Case 19

C.G. is a 45 year-old woman who developed polyarthritis involving her metacarpalphalangeal (MCP) joints, wrists, feet, ankles, and knees. Her family history was notable for a cousin with severe rheumatoid arthritis (RA); a photograph and X-ray of the cousin’s hands are shown below; Figs. 1-2). Physical examination was remarkable for ulnar deviation of multiple digits of both hands and mild tenderness of multiple MCP joints with decreased range of motion. Laboratory tests showed a positive rheumatoid factor of 1:320, mild anemia, and an ESR (erythrocyte sedimentation rate) of 65 (increased). RA was diagnosed and NSAIDs were started; the patient noted some improvement. Several months later her arthritis worsened and she became increasingly incapacitated with stiffness and pain especially in the morning. A short course of corticosteroids resulted in marked improvement but she relapsed when the steroids were discontinued. Hydroxychloroquine was added, followed by methotrexate. When first seen at CPMC she was taking hydroxychloroquine 200 mg twice a day, methotrexate 15 mg once a week, folic acid, and Celebrex (a selective COX-2 inhibitor) 200 mg twice a day. Despite these medications the patient had greater than an hour of morning stiffness, difficulty getting dressed, and pain upon walking. On review of systems she complained of a dry mouth and dry eyes for which she had begun using artificial tears. Physical exam was normal except for enlarged parotids, a dry oropharynx, and synovitis of MCPs, PIPs (proximal interphalangeal joints), and wrists with a large synovial cyst of the right wrist. She was unable to make a fist. Her ankles were tender, warm, and swollen. There were no nodules. Low dose prednisone (10 mg/day) and Enbrel (etanercept), 25 mg subcutaneously twice a week, were added to her regimen. Within several months she noted improvement in her symptoms with minimal joint stiffness. She had been able to taper the prednisone gradually to 4 mg daily and was exercising regularly. Physical exam showed only trace swelling over her MCP joints. She was able to make a tight fist with good grip strength. Laboratory tests showed an ESR of 8, a normal hematocrit, and a rheumatoid factor of 1:1280.

Fig. 1. Photograph of cousin’s hand demonstrating severe ulnar deviation of MCP joints.
**Questions for Case 19**

(1) Although synovial biopsies are not routinely performed in RA, they can sometimes be informative. Describe the typical features of a synovial biopsy in this disease and the cell types found in the biopsy.

(2) About 75% of patients with RA demonstrate elevated titers of rheumatoid factor. What role might rheumatoid factor or other antibodies play in the development of joint destruction? How can you account for the development of RA-like arthritis in patients with agammaglobulinemia?

(3) Rheumatoid arthritis, multiple myeloma, and osteolytic bone metastasis share the common manifestation of bone erosion and destruction. What is the major cell type responsible for this and what soluble factors promote its activity? What soluble factor inhibits its activity?

(4) Describe the potential roles of IL-2, IL-1, IFN-γ and TGF-β in the pathogenesis of RA.

(5) What are mechanisms of action of prednisone, hydroxychloroquine, methotrexate, etanercept, infliximab, NSAIDS, and COX-2 inhibitors in the therapy of RA?

(6) Bone erosion is halted in about 70% of patients treated with TNF-α antagonists. What are some biological effects of TNF-α relevant to the pathogenesis RA?

**Fig. 2.** X-ray of cousin’s hands demonstrating severe ulnar deviation of MCP joints.