CASE REPORT

IgA Vasculitis with scrotal involvement - a rare presentation in adults

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ABSTRACT

IgA vasculitis (IgAV) is a small-vessel vasculitis common in children but rare in adults. It is usually an auto-limited disease in children but has a more severe course and worse prognosis in adults. The classical manifestations are non-thrombocytopenic purpura, arthralgias, gastrointestinal involvement and renal involvement. Herein we report a case of a 39-year-old man with a rash of the lower limbs associated with testicular and lower abdominal pain. The initial study revealed increased inflammatory biomarkers and enlarged left testis with bilateral ischemic areas on doppler ultrasound. A cutaneous biopsy later revealed leukocytoclastic vasculitis, confirming the diagnosis of IgAV with scrotal involvement. The patient started prednisolone, with improvement in the first week and sustained remission after two years of follow-up. This case report describes an adult with IgAV and scrotal involvement, which is rarely reported in adults and appears to be different from the one in children. The prevalence of scrotal involvement is presumably underestimated. In all men with IgAV, a scrotal examination should be performed and ultrasonography accordingly since it affects the treatment and follow-up. Recommendations for IgAV diagnosis and treatment in adults are still lacking and more research is needed.

KEYWORDS: IgA Vasculitis; Henoch-Schönlein purpura; Scrotum; Doppler Ultrasound; Adult

INTRODUCTION

IgA vasculitis (IgAV), formerly known as Henoch-Schönlein purpura, is a small-vessel vasculitis mediated by IgA-dominant immune complex deposition and accompanied by high levels of IgA in up to 40% of cases [1].

IgAV primarily affects children and has been extensively studied in this population group, usually recognized as an auto-limited disease with a good prognosis. Nevertheless, IgAV can also affect adults, with a reported estimated annual incidence rate of 0.8-1.8 cases per 100 000 adults. More recent studies revealed approximately 3 to 6 times higher estimated incidence rates, suggesting an underestimation of IgAV cases in the adult setting [2,3]. The mean age of diagnosis in this population ranges from 32 to 50 years, with a slight male predominance [4]. In addition, unlike in children, IgAV is commonly associated with a more severe course and has a worse prognosis in the adult population [5,6].

IgAV is typically characterized by non-thrombocytopenic palpable purpura (the first manifestation in 75% of cases), arthritis/arthralgias, gastrointestinal symptoms, and renal involvement [1]. An upper respiratory infection commonly precedes this entity [4].

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Even though the *European League Against Rheumatism/ Paediatric Rheumatology International Trials Organization/Paediatric Rheumatology European Society* (EULAR/PRINTO/PRES) consensus criteria for IgAV is only validated for children, Hočevar et al. [7] and Perre et al. [8] demonstrated a 99% sensitivity and specificity for the diagnosis in adults, significantly higher than with the previous 1990 American College of Rheumatology criteria. These criteria include purpura or petechiae with lower limb predominance (mandatory and not related to thrombocytopenia) and at least one of the following: abdominal pain; histopathology findings of leukocytoclastic vasculitis with predominant IgA deposit or proliferative glomerulonephritis with predominant IgA deposit; arthritis or arthralgia; renal involvement [7].

Although there are classic features of IgAV, many other manifestations can occur. Herein we report a case of IgAV with testicular involvement, which has been rarely described in adults with IgAV.

CASE DESCRIPTION

A 39-year-old man presented to the Emergency department with a four-day history of a purpuric skin rash on the lower limbs associated with testicular pain. The day before admission he started exhibiting persistent lower abdominal pain, with no fever or other gastrointestinal or genitourinary

symptoms. He also denied a recent history of infection or trauma

He had a past medical history of obesity and dyslipidemia and was under no medication.

On physical examination, besides bilateral and symmetrical palpable purpura on the lower extremities (Figure 1), he presented abdominal tenderness in the lower quadrants, without signs of peritoneal irritation, and a tender and enlarged left testicle, with an elastic consistence and no skin alterations or palpable masses.

Blood tests showed a normal hemogram and clotting times with a slightly high erythrocyte sedimentation rate of 22mm/hr and C-reactive protein of 3.92mg/dL (NR < 0,50mg/dL). Creatinine, urea, liver enzymes and urinalysis were also within the normal range.

Testicular ultrasound revealed enlargement of the left testis, with areas of heterogeneous parenchyma without doppler signal, and a normal-sized right testis, with smaller areas with reduced doppler signal (Figure 2). The abdominal ultrasound was unremarkable.

He was admitted with a diagnosis of non-thrombocytopenic purpura with probable testicular vasculitis. A thorough study was performed to clarify the etiology: anti-streptolysin O (ASO), antinuclear antibodies (ANA), anti-double stranded deoxyribonucleic acid (anti-dsDNA), extractable nuclear antigens (ENA) screen, perinuclear and cytoplasmatic anti-neutrophil cytoplasmic antibodies (p-ANCA, c-ANCA), antiphospholipid antibodies, lupus anticoagulant and serum immunoglobulins were in the normal range, with a slight increase of C3 and C4 (C3 194mg/dL - NR 83-177mg/dL; C4 37.7mg/dL- NR 12-36mg/dL). A skin biopsy was performed which revealed leukocytoclastic vasculitis (immunofluorescence was not performed due to technical issues). A colonoscopy was performed to exclude colon involvement and no alterations were found.

A diagnosis of IgA vasculitis with cutaneous and testicular involvement was made, and he immediately started treatment with prednisolone 1mg/kg/day with clinical improvement in the first week of treatment. After discharge from hospital, he maintained prednisolone that was tapered for 2 months and then stopped. A follow-up testicular ultrasound was performed revealing a smaller testicular size, with heterogeneous structure and apparent scar tissue with preserved doppler signal (Figure 3).

After two years of follow-up without immunosuppressive treatment, the patient didn't present signs of relapse.

DISCUSSION

Several retrospective studies comparing IgAV in children and adults revealed that arthralgias, abdominal pain, and the pre-existence of an upper respiratory infection were less common in the latter group. However, in adults, skin ulceration seems to be more frequent and renal involvement is commonly described (68-79%). Regarding renal involvement, in the acute phase, hematuria ad proteinuria may be present, frequently with proteinuria in the nephrotic range and with a higher proportion of patients with impaired renal function (15.8-32% of cases). Furthermore, progression to chronic renal disease is more likely (10-30% of cases with IgAV nephropathy), even after adjustment for baseline estimated glomerular filtration rate [5,6,9,10].

Scrotal involvement in children with IgAV has a medium prevalence of 20% (2-38%) [11-13], but the prevalence of scrotal involvement in adults has not been described. Only a few case reports are published describing scrotal involvement in adults with IgAV (Table 1) [14-18]. Clinical presentation includes scrotal pain, tenderness, swelling and erythema due to acute scrotum, epididymitis, orchitis, or spermatic cord thrombosis, sometimes mimicking testicular torsion [11,19]. Bilateral involvement is seen in 20% of children with IgAV. It is important to emphasize that scrotum involvement can precede or succeed the other IgAV manifestations in days or weeks, which may lead to a delayed or wrong diagnosis [11,12].

Additionally, the frequency of elevated serum IgA in children with scrotal involvement was significantly lower than in patients without this involvement (18 vs 57%, $p < 0,05$) in one study [12], although this association was not seen in a previous study [11]. Ha et al. [11] also showed a significative higher C3 level in the group of patients with scrotal involvement. These findings were found in our patient and can be explained by a possible different

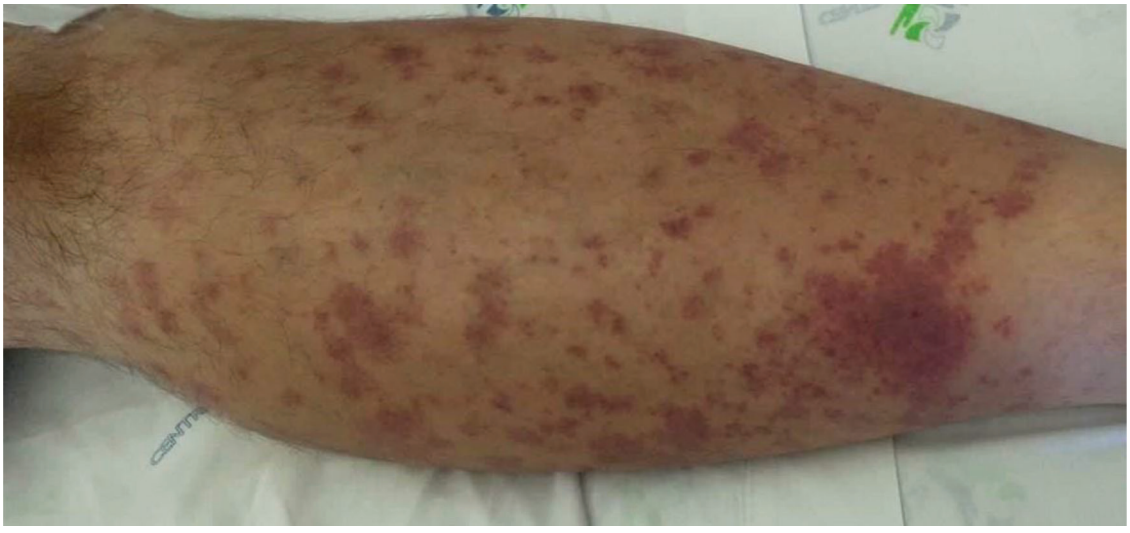

Fig. 1. Palpable purpura of the lower limbs.

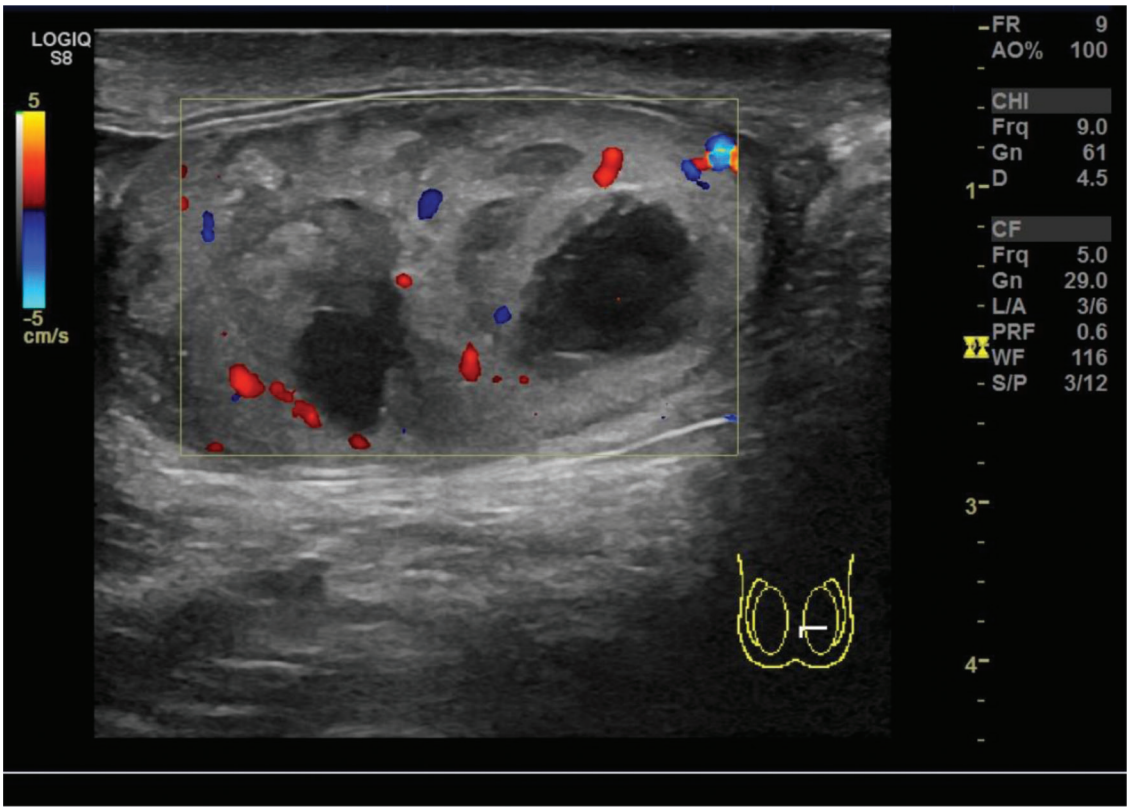

Fig. 2. Scrotal ultrasound with enlargement of the left testis, with areas of heterogeneous parenchyma with reduced doppler signal.

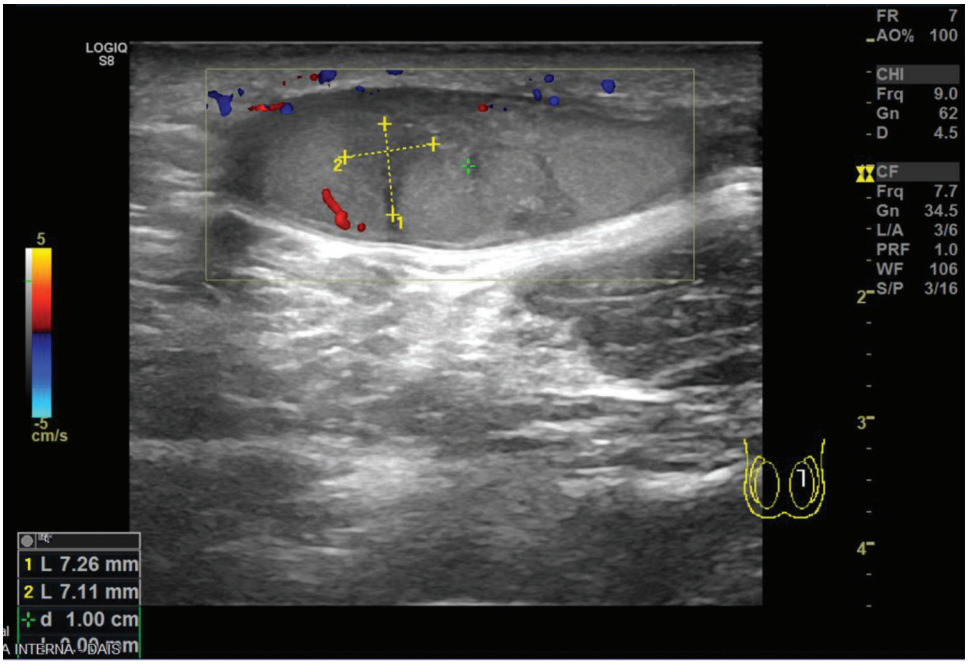

Fig. 3. Follow-up scrotal ultrasound with smaller testicular size, with heterogeneous structure and apparent scar tissue with preserved doppler signal.

pathophysiologic mechanism in these cases. Still, more studies are needed to clarify the pathways involved.

Ultrasonography with doppler in children with IgAV usually reveals epididymal enlargement, scrotal skin thickening, and hydrocele, with normal blood flow and normal morphology of the testis [13]. Scrotal involvement in adults is only described in a few cases, with apparent different findings on ultrasonography. Only three of the

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Table 1. Summary of published case reports of adults with IgA Vasculitis and scrotal involvement

Case	Author (Year)	Gender	Age	Clinical features(in order of appearance)	Scrotal ultrasound	Biopsy	Treatment
1	Mizuashi et al. (2009) [14]	Male	58	- Six-year course of relapsing purpura affecting eyelids, neck, and upper chest, fever and arthralgias - Hematuria and proteinuria - Four months after treatment with immunoglobulin: edematous swelling and tenderness in the scrotum	- Not reported	- Skin: Leukocytoclastic vasculitis, with IgA deposition	- Polyclonal immunoglobulin 20g/day for five days and tonsillectomy previously to the appearance of scrotal involvement - Not reported treatment regimen at the time of scrotal involvement
3	Maynard et al. (2010) [15]	Male	34	- Bilateral testicular pain - Microscopic hematuria - Left renal mass at abdominal CT - Generalized palpable purpura - Arthralgias - Severe abdominal pain and hematochezia	- Not reported	- Skin: Leukocytoclastic vasculitis positive for IgA and C3	- 60 mg of oral prednisone tapered over six months - Partial left nephrectomy
3	Aaron et al. (2013) [16]	Male	37	- Right testicular pain with tender bilateral scrotal swelling and abdominal pain - Generalized petechial rash - Arthralgias	- Bilateral epididymitis with hydrocele - No torsion	- Skin: Leukocytoclastic vasculitis, negative for IgG, IgA, IgM e c3	- Six-week course of oral prednisone
4	Toushan et al. (2017) [17]	Male	51	- Intermittent bloody bowel movements - Purpuric rash of lower extremities, abdomen and scrotum - Severe lower extremity and scrotal edema - Arterial hypertension - IgAV proliferative glomerulonephritis with presenting subnephrotic proteinuria and hematuria	- Hypoperfusion of the left testicle without evidence of torsion	- Skin: Leukocytoclastic vasculitis, positive for IgA, IgM, and C3 - Kidney: Proliferative glomerulonephritis with crescents, with positive IgA staining - Testicle: testicular infarction with testicular abscess with small vessel vasculitis on the spermatic cord with some scattered organizing thrombi in some; positive for IgA	- Broad-spectrum antibiotics - Initiated methylprednisolone 30mg intravenous every 8 hours - Bilateral orchiectomy
5	Lobl et al. (2019) [18]	Male	24	- Palpable purpura on the arms, trunk, and legs - Testicular acute pain, radiating to the lower abdomen - Urinalysis: elevated protein/creatinine ratio and hematuria - Abdominal pain and bloody stools	- Bilateral solid hypovascular or avascular masses - Hypervascular left testicle and epididymis - Repeated ultrasound: testicular infarcts	- Skin: Leukocytoclastic vasculitis positive for IgA	- Prednisone

reviewed cases reported ultrasonography results and, unlike children, some presented testicular morphologic changes and diminished doppler sign [17,18], which is concordant with this case report. These results emphasize the need for research and additional studies on this group, to better understand scrotal involvement, its severity and its consequences.

Differential diagnosis should be made with testicular torsion and other vasculitides like localized testicular vasculitis, polyarteritis nodosa, necrotizing granulomatous vasculitis and spermatic cord vasculitis [19].

Treatment in most cases of IgAV is mainly supportive, implying rest, hydration and symptom relief. Symptoms typically improve after two or three weeks. However, in adults, IgAV is often more severe, less responsive to initial treatment and with a relapsing pattern disease course, which can make the management more challenging [6,8,19,20].

The use of systemic glucocorticoids is controversial in the majority of cases and it doesn't seem to prevent renal involvement. However, systemic glucocorticoids are frequently used in cases of severe cutaneous involvement, IgAV nephritis or other severe extracutaneous manifestations [19]. A significantly higher use of glucocorticoids in children with scrotal involvement (93% vs 49%, $p < 0{,}0001$) has also been observed [12]. The *European consensus-based recommendations for diagnosis and treatment of immunoglobulin A vasculitis* in children [20] recommends the use of corticosteroids in IgAV nephritis, orchitis, pulmonary hemorrhage, cerebral vasculitis and other severe organ or life-threatening vasculitis manifestations. In patients with severe abdominal pain and/or rectal bleeding, glucocorticoids can also be considered. In some severe and refractory cases, the use of immunosuppressive drugs, plasmapheresis, dialysis, and even renal transplantation could be considered [19,20]. Despite these recommendations, specific adult considerations for the management of IgAV are lacking.

Regarding scrotal involvement in adults with IgAV, the severity and adequate treatment are also not defined. In most of the reviewed case reports in adults [15-18], the use of corticosteroids was implemented. In the presented case, corticosteroids were also employed, with an early improvement of scrotal manifestations and sonographic changes, as well as resolution of other IgAV-related symptoms.

CONCLUSION

This case report describes a patient with IgAV and scrotal involvement, which has only been described in a few cases in the literature. It is presumed that the prevalence of scrotal involvement in adults might be underestimated since symptoms are not always clear and the scrotum is not frequently examined in the absence of specific symptoms. The correct assessment of all manifestations of IgAV is essential for choosing adequate treatment and improving the prognosis.

The authors recommend a scrotal examination in all men with IgAV, as well as the performance of ultrasonography in suspicious cases, since it affects the treatment and follow-up of the patient. More studies are needed to evaluate the prevalence, severity, and sonographic changes of scrotal involvement in IgAV adults, which seem different from the ones reported in children. Furthermore, recommendations for IgAV diagnosis, evaluation and treatment in the adult population are still lacking and should be implemented for better clinical practice.

Declaration of interest

The authors have no competing interests to declare.

Informed consent

Informed consent was obtained from the patient for publication of this case report and accompanying images.

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