

Case report

Testicular involvement in rheumatoid vasculitis

D.F. Mayer, E.L. Matteson

Mayo Clinic College of Medicine,
Rochester, Minnesota, USA

Dean F. Mayer, MD; Eric L. Matteson,
MD.

Please address correspondence to: Dean
F. Mayer, MD, Division of Rheumatology,
Mayo Clinic College of Medicine, 200
First St SW, Rochester, MN 55905, USA.

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ABSTRACT

We report the case of an adult with rheumatoid arthritis (RA) who developed biopsy-confirmed testicular involvement of vasculitis in the setting of mononeuritis multiplex. This unusual presentation of rheumatoid vasculitis was successfully treated with a combination of corticosteroids and cyclophosphamide.

Introduction

Testicular involvement has been described in numerous autoimmune vasculitic conditions including polyarteritis nodosa, Henoch-Schönlein purpura, Wegener's granulomatosis, giant cell arteritis, Churg-Strauss syndrome, and isolated testicular vasculitis. However, only one case of testicular inflammation has been previously described in the setting of rheumatoid vasculitis (1). In that case, the patient was an 8-year-old boy with testicular swelling in the setting of seropositive juvenile rheumatoid arthritis whose symptoms responded to aspirin. To our knowledge, there are no previous published reports of an adult with testicular involvement of rheumatoid vasculitis.

Case report

A 53-year-old male machinist with a past history of epilepsy controlled by phenobarbital was admitted to the hospital with progressive weakness of the upper and lower extremities.

Seropositive (rheumatoid factor 100 IU/ml) RA was diagnosed 6 years prior to this admission following one year of pain, stiffness and swelling in multiple peripheral joints. Apart from nodules, there were no extraarticular manifestations evident at that time. Hydroxychloroquine 400 mg daily was prescribed, and joint symptoms improved. The patient later abandoned this medication in favor of shark cartilage supplements.

Five months prior to the admission the

patient developed escalating inflammatory joint symptoms. Methotrexate 7.5 mg weekly and prednisone at doses ranging from 5 to 15 mg a day were prescribed.

Two months thereafter he developed paresthesias of the left lower extremity that were followed by a left foot drop after another two months. By the time of admission, sensory disturbance and weakness had also developed in both upper extremities and the right lower extremity.

Examination revealed a well-developed man apart from early rheumatoid deformities and neurologic crippling of the arms and legs. Palpable purpuric lesions were evident on the extremities and flanks. There was active synovitis in the hands and feet in a typical rheumatoid distribution. Neurogenic peripheral paralysis was evident with bilateral claw hands and drop feet. Both distal lower extremities were completely insensate to light touch, and there was partial anesthesia of the distal upper extremities.

Laboratory studies revealed rheumatoid factor 765 IU/ml, and hand radiographs showed periarticular erosions consistent with rheumatoid arthritis. Assays for circulating antineutrophil cytoplasmic antibody (ANCA), hepatitis B and C virus antibodies and cryoglobulins were negative. Serum albumin was decreased to one-half the lower limit of normal. Serum creatinine, urine protein and urine microscopy were normal. Erythrocyte sedimentation rate was accelerated at 92/mm.

Electromyogram disclosed a severe polyradiculopathy, and sural nerve biopsy was consistent with necrotizing vasculitis. Biopsy of the purpuric skin lesions revealed a cutaneous leukocytoclastic vasculitis. Prednisone was increased to 60 mg daily. The neurologic and cutaneous manifestations stabilized and the joint inflammation improved.

After one week at the increased corticosteroid dose, the patient developed severe testicular pain. Urinalysis demonstrated sterile pyuria (21-30 WBC/hpf). The beta subunit of human chorionic gonadotropin (β -hCG) was elevated to ten times the upper limit of normal, and scrotal ultrasound revealed asymmetric hypoechoic regions of the testes consistent with infarction. Unilateral radical orchiectomy was performed which revealed a leukocytoclastic vasculitis of the testis (Figs. 1-3).

Intravenous methylprednisolone 1000 mg daily for 3 days was added to the oral prednisone 60 mg daily, oral cyclophosphamide 2 mg/kg (150 mg) daily was started, and phenobarbital was eliminated from the regimen to avoid the enhancement of corticosteroid metabolism. The vasculitic process stabilized and pain in the remaining testicle subsided. The patient was discharged from the hospital after a period of rehabilitation on cyclophosphamide and a tapering course of prednisone. During outpatient follow-up he did have one recurrent episode of scrotal pain but no evidence for further infarctive tissue necrosis.

Discussion

Overt vasculitis is regarded as an infrequent extraarticular complication of RA, with an estimated 30-year cumulative incidence of less than 5% (2). The majority of cases involve cutaneous manifestations, with internal organ involvement being less common (2). Rheumatoid vasculitis can involve virtually every organ in the body, but apart from the adrenal glands and pancreas, those in the endocrine system are usually spared (3, 4). Testicular involvement of rheumatoid vasculitis in an adult has not been previously reported. Rheumatoid vasculitis may not only be associated with a significant increase in mortality when compared to RA controls (5), but can cause substantial morbidity due to organ injury as illustrated in this case with crippling neurologic involvement and necrotic testicular involvement. Compounding the disease effects, treatment with immunosuppressants may also prove toxic, and infections were found to be the leading



Fig. 1. Left testis showing necrotic tissue.

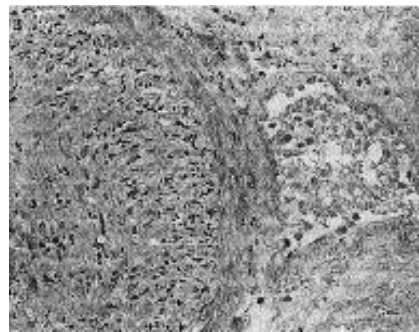


Fig. 2. Leukocytoclastic vessel inflammation and necrotic seminiferous tubule

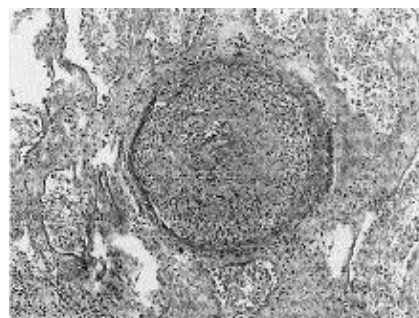


Fig. 3. Thrombosed inflamed vessel with surrounding seminiferous tubules and necrotic germ cells.

cause of death in one series (6). Factors associated with the development of rheumatoid vasculitis include high-titer rheumatoid factor, other extraarticular features, joint erosions, and male gender (5, 7). Other suggested

associations have included ANCA specific for myeloperoxidase (8) or lactoferrin (9) and HLA-DRB1*0401 allele homozygosity (10).

As a result of the rarity of rheumatoid vasculitis, the lack of accepted diagnostic criteria, and the protean manifestations of the syndrome, there are no guidelines to direct treatment and controlled clinical trials are few. Over three decades ago a randomized controlled trial compared azathioprine 2.5 mg/kg daily with placebo in a small number of patients said to have rheumatoid vasculitis (11). There was felt to be no ascertainable benefit, with very scant details provided in the publication. Other treatment strategies have included corticosteroids, cyclophosphamide, d-penicillamine and plasmapheresis, and there are various published anecdotal case reports or case series that suggest some success with each therapy. Recently, the role of cytokines including tumor necrosis factor alpha (TNF- α) has become of interest (12), and there are several reports of successful treatment of rheumatoid vasculitis with the TNF- α antagonists etanercept (13), lenercept (14) and infliximab (15, 16).

Rheumatoid vasculitis is a rare but serious extraarticular manifestation of RA that carries the risk of substantial morbidity. Although cutaneous vasculitis is most common, unusual presentations with internal organ involvement may occur and require vigilant awareness on the part of the treating physician. Optimal treatment of this complication is not well defined, but various therapies including the combination of corticosteroids and cyclophosphamide administered in this case have been used with success. The role of biologic agents in the management of rheumatoid vasculitis remains uncertain.

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