CASE REPORT

Orchitis in lupus/scleroderma overlap syndrome: a case report and literature review

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Testicular involvement in connective tissue diseases (CTD) is typically caused by medium vessel vasculitis as in polyarteritis nodosa. Systemic lupus erythrematosus (SLE) and systemic sclerosis cause small vessel vasculitis, which is an unusual cause of orchitis. We hereby report a case of orchitis in a 28-year-old patient caused by vasculitis related to his lupus/scleroderma overlap CTD. He had an excellent response to steroids and azathioprine with complete resolution of his testicular and systemic symptoms. Our case highlights that although testicular involvement secondary to small vessel vasculitis in CTD is uncommon, it is still possible and should be evaluated.

Key Words: testicular, vasculitis, autoimmune diseases, systemic lupus erythematosus, systemic sclerosis

Introduction

Testicular involvement secondary to systemic vasculitis is frequent in diseases like polyarteritis nodosa. Orchitis in connective tissue diseases (CTD) is usually secondary to medium vessel vasculitis. Systemic lupus erythrematosus (SLE) and systemic sclerosis cause small vessel vasculitis, which is an unusual cause of orchitis. We here present a case of orchitis in a patient with overlap connective tissue disease systemic lupus erythrematosus and systemic sclerosis.

Case presentation

A 28-year-old African American male presented with a 3 day history of acute right testicular pain associated with general malaise, abdominal pain, nausea, vomiting and diarrhea.

He had a history of overlap connective tissue disease (systemic lupus erythrematosus and systemic sclerosis) diagnosed in 1995. His clinical features for SLE were: polyarthritis and serositis as well as laboratory findings of lymphopenia, positive antinuclear antibody, double stranded DNA and anti-Smith antibodies. His clinical features for systemic sclerosis were: sclerodactyly, diffuse skin thickening along his upper extremities and chest, severe raynaud's complicated with digital ischemia requiring surgical amputation as well as laboratory findings of positive anti-centromere antibodies. He smokes one pack per day for the past 2 years and drinks three cans of beer every week. He uses marijuana occasionally and last use was 2 months prior to his presentation. Prior to his admission, he was on prednisone 5 mg daily, nifedipine 30 mg daily, aspirin 81 mg daily and hydrocodone as needed. He was allergic to penicillin (developed rash).

On presentation patient was afebrile. Examination revealed lower abdominal tenderness and bilateral swollen, tender and erythematous scrotum. Laboratory tests showed: WCC 4.4 TH/CMM (with 11% lymphocytes), C_3 89 mg/dL, C_4 13 mg/dL, ESR 120 mm/hr, CRP 7.7 mg/dL, and DsDNA 488 U/mL. The rest of the CBC, complete metabolic panel and urine analysis were within normal limits. Blood and urine cultures, chlamydia and gonorrhea PCR, antiphospholipid antibody panel, lupus anticoagulant, hepatitis panel, cryoglobulins, myeloperoxidase and anti-proteinase 3 antibodies were all negative. Testicular MRI and ultrasound showed bilateral testicular wedge shaped areas of decreased enhancement and echogenecity, representing areas of infarction, Figure 1. There was no evidence of microaneurysms or testicular torsion. CT abdomen and pelvis and liver ultrasound showed cholelithiasis with no biliary ductal dilatation or pericholecystic fluid collection. We recommended a testicular biopsy for histological confirmation but the patient declined.

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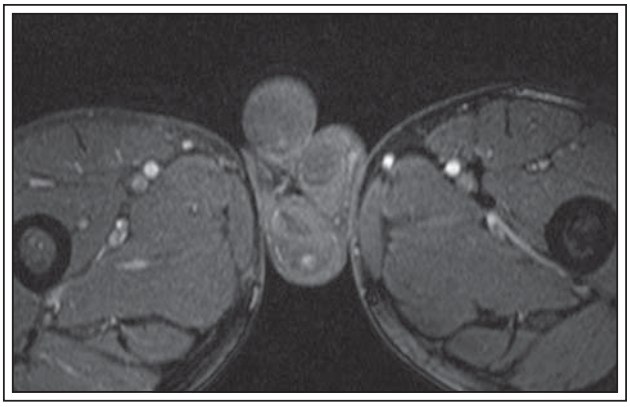

Figure 1. Testicular MRI showing wedge shaped areas of decreased enhancement in bilateral testicles representing areas of infarction.

A clinical diagnosis of bilateral orchitis and serositis was made. There was no evidence of infection as the underlying cause of his orchitis-blood and urine cultures, chlamydia and gonorrhea PCR were all negative. His testicular symptoms were likely caused by vasculitis related to his overlap syndrome. This also seemed to be a flare up of SLE rather than systemic sclerosis due to low complements, elevated DsDNA, lymphopenia, serositis and disproportionately high ESR compared to CRP. He was so treated with intravenous methylprednisolone (1mg/kg every 8 hours slowly tapered to 1 mg/kg/day) followed by oral prednisone (1 mg/kg/day) along with azathioprine (initially 100 mg daily then increased to 150 mg daily) and hydroxychloroquine (400 mg daily). Aspirin and the calcium blocker were continued.

Upon 4 weeks follow up, his testicular and systemic symptoms resolved and laboratory values markedly improved including ESR, CRP and complements as shown in Table 1.

TABLE 1. **Laboratory values on presentation and at follow up**

	On presentation	**4 weeks follow up**	**8 weeks follow up**
White cell count (4.0-11.0) TH/CMM	4.4	7.8	10.3
Lymphocytes % (25-46) %	11.0	24.0	26.5
Westergren sed rate (1-9) mm/hr	120	26	6
C-reactive protein (0.0-0.9) mg/dL	7.7	1.6	< 0.5
Ds DNA antibody (0-99.9) u/mL	488		279
Complement 3 (90-180) mg/dL	89	85	101
Complement 4 (16-47) mg/dL	13	20	27

Discussion

Acute scrotal pain is one of the most common presenting symptoms in urology. Epididymo-orchitis, testicular torsion and testicular tumors are common reasons for this symptom.

Epididymo-orchitis is predominantly caused by bacterial or viral infections. Sexually transmitted epididymitis is usually secondary to chlamydia trachomatis or neisseria gonorrhea and represents the most frequent cause of acute scrotal swelling in men younger than 35 years of age.[1] Mumps is the most frequent cause of viral orchitis.[1]

In rare cases, epididymo-orchitis can be secondary to systemic vasculitis as in polyarteritis nodosa, churg-Strauss angiitis, Henoch-Schonlein's purpura, Wegner's granulomatosis, behcet's, relapsing polychondritis, dermatomyositis or isolated testicular vasculitis.[2-11]

As summarized in Table 2, testicular involvement has been reported in only two cases of SLE, one case of lupus-like disease and none in systemic sclerosis. The first case was a 31-year-old man presenting with isolated testicular pain with no other systemic features of lupus.[12] He had a positive ANA and DsDNA antibodies, elevated ESR and anemia. Biopsy of the testis showed acute vasculitis matching the clinical diagnosis of SLE. He was successfully treated with steroids.

The second case was a 37-year-old South Asian man who presented with fever, joint pain, rash and testicular pain.[13] He had a positive ANA and DsDNA antibodies, lymphopenia, low complements and a kidney biopsy showing Class III lupus nephritis. His testicular pain and systemic symptoms responded well to steroids and azathioprine.

The third case was a 58-year-old patient with lupus-like disease who fulfilled 3 of the 11 ACR classification criteria for SLE: positive ANA (but DsDNA antibodies were negative), arthritis and photosensitive rash.[14,15] He had recurrent episodes of testicular pain and swelling, treated as infected epididymo-orchitis with antibiotics but infection was never proven. He eventually had a testicular biopsy showing evidence of vascular involvement and tubular damage with lymphocytic infiltration, but the specimen was too small to show a clear vasculitis. He was treated as lupus with steroids and azathioprine with a good response.

TABLE 2. **Reported cases with lupus orchitis**

Author	Age (yrs)	ANA	Ds DNA antibodies	Other features	Testicular biopsy	Treatment	Response
Kuehn[12]	31	Positive	Positive	No other systemic features of lupus	Acute vasculitis	Steroids	Good
MacIver[13]	37	Positive	Positive	Joint pain, rash, lymphopenia, biopsy proven Class III lupus nephritis	Not done	Steroids and azathioprine	Good
Walker[14]	58	Positive	Negative	Arthritis, photosensitive rash	Vascular involvement with lymphocytic infiltration	Steroids and azathioprine	Good

We treated our patient as vasculitis related orchitis without histological confirmation, given he had no evidence of infection – negative urine and blood cultures, negative chlamydia and gonorrhea PCR. Moreover, in favor of a vasculitic origin was the correlation between his testicular symptoms and the flare of his systemic disease. His dramatic clinical response to steroids and steroid sparing drugs was again more compatible with a vasculitic origin.

This patient highlights that testicular involvement secondary to small vessel vasculitis can be encountered during the course of the underlying illness and should be aggressively worked up and treated. It may not always be possible to get a histological confirmation of the vasculitis and may need to be treated clinically. All reported cases had a good response to steroids and steroid sparing agents without the need for more aggressive treatment with cytotoxic drugs like cyclophosphamide. It is prudent to closely follow up these patients as there is still not much known at this point on their long term outcome. Further insight is needed regarding the reccurence rate, long term effects on sexual function and testosterone levels.

Conclusion

Testicular involvement secondary to small vessel vasculitis, specifically SLE, is rare but this differential diagnosis should be kept in mind when dealing with patients known to have autoimmune disease.

Although testicular involvement of autoimmune disease can be proven only by histology, in some patients conservative treatment of the primary disease without surgical intervention is possible.

Treatment of testicular vasculitis secondary to SLE includes steroids with or without a steroid sparing agent, usually with a good outcome. □

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