Acute Pneumonitis in a Patient with Celiac Disease and Dermatitis Herpetiformis

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Celiac disease is associated with several extragastrointestinal manifestations, including autoimmune diseases [1,2]. Pulmonary disease has been described in the form of chronic interstitial lung disease, such as fibrosing alveolitis and hypersensitivity pneumonitis [3,4]. We describe a case of acute pneumonitis and wrist arthritis presenting as unusual extra- intestinal manifestations of celiac disease.

Patient Description

A 72 year old man with a long-standing history of dermatitis herpetiformis was admitted for investigation of fever and dyspnea of 3 days duration. Dermatitis herpetiformis had been diagnosed 20 years previously by a skin biopsy demonstrating immunoglobulin A granular deposits. Serologic tests for celiac disease on several occasions were negative and a small bowel biopsy was not performed. The patient was treated with dapsone combined with a gluten-free diet, resulting in a complete clinical remission. Two months prior to admission the patient stopped both the dapsone treatment and the gluten-free diet. He denied previous gastrointestinal symptoms but had been treated for iron deficiency anemia 10 years previously.

Five weeks prior to the present admission the patient was hospitalized because of acute wrist monoarthritis. Repeated joint aspirations were unsuccessful, but an infectious cause was suspected because of the clinical and radiologic findings. Moderate improvement was observed following treatment with broad-spectrum antibiotics and he was discharged; prolonged home treatment with intravenous ceftriaxone was recommended.

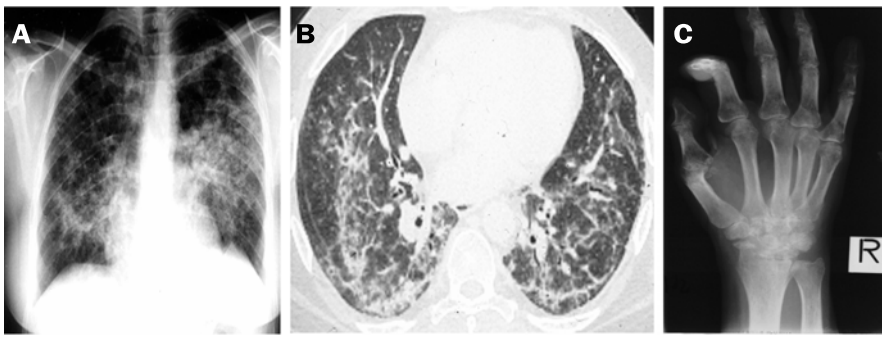
The patient was admitted to our department because of fever (38.0–38.5°C) and progressive dyspnea without cough that had begun 3 days previously. On physical examination he was dyspneic and diaphoretic; his temperature was 38.2°C, pulse 120/minute, respiratory rate 26/min, blood oxygen saturation 82% on room air. Lung auscultation revealed coarse crackles over both lung bases. Skin examination disclosed scattered erythematous lesions with central papules, compatible with the first stage of dermatitis herpetiformis. The rest of the physical examination was normal.

Complete blood count was normal, as was complete biochemical profile. Repeated blood, urine and sputum cultures did not yield any pathogenic microorganisms. Serologic tests for human immunodeficiency virus, antinuclear and antineutrophil cytoplasmic antibodies and rheumatoid factor were negative; IgA antigliadin antibodies were positive at 520 IU/L (normal 0–80) and endomysial antibodies were strongly positive. Chest X-ray revealed bilateral interstitial and alveolar infiltrates [Figure A].

The patient was treated with intravenous vancomycin + ceftazidime but his respiratory status deteriorated rapidly with decreased blood oxygen saturation and propagation of lung infiltrates in multiple lung segments. Chest computerized tomography revealed interstitial and alveolar infiltrates without pleural effusion [Figure B]. An X-ray film of his right wrist demonstrated erosive changes of metacarpopharangeal and distal interphalangeal joints [Figure C].

Bronchoscopic examination was performed and transbronchial biopsies were taken. Bacteriologic studies of alveolar lavage, including bacterial, viral and fungal cultures, silver staining for *Pneumocystis carinii* and Ziehl-Neelsen acid-fast stain were all negative. On pathologic examination, diffuse non-specific alveolar infiltrates were seen with a mixture of different

IgA = immunoglobulin A



[A] Chest X-ray during the acute phase of pneumonitis. **[B]** Chest CT scan. **[C]** X-ray of the patient's right wrist, demonstrating erosive changes of the carpometacarpal and distal interphalangeal joints.

inflammatory cells including several eosinophils (less than 15% of the cells). Antibiotic treatment was discontinued and a course of high dose corticosteroids (prednisone 100 mg per day per os) was begun, which resulted in rapid resolution of lung infiltrates. Concomitantly the patient was put on a gluten-free diet.

Further improvement in his wrist arthritis, dermatitis and well-being were noted along with rapid and complete disappearance of fever and dyspnea. After 10 days of the corticosteroid therapy he denied any respiratory complaints and his chest X-ray was near normal.

Comment

Several extra-intestinal manifestations of celiac disease have been described previously [1]. These include iron deficiency anemia, metabolic bone disease due to vitamin D and calcium deficiency, various rheumatic disorders, IgA deficiency, skin manifestations (most commonly dermatitis herpetiformis), diverse neurologic and psychiatric derangements, and myopathy.

Ventura et al. [2] recently reported that the development of autoimmune disorders such as autoimmune hepatitis and thyroiditis increases with the duration of exposure to gluten. In the present case, we describe autoimmune disease shortly after re-exposure to gluten.

Reports in the early 1970s pointed to a possible association between celiac disease and pulmonary involvement, mainly in the form of hypersensitivity pneumonitis [3]. However, a later study did not confirm this association [4]. Although fibrosing alveolitis has also been reported in association with celiac disease as a late, progressive and irreversible stage of pneumonitis, the pulmonary disease may be mild with symptoms of chronic unexplained cough.

To the best of our knowledge, the current case is unique because of the severe and rapidly progressing alveolitis after gluten rechallenge, followed by a rapid and complete response to corticosteroid treatment combined with a gluten-free diet. In support of a causative link between pulmonary involvement and gluten rechallenge is the fact that the patient's celiac serology was negative 2 months prior to his admission while he was adhering to a gluten-free diet. Gluten rechallenge resulted in a flare-up of the dermatitis herpetiformis, accompanied by pulmonary and articular manifestations. Furthermore, the patient became seropositive for antigliadin and endomysial antibodies. Indeed, it is well established that celiac patients on a gluten-free diet may have very low or even undetectable titers of anti-endomysial and antigliadin antibodies, which may increase upon gluten rechallenge, as observed in our patient.

The inflammatory intestinal process characterizing celiac disease includes activation of the main "participants" of the immune system, such as large numbers of T cells (CD4 and CD8). This is the basis of several previous reports on the use of corticosteroids and cyclosporine for the treatment of refractory celiac disease. The prompt response of pulmonary as well as articular (wrist arthritis) and dermatologic manifestations (dermatitis herpetiformis) to corticosteroid treatment in the present case supports the notion of an autoimmune basis for these extra-intestinal manifestations of celiac disease.

Celiac disease-associated arthritis is well recognized and may be associated with "enteroarthritis," which refers to a number of intestinal diseases (e.g., inflammatory bowel disease and Whipple's disease). This is characterized by nonerosive mono- or oligoarthritis [5]. Our patient's arthritis was associated with rapid bone destruction, suggesting infection. Yet the lack of response to a broad-spectrum antibiotic treatment and failure to grow bacteria from the joint aspirate strongly negated a septic etiology. Furthermore, the patient's arthritis rapidly and completely resolved after initiation of prednisone treatment, indicating an autoimmune etiology and exacerbation of celiac disease.

We contend that interstitial pneumonitis and destructive arthritis should be considered among the extra-intestinal manifestations of celiac disease. Both may rapidly respond to a gluten-free diet and/or corticosteroid therapy.

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It took me fifteen years to discover that I had no talent for writing, but I couldn't give up because by that time I was too famous

Peter Benchley (1940-), author and environmentalist, most famous for his 1974 book *Jaws* that was made into a blockbuster movie