Polyarteritis nodosa isolated to the testis and urinary bladder in the setting of cryptorchidism: a case report and literature review

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Abstract

Background: Polyarteritis nodosa is a small vessel to medium vessel vasculitis that frequently presents with multi-organ involvement, but can sometimes be limited to single organs such as the testes. Patients often require treatment with glucocorticoids, plus or minus additional immunosuppressive therapy depending on the severity of the disease. We describe a rare case of polyarteritis nodosa involving the right testis and urinary bladder without other systemic features of vasculitis.

Case presentation: A previously healthy 54-year-old First Nations Canadian man presented with intermittent gross hematuria. He underwent surgical excision of his right testis for cryptorchidism and a transurethral resection of a bladder mass. Histology showed an active medium vessel vasculitis in both organs. On extensive clinical, laboratory, and radiographic review, he had no systemic features of vasculitis. On 2-year follow-up, he has not required any systemic therapy and has not developed further symptoms.

Conclusion: Single organ polyarteritis nodosa can sometimes be managed with surgical excision of the involved organ alone. Although our patient had two organs involved, we extrapolated the results of our literature search to guide his care. This case highlights the potential for surgical excision to cure polyarteritis nodosa despite the involvement of two organs in the absence of symptoms and signs of systemic vasculitis.

Keywords: Polyarteritis nodosa, Testis, Bladder, Single organ vasculitis

Introduction

Polyarteritis nodosa (PAN) is a vasculitis characterized by necrotizing inflammation of medium and small arteries. It can affect many organ systems; most often, it affects the peripheral nerves, skin, gastrointestinal system, muscles, and kidneys. The disease often presents with multi-organ involvement, but cases of isolated organ involvement have been described [1, 2]. A detailed history and physical examination are required to identify features consistent with PAN, such as constitutional symptoms, skin lesions, abdominal pain, and peripheral neuropathy. Once PAN is suspected, a biopsy is usually required to confirm the diagnosis. If a biopsy is not possible, angiography is a reasonable alternative [1]. Treatment is based on the severity of illness and involved organs.

In general, cases of mild PAN can be treated with glucocorticoids alone. More severe cases necessitate the addition of immunosuppressive agents, such as cyclophosphamide. Isolated or single organ PAN can be managed by excision of the organ involved (for example, testis) and serial follow-up to ensure that systemic features do not develop [1, 2].

Our case report explores a rare case of PAN affecting both the testis and urinary bladder.

Case presentation

A previously healthy 54-year-old First Nations Canadian man presented with a several-month history of urinary retention and intermittent gross hematuria. In the course
of his initial evaluation, he was found to have an enlarged prostate and was started on tamsulosin with improvement in his urinary symptoms. He noted the absence of his testicle on the right side for at least 30 years, consistent with cryptorchidism. He subsequently underwent cystoscopy, which demonstrated a superficial-appearing mass at the dome of his bladder. A radical right orchiectomy and transurethral resection of the bladder tumor (TURBT) were performed. Surprisingly, a pathologic examination revealed the presence of small and medium vessel vasculitis in both the urinary bladder and undescended testis (Fig. 1). There was no evidence of malignancy. He was referred to rheumatology for further evaluation.

An extensive review revealed no evidence of systemic vasculitis. He had no features of another underlying rheumatologic disorder. His investigations including basic blood work, C-reactive protein (CRP)/erythrocyte sedimentation rate (ESR), and antineutrophil cytoplasmic antibody (ANCA) were normal. Although antinuclear antibody (ANA) was positive (1:320), double-stranded deoxyribonucleic acid (DNA) (dsDNA) and extractable nuclear antigen (ENA) were negative and complements were normal. Rheumatoid factor (RF) was positive at 43 kU/L (reference range < 12 kU/L), but anti-cyclic citrullinated peptides (CCP) antibody was negative and our patient had no features of an inflammatory arthritis. Hepatitis B and C serologies were negative. A diagnosis of PAN was made. His testicular involvement and findings of active small and medium vessel vasculitis on urinary bladder and testis pathology were most consistent with this diagnosis. Given the lack of clinically apparent systemic vasculitis, no immunosuppressive therapy was initiated. Following his radical orchiectomy and TURBT, he had ongoing intermittent hematuria that was investigated with several repeat cystoscopies. An area of erythema was identified on one occasion. A repeat biopsy of the site demonstrated reactive changes and no evidence of vasculitis. A computed tomography (CT) angiogram was done of his abdomen and pelvis to evaluate the possibility of occult vessel involvement elsewhere, and was negative other than wall thickening and fat stranding noted at the anterior bladder. His symptoms have completely resolved following surgery and he has remained asymptomatic over the last 2 years.

**Discussion**

To the best of our knowledge, this is the first case reported in the literature of PAN affecting both the bladder and testis in the absence of systemic involvement. Moreover, this is also the first case of PAN reported in the setting of cryptorchidism. We performed a literature search to find reports of patients with isolated testicular or bladder vasculitis and found 45 such cases (Table 1). The average age of presentation was 39 years (median, 36 years). Of the 45 cases, 39 had isolated testicular vasculitis and 6 had isolated bladder vasculitis. Most cases (34/45) had biopsies that were pathologically consistent with PAN.

For the patients with isolated testicular vasculitis in whom treatment information was available, most (21/32) were treated with surgical excision alone with no reported cases of emergent systemic disease over a mean follow-up of 29 months (median, 24 months). Of the 11 patients who were treated with surgical excision as well as glucocorticoids +/- additional immunosuppressive therapy, 8/11 had evidence of more systemic illness at disease onset (for example, elevated CRP/ESR or constitutional symptoms) (Fig. 2). It is unclear what prompted treatment in the other three cases. Three patients were treated with glucocorticoids alone. Eight patients were treated with glucocorticoids in conjunction with at least one other immunosuppressive therapy [19–23]. Of those eight, four were treated with steroids and cyclophosphamide and the other four were treated with steroids in conjunction with cyclophosphamide and methotrexate, mycophenolate mofetil, methotrexate alone, or azathioprine and rituximab.

Of the 11 patients with isolated testicular vasculitis who received systemic therapy, three went on to develop

![Fig. 1 Bladder and testis histology. Hematoxylin and eosin stains. Sections of both bladder (left) and testis (right) demonstrate active small and medium vessel vasculitis with predominantly mononuclear infiltrate and fibrinoid medial necrosis. Scale bars shown](image-url)
| Authors                    | Age/ gender | Organ affected | Systemic symptoms | ANCA | ESR/CRP | Pathology                                                                 | Systemic therapy^a |
|---------------------------|-------------|----------------|-------------------|------|---------|---------------------------------------------------------------------------|-------------------|
| Persellin and Menke (1992) [3] | 29/M        | Testis         | None              | N/A  | N/A     | Necrotizing small and medium vessel vasculitis consistent with PAN       | None (F/u 17 months) |
| Halim et al. (1994) [4]    | 71/M        | Testis         | None              | Neg  | Normal  | Necrotizing granulomatous vasculitis                                      | None (F/u 24 months) |
| Mukamel et al. (1995) [5]  | 28/M        | Testis         | None              | N/A  | Normal  | Necrotizing small vessel vasculitis consistent with PAN                  | None (F/u 27 months) |
| Mukamel et al. (1995) [5]  | 35/M        | Testis         | None              | N/A  | Normal  | Necrotizing vasculitis consistent with PAN                               | None (F/u 36 months) |
| Kessel et al. (2001) [6]   | 13.5/M      | Testis         | None              | Neg  | Elevated| Necrotizing small and medium vessel vasculitis consistent with PAN       | None (F/u 24 months) |
| Hashiguchi et al. (2001) [7] | 37/M        | Testis         | None              | N/A  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN       | None (F/u 9 months)  |
| Eilber et al. (2001) [8]   | 43/M        | Testis         | Fever, myalgia, and hematuria | N/A  | Elevated| Necrotizing vasculitis consistent with PAN (cystoscopy normal)           | Not reported (F/u unclear) |
| Fraenkel-Rubin et al. (2002) [9] | 26/M        | Testis         | None              | Neg  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN       | None (F/u 30 months) |
| Dotan et al. (2003) [10]   | 32/M        | Testis         | None              | Neg  | Normal  | Necrotizing medium vessel vasculitis consistent with PAN                 | None (F/u 60 months) |
| Tanuma et al. (2003) [11]  | 40/M        | Testis         | None              | N/A  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN       | None (F/u 22 months) |
| Fleischmann and Studer (2007) [12] | 21/M        | Testis         | None              | N/A  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN       | None (F/u 24 months) |
| Giannarini et al. (2009) [13] | 36/M        | Testis         | None              | Neg  | Normal  | Necrotizing medium vessel vasculitis consistent with PAN                 | None (F/u 60 months) |
| Atis et al. (2010) [14]    | 57/M        | Testis         | None              | Neg  | Normal  | Necrotizing medium vessel vasculitis consistent with PAN                 | None (F/u unclear) |
| Saito et al. (2013) [15]   | 78/M        | Testis         | None              | Neg  | N/A     | Necrotizing vasculitis of epididymis consistent with PAN                 | None (F/u 12 months) |
| Lintern et al. (2013) [16] | 21/M        | Testis         | None              | Neg  | Normal  | Necrotizing medium vessel vasculitis consistent with PAN                 | Not reported (F/u unclear) |
| Garg and Dawson (2015) [17] | 36/M        | Testis         | None              | Neg  | N/A     | Necrotizing small and medium vessel vasculitis consistent with PAN       | None (F/u 3 months) |
| Dixit et al. (2017) [18]   | 84/M        | Testis         | None              | Pos  | Elevated| Non-granulomatous medium vessel vasculitis                             | Not reported (lost to follow-up) |
| Brimo et al. (2011) [19]   | 35/M        | Testis         | None              | Neg  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN       | None (F/u unclear) |
| Brimo et al. (2011) [19]   | 31/M        | Testis         | None              | Neg  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN       | None (F/u unclear) |
| Brimo et al. (2011) [19]   | 63/M        | Testis         | None              | Neg  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN       | None (F/u unclear) |
| Brimo et al. (2011) [19]   | 38/M        | Testis         | None              | Neg  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN       | None (F/u unclear) |
| Brimo et al. (2011) [19]   | 38/M        | Testis         | None              | N/A  | N/A     | Lymphocytic vasculitis                                                 | Not reported (F/u unclear) |
| Brimo et al. (2011) [19]   | 31/M        | Testis         | None              | Neg  | Normal  | Necrotizing small and medium vessel vasculitis                           | None (F/u unclear) |
| Authors               | Age/gender | Organ affected | Systemic symptoms | ANCA | ESR/CRP | Pathology                                           | Systemic therapy |
|----------------------|------------|----------------|-------------------|------|---------|-----------------------------------------------------|------------------|
| Brimo et al. (2011) [19] | 53/M       | Testis         | None              | Neg  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN | None (F/u unclear) |
| Brimo et al. (2011) [19] | 31/M       | Testis         | N/A               | N/A  | N/A     | Necrotizing small and medium vessel vasculitis consistent with PAN | Not reported (F/u unclear) |
| Brimo et al. (2011) [19] | 23/M       | Testis         | None              | Neg  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN | None (F/u unclear) |
| Brimo et al. (2011) [19] | 40/M       | Testis         | N/A               | N/A  | N/A     | Necrotizing small and medium vessel vasculitis consistent with PAN | Not reported (F/u unclear) |
| Brimo et al. (2011) [19] | 34/M       | Testis         | N/A               | N/A  | N/A     | Necrotizing granulomatous vasculitis                  | Not reported (F/u unclear) |
| Brimo et al. (2011) [19] | 27/M       | Testis         | None              | Neg  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN | Prednisone (F/u unclear) |
| Brimo et al. (2011) [19] | 20/M       | Testis         | Fever, night sweats | Pos  | Elevated | Non-necrotizing granulomatous vasculitis             | Prednisone, cyclophosphamide (F/u unclear) |
| Brimo et al. (2011) [19] | 40/M       | Testis         | Fatigue           | Neg  | Elevated | Necrotizing small and medium vessel vasculitis consistent with PAN | Prednisone, MMF (F/u unclear) |
| Brimo et al. (2011) [19] | 28/M       | Testis         | Fever, myalgia    | Neg  | Elevated | Necrotizing small and medium vessel vasculitis consistent with PAN | Prednisone, cyclophosphamide (F/u unclear) |
| Brimo et al. (2011) [19] | 44/M       | Testis         | Fevers, sweats, weight loss | Neg  | Elevated | Necrotizing small and medium vessel vasculitis consistent with PAN | Prednisone, cyclophosphamide (F/u unclear) |
| Brimo et al. (2011) [19] | 38/M       | Testis         | None              | Neg  | Elevated | Necrotizing small and medium vessel vasculitis consistent with PAN | Prednisone (F/u unclear) |
| Brimo et al. (2011) [19] | 34/M       | Testis         | N/A               | Neg  | Normal  | Necrotizing small and medium vessel vasculitis consistent with PAN | Prednisone, cyclophosphamide (F/u unclear) |
| Pastor-Navarro et al. (2007) [20] | 26/M | Testis         | None              | Neg  | N/A     | Necrotizing vasculitis consistent with PAN            | Steroids (F/u 12 months) |
| Breuer et al. (2015) [21] | 19/M       | Testis         | Erythema nodosum (8 years after initial episode of testicular symptoms) | N/A  | Normal  | Vasculitis with fibrinoid necrosis consistent with PAN | Prednisone, AZA, rituximab (F/u > 8 years) |
| Bhatia et al. (2018) [22] | 52/M       | Testis         | None              | Neg  | Elevated | Necrotizing vasculitis consistent with PAN            | Prednisone, cyclophosphamide, methotrexate (F/u 8 months) |
| Islam et al. (2018) [23] | 41/M       | Testis         | Polyarthritis, weight loss, rash | Neg  | N/A     | Necrotizing vasculitis of medium and large vessels consistent with PAN | Steroids, methotrexate (F/u unclear) |
| Fischer et al. (1998) [24] | 32/M       | Bladder        | None              | Neg  | Elevated | Necrotizing vasculitis of the medium-sized arteries consistent with PAN. Positive for hepatitis B surface antigen immunostaining | TURBT, steroids (F/u 18 months) |
| Fischer et al. (1998) [24] | 61/F       | Bladder        | None              | Neg  | N/A     | Small vessel vasculitis                              | Steroids, cyclophosphamide (F/u 12 months) |
systemic vasculitis [19] and one patient had persistent episodes of mild cutaneous vasculitis [21]. All four patients had evidence of more systemic disease on initial presentation.

Six patients who had isolated bladder vasculitis were included in our literature review. Four of the patients had evidence of more systemic illness at disease onset. The patients who did not have any systemic features underwent either a TURBT as well as therapy with prednisone and azathioprine, or treatment with steroids and cyclophosphamide without surgical excision [24, 26]. Of the other four patients, one underwent TURBT alone [27], two underwent TURBT as well as systemic therapy [24, 26], and one received prednisolone alone [25]. All six patients had no evidence of emergent systemic vasculitis over a mean follow-up of 17.2 months (median, 10.5 months).

It appears from the result of our literature review that patients who present with isolated testicular vasculitis and no evidence to suggest more systemic disease do not go on to develop systemic vasculitis after orchiectomy, regardless of whether or not they receive concomitant immunosuppressive therapy. Therefore, orchiectomy alone in isolated testicular vasculitis seems to be a reasonable option.

Table 1 Summary of cases of isolated testicular or bladder vasculitis from literature search (Continued)

| Authors            | Age/ gender | Organ affected | Systemic symptoms                      | ANCA  | ESR/CRP | Pathology                                                                 | Systemic therapy a |
|--------------------|-------------|----------------|----------------------------------------|-------|---------|---------------------------------------------------------------------------|-------------------|
| Katz et al. (2005) | 59/M        | Bladder        | Fatigue, sweats, weight loss           | Neg   | Elevated| Necrotizing vasculitis of small and large vessels                          | Prednisolone (F/u 3 months) |
| Becker et al. (2008) | 53/M        | Bladder        | None                                   | Neg   | Elevated| Necrotizing vasculitis of small vessels                                  | TURBT, prednisone, cyclophosphamide (F/u 1 month) |
| Kassir et al. (2013)| 31/M        | Bladder        | Fever                                  | N/A   | Elevated| Non-granulomatous, small and medium vessel thrombotic vasculitis          | TURBT (F/u 9 months) |
| Fall et al. (2018) | 45/M        | Bladder        | None                                   | Neg   | Normal  | Fibrinoid degeneration with neutrophil infiltration into vessel walls consistent with vasculitis | TURBT, Prednisone, AZA (F/u 60 months) |

ANCA antineutrophil cytoplasmic antibody, AZA azathioprine, CRP C-reactive protein, ESR erythrocyte sedimentation rate, F female, F/u follow-up, M male, MMF mycophenolate mofetil, N/A not applicable, Neg negative, PAN polyarteritis nodosa, Pos positive, TURBT transurethral resection of bladder tumor

a All patients with isolated testicular vasculitis underwent orchiectomy

b These patients went on to develop systemic vasculitis or persistent mild cutaneous vasculitis

Fig. 2 Summary of treatment regimens and outcomes for patients with isolated testicular vasculitis
therapeutic approach. There were only six patients with isolated bladder vasculitis, and one of them underwent TURBT alone with no emergent systemic illness. We used these findings to guide our management of a patient with PAN affecting both the right testis and urinary bladder.

**Conclusion**

This case summarizes the current literature regarding the treatment of isolated testicular or bladder vasculitis. Our findings support withholding immunosuppressive therapy after surgical excision in these patients if there is no evidence of more systemic disease at onset. While single organ PAN has been treated in the past with surgical excision, there is a lack of data regarding treatment of PAN involving two organs, with no other systemic features. We extrapolated the results of our literature review to guide the management of a patient who presented with PAN affecting both the urinary bladder and right testis. He underwent radical right orchiectomy and TURBT, with no systemic therapy. On 2-year follow-up, he has not developed any systemic PAN symptoms. The risk of developing future extratesticular and vesicovasculare involvement appears to be low.

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**Authors’ contributions**

MS and GM made substantial contributions to the literature review and compilation of data from previously published case reports, as well as writing the manuscript. MAS provided the histologic analysis and interpretation, the histology figures, and revised the manuscript. ND performed the initial assessment and ongoing management of the patient, and revised the manuscript. All authors read and approved the final manuscript.

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**Ethics approval and consent to participate**

The patient involved in the case report gave consent to participate prior to inclusion in the manuscript. As per the University of British Columbia Clinical Research Ethics Board guidelines, individual case reports do not require ethics review. More information is available at https://ethics.research.ubc.ca/ore/ubc-clinical-research-ethics-general-guidance-notes section 4.4.2.

**Consent for publication**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Competing interests**

The authors declare that they have no competing interests.

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