

Synovial fluid examination for the diagnosis of amyloidosis

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Amyloidosis is a well-recognized complication of multiple myeloma. Examples of patients with myeloma having a symmetrical polyarthritis resembling rheumatoid disease as a consequence of synovial deposition of amyloid have also been documented (Stewart and Weber, 1938; Tarr and Ferris, 1939; Hoessly and Greenberg, 1952; Davis, Weber, and Bartfeld, 1957; Hamilton and Bywaters, 1961; Goldberg, Brodsky, and McCarty, 1964; Arkin and Ward, 1968; Bernhard and Hensley, 1969). Recently we have encountered three patients with kappa light chain disease who were erroneously considered to have rheumatoid arthritis. In the course of synovial fluid examination, the aspirates obtained from these patients revealed small sequestered fragments of synovial villi containing amyloid, thereby establishing the diagnosis of amyloidosis before confirmation by tissue biopsy (Cohen, 1967).

Case reports

Case 1 (a 67-year-old man), Case 2 (a 77-year-old man), and Case 3 (a 75-year-old woman), presented in 1968, 1970, and 1971 respectively, with a polyarthritis clinically indistinguishable from rheumatoid arthritis.

All had involvement of wrists, fingers, elbows, shoulders, knees, ankles, and feet of approximately 2 years' duration. None had nodules and the latex-fixation and L.E. tests were negative. Marrow aspirates showed a predominance of atypical plasma cells and isolated osteolytic lesions were seen on x ray in each case. All three had a visible spike of Bence Jones globulin on urine protein electrophoresis. Immunoelectrophoresis demonstrated Bence Jones type kappa globulin in the serum and urine of all cases and in the synovial fluid of two patients. Yellowish, viscous fluid having a good mucin clot was aspirated from the right wrist and left knee of Case 1, from the left shoulder and knees of Case 2, and from the shoulders of Case 3.

The mean white cell count of 2,460/mm³. (440-4,560) from these aspirates consisted predominantly of large mononuclear cells (Fig. 1), although polymorphonuclears and plasma cells were also seen. Synovial fluid from the right knee of Case 3 had a poor mucin clot and a white cell count of 10,440/mm³ with 94 per cent. polymorphonuclears. No crystals were detected by polarizing microscopy.

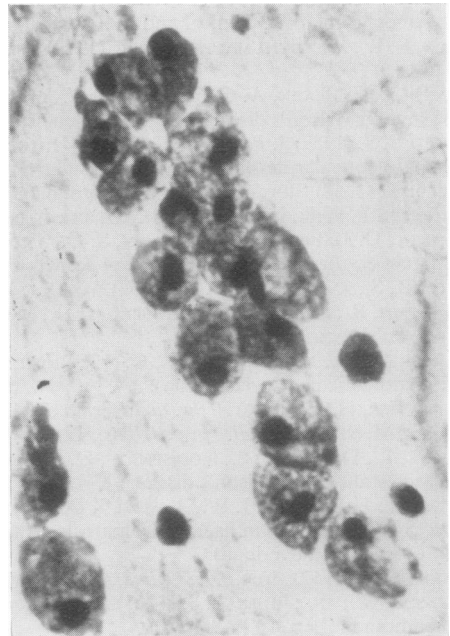


FIG. 1 Case 1. High-power view of aspirated synovial fluid, showing predominantly mononuclear cells. $\times 300$

When the synovial fluids from these patients were centrifuged, paraffin sections of the sediment showed papillary fragments having the appearance of synovial villi which stained vividly with Congo red (Fig. 2). Little associated cellular reaction was evident. On polarizing microscopy, the Congo red positive areas (Fig. 3, left) also showed green birefringence (Fig. 3, right) typical of amyloid (Cohen, 1967). Biopsies of synovium were obtained later from the right wrist of each patient and revealed similar histological findings.

Discussion

The diagnosis of multiple myeloma (kappa light chain disease) appears to have been well established in our cases, based on the evidence of marrow plasmacytosis, bony involvement, and Bence Jones type kappa protein in the serum, urine, and synovial fluid. No radio-

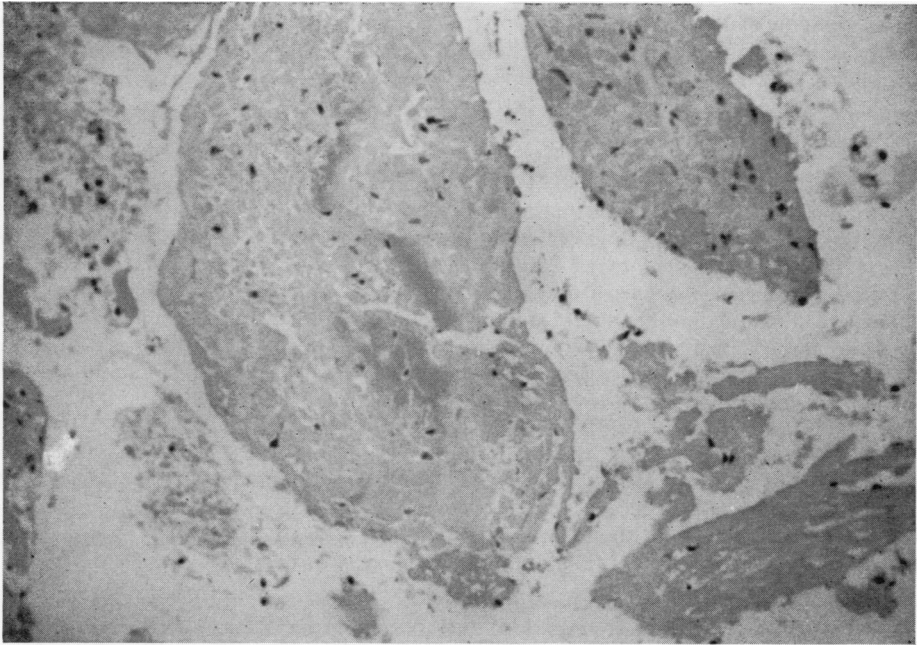


FIG. 2 Case 2. Medium-power view of synovial fluid aspirates which contained fragments of synovial villi with amyloid deposition. Congo red stain. $\times 50$

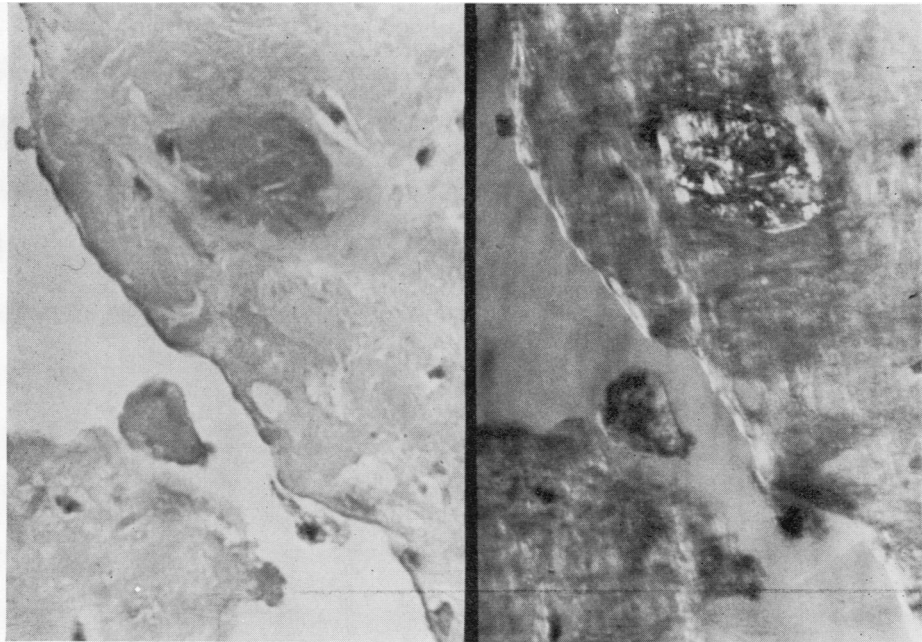


FIG. 3 Case 3. High-power view of aspirated synovial fragments, showing amyloid deposition by direct microscopy. Congo red stain (left) and birefringence by polarizing microscopy (right). $\times 300$

logical, serological, or histological evidence of coincidental rheumatoid arthritis was found. Furthermore, with the exception of the synovial fluid from the right knee of Case 3, all the synovial fluids examined lacked the inflammatory characteristics of rheuma-

toid arthritis (Goldberg and others, 1964; Arkin and Ward, 1968; Bernhard and Hensley, 1969). The presence of amyloid in synovial fluid and synovial biopsies in these cases is consistent with an arthropathy resulting from amyloid infiltration of synovial

tissues. The association of Bence Jones type kappa protein and amyloidosis in our cases is also in keeping with recent evidence that light chains may be important constituents of amyloid (Glenner, Ein, and Terry, 1972).

Tarr and Ferris (1939) made the *post mortem* observation that free gelatinous masses of amyloid may be sequestered in the joint cavity. However, the significance of their observation appears to have been overlooked, since the examination of synovial fluid for amyloid has to our knowledge not been previously reported. Our cases illustrate that the examination of synovial aspirates for fragments of villi containing amyloid may be of diagnostic assistance and a valuable aid in distinguishing amyloid synovial involvement from that of rheumatoid arthritis. In fact, amyloid deposition in synovium may be more common than is generally suspected, even in the absence of obvious joint manifestations. In one recent example of proven generalized amyloidosis without articular complaints seen in our unit, careful examination of

the joints revealed a small effusion in one knee, which on aspiration showed synovial fragments containing amyloid.

Summary

Three patients presenting with a polyarthritis resembling rheumatoid arthritis were found to have kappa light chain disease. Synovial fluids aspirated from these patients were yellow and viscous with a good mucin clot test. The mean cell counts were 2,460/mm.³ and consisted predominantly of mononuclear cells. Fluids from two patients contained Bence Jones type kappa globulins. Of interest was the observation that small fragments of villi containing amyloid tissue were detectable in the sediment of these fluids. Examination of synovial fluid, therefore, may be helpful in distinguishing rheumatoid disease from amyloid arthritis without the necessity of tissue biopsy.

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