA/ml (4.62 log) and CD4 lymphocyte count was 402/μl (30%), whereas it was 248/μl (21%) 1 month earlier, with an HIV viral load of 4.40 log. Examination showed only nape stiffness and superficial lymphadenopathy. She was afebrile. CSF analysis showed 49 leukocytes/mm^3 (76% lymphocytes); protein level was 1.53 g/l and glucose 2.3 mmol/l. Gram stain was negative, but cultures grew secondarily to *P. acnes*, and confirmation was obtained with RNA 16s RT-PCR. *P. acnes* was not quantified. Interferon and viral PCR results were negative, as were cryptococcic antigen and mycobacteria cultures. C-reactive protein level was 3.3 mg/l. She was treated with intravenous amoxicillin (12 g/day) for 3 weeks, without clinical improvement.

Ten days later, CSF examination showed persistent meningitis (CSF leukocyte count 35/mm^3, 88% lymphocytes), but culture results were negative. Given the potential chronicity of this lymphocytic meningitis, with a first episode 6 years earlier, sarcoidosis was considered. Serum angiotensin-converting enzyme (ACE) was 56 IU/l (normal value < 52 IU/l). The Mantoux test was negative, and the patient had been vaccinated with BCG. Analysis of bronchoalveolar lavage (BAL) showed a lymphocytic alveolitis (271 cells/mm^3, 21% lymphocytes), mostly related to an increase in the CD4 cell subset (74% of lymphocytes). Lung computed tomography scan was normal, but pulmonary function tests (PFT) showed a moderate diffusion disorder (diffusing capacity for carbon monoxide was 76% of normal value). Gallium-67 scan showed strong accumulation of the isotope in liver, spleen, and parotid and lacrymal glands. However, accessory salivary gland biopsy revealed only chronic sialadenitis. Cerebral magnetic resonance imaging was normal. Calcium and phosphorus concentrations in blood and urine were normal. The results of the BAL, serum ACE, PFT, and gallium-67 scan allowed us to propose the diagnosis of sarcoid-like reaction even though no histological evidence of noncaseating granuloma was available.

No indication for treatment was suggested by these investigations. Moreover, because of the potential implication of HAART in this syndrome, it was decided to stop this treatment. Symptoms resolved within 2 months, and no recurrence occurred after HAART was restarted. At present, the patient remains asymptomatic for chronic meningitis and pulmonary disease.

DISCUSSION

Our patient developed a sarcoid-like reaction with chronic meningitis under HAART, associated with a *P. acnes* infection, which resolved after treatment of *P. acnes* and HAART were stopped. These features are compatible with an IRIS-related sarcoid-like reaction triggered by *P. acnes*. We cannot rule out *P. acnes* contamination, but such identification was never noted on CSF specimens in our department.

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Sarcoidosis can be considered a syndrome rather than an illness. It is probably an immune response to an as yet unidentified agent. Multiple agents may be causative, including mycobacteria and propionibacteria. The role of Mycobacteria is controversial, but *P. acnes* seems more and more susceptible to be involved in sarcoidosis[4]. In murine models, cutaneous immunization against *P. acnes* may induce pulmonary and hepatic Th-1 granuloma formation[1]. In humans, Ishige, *et al* used PCR amplification of biopsied thoracic lymph nodes to identify propionibacterial DNA, and found that significantly higher propionibacterial DNA copy numbers were seen in thoracic lymph nodes of patients with sarcoidosis compared with controls[2]. *P. acnes* DNA was also detected in renal parenchyma in a case of renal sarcoidosis[5], and in vitreous fluid of patients with sarcoidosis-related uveitis[6].

The immune restoration inflammatory syndrome, a reaction following institution of HAART, can be the source of a paradoxical decline in clinical status. IRIS is believed to result from a specific immune response to strong microbial antigenic stimulation[3]. IRIS has been mostly described with *Mycobacterium avium* complex, *Mycobacterium tuberculosis*[7], *Cryptococcus neoformans*[8], and *Cytomegalovirus*[9]. Indigenous bacteria of low virulence may also trigger such reactions. However, this inflammatory disease has been described without evidence of occult concomitant infection as well. Sarcoidosis has already been described in this feature[10], and is the more frequent IRIS-related rheumatologic disorder[11].

To our knowledge, this report is the first description of a chronic meningitis in a sarcoid-like reaction with *P. acnes* detected in CSF. This case emphasizes the potential importance of this pathogen to trigger sarcoidosis, and expands the variety of descriptions of *P. acnes* infection-associated sarcoidosis. As well, this is the first report of an IRIS triggered by Propionibacterium infection.

Further studies with quantitative PCR may elucidate the causes of sarcoidosis and sarcoid-like reactions, and especially in the HAART-induced immune restoration syndrome.

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