

Polymyalgia rheumatica and renal amyloidosis

REPORT OF A CASE

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POLYMYALGIA rheumatica is a common but frequently unrecognized syndrome of widespread muscular and periartritic pains, muscle stiffness, and constitutional disturbance.¹⁻⁵ The cause of polymyalgia rheumatica is not known, but it is often regarded as a variant of rheumatoid arthritis,^{1, 3, 6} and has been designated by various names.^{3, 5-7} The term polymyalgia rheumatica is more suitable than any other because it carries no etiologic connotations.^{1, 8}

Our report concerns a patient in whom renal amyloidosis developed five years after the onset of polymyalgia rheumatica. This association of diseases illustrates an unusual facet of a usually benign syndrome.

REPORT OF A CASE

A 57-year-old man was first examined at the Cleveland Clinic, in February 1963, because of pyrosis and abdominal discomfort. He had a five-year history of migratory pains in the back, chest, ankles, knees, shoulders, wrists, and neck. The pains were usually most severe at night and seemed most noticeable when he was not active. The pains in the ribs were worst on deep inspiration. Severe attacks of pain would sometimes last for several days. There was morning stiffness but no swelling of the joints. The patient had nocturnal sweating, slept badly, had lost weight, and had become depressed. Physical examination revealed no abnormality. Neither synovitis nor temporal artery tenderness was present.

Special determinations disclosed the following values: erythrocyte sedimentation rate, 1.45 mm per minute (normal, less than 0.65 mm); serum glycoprotein concentration, 200 mg per 100 ml (normal, less than 160 mg); serum uric acid content, 3.6 mg per 100 ml; lupus erythematosus test, negative; latex flocculation test, negative; urinalysis, normal; and serum protein electrophoresis—albumin, 3.42 g per 100 ml; globulins, α_1 , 0.43 mg, α_2 , 0.88 mg, β , 0.79 mg, γ , 0.88 mg per 100 ml. A cholecystogram and an upper gastrointestinal roentgenogram were normal.

A possible diagnosis was episodic rheumatoid arthritis, and the patient was given salicylates.

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A psychiatric examination revealed a compulsive personality. There was "anxiety in the form of muscular pain and tension with evidence of depression and involuntal overtones." He was given a course of imipramine and chlordiazepoxide.

In October 1964, one year and eight months after the initial examination, he was readmitted to the Cleveland Clinic Hospital for further investigation. The symptoms had persisted, and ankle edema and proteinuria had now developed. He mentioned especially the discomfort in the lower part of the abdomen. He was normotensive and had no other abnormal physical signs.

At this time, special studies disclosed the following values: sedimentation rate, 1.35 mm per minute; blood sugar concentration, 82 mg per 100 ml; serum cholesterol content, 250 mg per 100 ml; blood urea content, 30 mg per 100 ml; serum creatinine concentration, 2.7 mg per 100 ml; creatinine clearance, 49 ml per minute; serum calcium concentration, 9.9 mg per 100 ml; serum phosphate concentration, 3.6 mg per 100 ml; blood hemoglobin content, 12.2 g per 100 ml; leukocyte count, 10,900 per cubic millimeter; serum glycoprotein concentration, 186 mg per 100 ml; sulfobromophthalein retention, 13 percent at 45 minutes; urinary protein, 6 g per 24 hr; urine culture, sterile; serum proteins—albumin, 2.9 g per 100 ml; globulins: α_1 , 0.36 mg, α_2 , 1.32 mg, β , 0.91 mg, γ , 1.01 mg per 100 ml; bone marrow, normal (no increase in plasma cells). Roentgenograms of the chest, lumbosacral spine, left ankle, left wrist, and of the lower gastrointestinal tract after barium enema, were normal. An intravenous pyelogram showed incomplete opacification bilaterally. The kidneys were small but not otherwise abnormal. It was apparent that now a nephrotic syndrome and some renal insufficiency were superimposed on his previous condition. A renal biopsy was performed and showed foci of amyloidosis in arterioles and glomeruli (*Fig. 1*). There were no giant cells in any of the arteries.

He was treated with diuretics and a low-salt diet, and the ankle edema gradually subsided. It was believed that the administration of corticosteroids was not indicated, although chloroquine phosphate was prescribed in an effort to control the patient's rheumatic symptoms. He

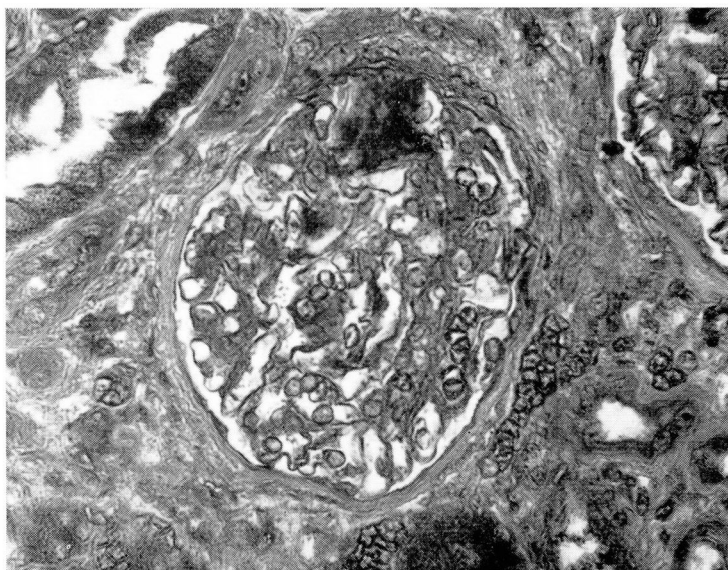


Fig. 1. Photomicrograph of renal biopsy specimen from patient with polymyalgia rheumatica, showing focal distribution of amyloid in the arterioles of a glomerular tuft. Hematoxylin and eosin stain; magnification $\times 400$.

resumed work for several months but fatigue and joint and muscle aching increased, weight loss became severe, anemia was noted, and transfusions were necessary.

In August 1965, two and one-half years after initial examination, the patient was readmitted to the Cleveland Clinic Hospital because of purpura and severe renal insufficiency, both considered to be due to amyloidosis. His condition worsened rapidly and pulmonary edema developed, resulting in death one week after admission to the hospital. Autopsy disclosed systemic amyloidosis affecting kidneys, spleen, liver, adrenals, thyroid, pancreas, and heart, and also pulmonary edema.

DISCUSSION

Polymyalgia rheumatica is a distinctive and easily recognizable syndrome,³ although the clinical features frequently appear to be subjective and non-specific. Most patients are middle-aged or elderly. There are widespread muscular and periarticular pains, joint stiffness, generalized weakness, weight loss, and frequently nocturnal sweating and mental depression. Though swelling of joints is unusual,⁵ limitation of movement may be severe.² The pains are migratory, often influenced by the weather, worst at night, and relieved by phenylbutazone and corticosteroids, and, to some extent, by salicylates. The limb-girdles, chest, neck, and back are most frequently affected. The erythrocyte sedimentation rate is always high. A hypochromic anemia and slight hyperglobulinemia are usual. The serologic tests for rheumatoid arthritis are negative. Lupus erythematosus cells are not found. Thrombocythemia⁷ and plentiful or abnormal plasma cells in the bone marrow⁶ may occur. The disease may last for several years and usually runs a benign course with complete recovery.⁵ Our case constitutes an exception to the usual course of the disease.

Todd³ has emphasized that there is a lack of awareness by clinicians of the existence of this syndrome. Patients with mild disease often may be diagnosed as having fibrositis or psychoneurosis,³⁻⁵ while those with severe disease may be extensively and sometimes unnecessarily investigated. Many patients undergo psychiatric treatment. Barber¹ stated that the patient's melodramatic description of the pains tends to suggest psychoneurosis, until the erythrocyte sedimentation rate has been measured.

As mentioned before, the etiology of polymyalgia rheumatica is not known. It has been considered to be a variant of rheumatoid arthritis,^{1, 3, 6} a form of giant-cell or Takayasu's arteritis,^{7, 9, 10} or an arthritis of the spine and limb-girdles with referred pain.¹¹ Psychologic factors have been thought by some to play a part in precipitating this condition.⁹ Muscle tissue is usually normal,² but nonspecific inflammatory changes have been found in the periarticular structures (joint capsule, bursa, and deep fascia) and in the tendinous septa of muscles.⁸

An interesting diagnostic dilemma is posed by the association in one patient of two entities, each of which is subclassified as primary or as secondary based on the coexistence of other illness. Is myalgia an early symptom of

primary amyloidosis that terminates in renal failure? Or, can polymyalgia rheumatica result in secondary systemic amyloidosis? We do not know.

The frequent association of amyloidosis with rheumatoid arthritis may support the view that polymyalgia rheumatica is an anarthritic form of rheumatoid disease. However, connective tissue disorders frequently overlap, and their definition as entities has a descriptive rather than an etiologic basis. An arthritis that may be indistinguishable from rheumatoid arthritis has been reported to coexist with both giant-cell⁹ and Takayasu's arteritis.¹² Furthermore, Heptinstall, Porter, and Barkley¹³ have described a patient who had renal amyloidosis, temporal arteritis, and an arthritis with rheumatoid features.

One may conclude that the formal classification of polymyalgia rheumatica within the realm of the connective tissue disorders remains unsettled. At present, it is best placed in the vague borderland between rheumatoid arthritis and giant-cell arteritis, and may be related to both. It is of interest that a syndrome indistinguishable from polymyalgia rheumatica has been reported to herald malignant tumor¹⁴ in some patients in whom metastases did not account for the symptoms.

SUMMARY

The syndrome of polymyalgia rheumatica may have serious consequences. This fact is illustrated by the association of polymyalgia rheumatica with renal amyloidosis in the reported case. While polymyalgia rheumatica often follows a benign course, the syndrome may be the earliest manifestation of more serious disease, such as rheumatoid arthritis, giant-cell arteritis, necrotizing arteritis, polymyositis, scleroderma, amyloidosis, or neoplasm.

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