

## Case 21

RN is a 16 year-old male of Finnish extraction. During the summer, shortly after a strenuous year of competitive swimming meets, he became aware of a discomfort deep in his lower back and buttocks that awakened him from sleep. He could not localize the discomfort to a single area. The discomfort grew in intensity during the night and often he would awaken feeling “stiff in the back”. The stiffness and discomfort usually disappeared shortly after arising and walking around for a few minutes or while taking a hot shower and it responded slightly to NSAIDs.

Once in college, RN noticed his left eye was becoming red and felt “gritty.” He noted blurry vision and went to the college health service complaining of “pink eye”. The examining physician said the problem was not in the conjunctiva, but that there was a ciliary flush indicative of acute anterior iritis. She took a family history that revealed a maternal uncle developed a “poker spine” as a young adult (Fig. 1) and that RN’s mother had Crohn’s disease as a young adult, but that it was in full remission for many years.

Physical examination revealed tenderness over RN’s sacroiliac joints, a loss of the normal lumbar lordosis, and the inability to come no closer than 12” from touching the floor. Both hips were found to be limited in internal and external rotation by 15-20° and there was a 30° loss in flexion bilaterally. Chest expansion was unimpaired. The remainder of the physical examination was normal. X rays of the spine, SI joints, and hips were normal except for loss of the lumbar lordosis. He was referred to a New York institution for further evaluation. MRI with gadolinium enhancement revealed extensive bilateral inflammation of the SI joints, hip joints, and extensive involvement of the lumbar and sacral spine. Pulmonary function tests, an aortic root echocardiogram, and an EKG were all normal. HLA typing performed by a research laboratory revealed the father to be HLA-A1, A3, B7, B8; the mother HLA-A1, A2, B12, B27; RN HLA-A2, A3, B7, B27; and a healthy sister to also be HLA-A2, A3, B7, B27.



**Fig. 1.** Typical “poker” or “bamboo” spine in a patient with advanced ankylosing spondylitis.

RN was placed on various NSAIDs with minimal relief in his symptoms. RN agreed to a synovial biopsy for research purposes. A biopsy of his right hip revealed proliferation of the synovial lining and infiltration of the synovium with both CD4<sup>+</sup> and CD8<sup>+</sup> lymphocytes, plasma cells, and many activated macrophages. In addition to the inflammation, there was fibrosis of the joint and capsular ossification. RN's physician next decided to put him on Methotrexate. RN reported marked improvement and remained well for approximately two years. He then experienced a severe flare of his arthritis after being noncompliant with the medication. Because of progressive hip arthritis and back pain RN was started on intravenous Infliximab (a TNF- $\alpha$  inhibitor), which resulted in a prolonged remission.

### **Questions for Case 21**

- (1) Explain how HLA genes play a role in disease pathogenesis. What reasons could you give to explain why RN's sister is not affected despite sharing the same HLA genes?
- (2) The research report of the synovial biopsy revealed most of the lymphocytes were non-clonally expanded polyclonal CD4<sup>+</sup> T cells and a minor proportion of highly clonally expanded CD8<sup>+</sup> T cells. What does this tell you about some of the events responsible for the accumulation of lymphocytes in the synovium? Why might there be plasma cells in the synovium if there are no autoantibodies?
- (3) Why does methotrexate work for inflammatory diseases? Explain how TNF- $\alpha$  blockade is useful in treating spondyloarthritis.
- (4) Provide an explanation for why patients with advanced AIDS, who virtually lack all CD4 T cells still get an initial episode of an immunologically-mediated spondyloarthritis disease in their immunosuppressed state.
- (5) Extra-articular manifestations of AS are common and significant. What cardiac and pulmonary manifestations of AS occur and how common are they?