CASE REPORT

Rheumatoid vasculitis: early presentation of rheumatoid arthritis

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SUMMARY

Rheumatoid vasculitis is a rare and late complication of rheumatoid arthritis and may affect small-to-medium-sized vessels. Here, we report a case of a 49-year-old man who presented with amaurosis fugax in the left eye, symmetric polyarthritis, Raynaud's symptoms and paraesthesia in both lower extremities. The patient subsequently experienced right foot drop, nail fold infarcts and gangrene of his right second toe. He was found to have a high titre of rheumatoid factor and treatment with rituximab and high dose of corticosteroids led to significant improvement of his symptoms. This is rare case describing the early onset of rheumatoid vasculitis in a patient with rheumatoid arthritis.

BACKGROUND

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterised by chronic symmetric polyarthritis and by the presence of autoantibodies including rheumatoid factor (RF) and anticyclic citrullinated peptide (anti-CCP) antibodies. Rheumatoid vasculitis (RV) is an unusual manifestation of chronic, deforming RA and may affect multiple systems.^{1 2} The skin is commonly affected but other organs can be involved. RV should be in the differential diagnosis of patients presenting with multiple organ dysfunction and high titre of RF. We report a case of a patient with recently diagnosed RA which was complicated with systemic RV. Most often it occurs in patients with long-standing disease but in our case it was an initial presentation of the disease.

CASE PRESENTATION

A 49-year-old African-American man, a chronic smoker, with no significant medical history presented with 3-day history of painless vision loss in the left eye, which resolved spontaneously, accompanied with a 2-month history of persistent bilateral hand, knee and elbow pain. He also experienced numbness of his lower extremities and intermittent bluish discolouration of the fingers and toes when exposed to cold. On examination, he was found to have synovitis bilaterally in the proximal interphalangeal and the metacarpophalangeal joints. Eye examination showed no evidence of retinal vein or artery occlusion.

INVESTIGATIONS

The following laboratory values were significant for RF of 4350 IU/mL, positive antinuclear antibodies with titre of 1:160, erythrocyte sedimentation rate

of 80 mm/hour, C reactive protein of 9.47 mg/L, slightly elevated C3 and C4, 185 and 54 mg/dL, respectively. Anti-CCP antibodies, antineutrophil cytoplasmic antibodies (ANCA), HIV antibodies, acute hepatitis panel, scleroderma-70 antibody, double-stranded DNA antibody, anti-SSA/anti-SSB autoantibodies, anti-Smith, antiphospholipid antibodies and cryoglobulins were all negative. X-rays of bilateral hands and feet showed no erosive changes or joint space narrowing.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses included vasculitis, infective endocarditis, peripheral artery disease, cryoglobulinaemia and thromboembolic disease.

Cerebrovascular accident was excluded by MRI and MR angiogram (MRA) of the brain and bilateral carotids ultrasound scan were within normal limits. Echocardiogram did not show any evidence of valve vegetation, intracardiac masses or thrombi. Blood cultures were obtained and were negative. The ankle brachial index test was within normal limit. CT angiogram of the abdomen was performed to rule out polyarteritis nodosa and there were no radiographical findings of intra-abdominal vascular aneurysms or stenosis.

TREATMENT

The patient was started on prednisone 60 mg daily with taper instructions and methotrexate 15 mg weekly with folic acid 1 mg daily. Two months later, the patient stopped taking his medications and he developed worsening purple discolouration of his hands and feet, worse when exposed to cold, associated with nail fold and digits infarctions in his hands and feet. He also presented with a necrotic ulcerative lesion on his right second toe and difficulty ambulating due to right foot drop (figure 1A, B).

He was admitted with the working diagnosis of RV based on the presence of ulcerative necrotic lesion of his toe, mononeuritis multiplex with foot drop, history of polyarthritis, unexplained vision loss and high titre of RF. His RF was rechecked and found to be 7000 IU/mL. He received pulse dose of corticosteroids (1000 mg methylprednisolone for 3 days and then prednisone 60 mg daily while in the hospital), and total of two doses of Rituximab 1000 mg 2 weeks apart. For his ischaemic lesions and Raynaud's, the patient was treated with amlodipine 10 mg daily, aspirin 325 mg daily and topical nitroglycerine. The patient showed improvement of his symptoms except the right second toe's ulcerative lesion which worsened and he underwent amputation. Two days after the

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Figure 1 (A and B) A necrotic ulcerative lesion on the right second toe.

procedure the patient was discharged on prednisone 60 mg daily with tapering 5 mg every 1 week and methotrexate 20 mg weekly.

OUTCOME AND FOLLOW-UP

In a follow-up visit 3 months later, the patient noted improvement of his skin lesions, right foot strength, paraesthesia, Raynaud's phenomenon and denied joint pain or swelling. Repeated inflammatory markers showed a C reactive protein of 6.68 mg/L and sedimentation rate of 31 mm/hour.

DISCUSSION

RV is an unusual complication of long-standing, severe RA. It is characterised by an inflammatory process affecting small-to-medium-sized vessels and may involve any organ of the body. The mean duration between the diagnosis of RA and the onset of vasculitis is 10–14 years and it is unusual to be presented within the first 5 years of RA diagnosis though it has been reported before.^{1 2} The 30-year incidence of vasculitis in patients with RA was estimated to be 3.6%.¹ Over the past 15 years, with the widespread use of biological agents early in the treatment of RA, has led to a decline in the prevalence of RV.³

The postulated pathogenic mechanism of RV is complex, involving the activation of the endothelial cells, with upregulated expression of HLA-DQ, interleukin-1 α and expansion of CD28^{null} T cells.^{4 5} Several clinical studies suggest that RV may be caused by circulating immune complexes containing RF and autoantibodies such as antiendothelial cell antibodies, forming deposits in vessel walls and triggering an inflammatory reaction, which may lead to endothelial cell injury.^{6 7}

Risk factors for RV include long-standing RA, male, smoking, rheumatoid nodules and HLA class I and class II genotypes.^{8 9} A genetic predisposition appears to be related to the development of RV in patients with RA. A meta-analysis that compiled 14 studies encompassing more than 1500 patients with RA revealed a strong relationship between RV and three specific genotypes of the HLA-DRB1.¹⁰

The two most common organs to be involved are the skin and the peripheral nerves in more than 80% of patients.¹¹ Other system involvement includes heart, bowel and kidney which are much less common but can lead to significant

morbidity and mortality, including myocardial infarction, bowel ischaemia and renal failure.^{12 13}

Cutaneous manifestations of RV include palpable purpura, nodules, ulcers, nail fold infarctions, digital necrosis, livedo reticularis and urticarial vasculitis.

Diagnostic criteria for systemic RV were proposed by Scott and Bacon as having one or more of the following in the presence of RA: (1) mononeuritis multiplex or peripheral neuropathy, (2) peripheral gangrene, (3) biopsy evidence of acute necrotising arteritis in addition to systemic illness (fever and weight loss), and (5) deep cutaneous ulcers or extra-articular disease (eg, pleurisy, pericarditis and scleritis) if associated with typical digital infarcts or biopsy evidence of vasculitis.^{14 15}

Laboratory tests may support, but do not confirm the diagnosis of RV. Some studies have shown an association between high titres of RF or anti-CCP antibodies and RV.¹⁶ Low complement has been associated with RV in 20–57% of the patients based on different studies.^{17 18}

Management includes the use of corticosteroids, cyclophosphamide, traditional and biological disease-modifying antirheumatic drugs (DMARDs).¹⁹ The emergence of rituximab during the past decade as a new treatment of ANCA-associated vasculitis and RA was followed by the use of rituximab in RV. It showed a remarkable effect in inducing and maintaining remission, plus decreasing the incidence of relapse.²⁰

The prognosis in RV depends in part on the severity of the damage to the organs involved. Infection and end-organ damage from active vasculitis are the main causes of death; 40% of patients die within 5 years of disease onset.²¹

Learning points

- ▶ This case report highlights that rheumatoid vasculitis (RV) can be, even though rare, the initial presentation of rheumatoid arthritis (RA).
- ▶ RV, although it is a late complication of chronic RA, can be presented at any time during the disease process.
- ▶ Mononeuritis multiplex, manifested with foot drop in a patient with RA, could be a warning sign of RV.
- ▶ RV should be in the differential diagnosis of patients presenting with multiple organ dysfunction and high titre of rheumatoid factor.
- ▶ High-dose glucocorticoids and rituximab help in inducing remission in active RA, while methotrexate or azathioprine might help in maintenance therapy. Rituximab has been shown to be effective in treating RV. The effect of tumour necrosis factor inhibitors and other biological agents in treating severe, active RV still require further investigations.

Competing interests None declared.

Patient consent Obtained.

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REFERENCES

- 1 Makol A, Crowson CS, Wetter DA, et al. Vasculitis associated with rheumatoid arthritis: a case-control study. *Rheumatology (Oxford)* 2014;53:890–9.
- 2 Turesson C, O'Fallon WM, Crowson CS, et al. Extra-articular disease manifestations in rheumatoid arthritis: incidence trends and risk factors over 46 years. *Ann Rheum Dis* 2003; 62:722–7.

- 3 Bartels C, Bell C, Rosenthal A, *et al.* Decline in rheumatoid vasculitis prevalence among US veterans: a retrospective cross-sectional study. *Arthritis Rheum* 2009;60:2553–7.
- 4 Martens PB, Goronzy JJ, Schaid D, *et al.* Expansion of unusual CD4+ T cells in severe rheumatoid arthritis. *Arthritis Rheum* 1997;40:1106–14.
- 5 Michel JJ, Turesson C, Lemster B, *et al.* CD56-expressing T cells that have features of senescence are expanded in rheumatoid arthritis. *Arthritis Rheum* 2007;56:43–57.
- 6 Jans H, Halberg P, Lorenzen I. Circulating immune complexes in rheumatoid arthritis with extra-articular manifestations. *Scand J Rheumatol* 1983;12:215–18.
- 7 Scott DGI, Bacon PA, Allen C, *et al.* IgG rheumatoid factor, complement and immune complexes in rheumatoid synovitis and vasculitis: comparative and serial studies during cytotoxic therapy. *Clin Exp Immunol* 1981;43:54–63.
- 8 Turesson C, Schaid DJ, Weyand CM, *et al.* Association of HLA-C3 and smoking with vasculitis in patients with rheumatoid arthritis. *Arthritis Rheum* 2006;54:2776–83.
- 9 Struthers GR, Scott DL, Delamere JP, *et al.* Smoking and rheumatoid vasculitis. *Rheumatol Int* 1981;1:145–6.
- 10 Gorman JD, David-Vaudey E, Pai M, *et al.* Particular HLA-DRB1 shared epitope genotypes are strongly associated with rheumatoid vasculitis. *Arthritis Rheum* 2004;50:3476–84.
- 11 Puechal X, Said G, Hilliquin P, *et al.* Peripheral neuropathy with necrotizing vasculitis in rheumatoid arthritis. A clinicopathologic and prognostic study of thirty-two patients. *Arthritis Rheum* 1995;38:1618–29.
- 12 Caballol Pons N, Montalà N, Valverde J, *et al.* Isolated cerebral vasculitis associated with rheumatoid arthritis. *Joint Bone Spine* 2010;77:361–3.
- 13 Zolcinski M, Bazan-Socha S, Zwolinska G, *et al.* Central nervous system involvement as a major manifestation of rheumatoid arthritis. *Rheumatol Int* 2008;28:281–3.
- 14 Scott DG, Bacon PA. Intravenous cyclophosphamide plus methylprednisolone in treatment of systemic rheumatoid vasculitis. *Am J Med* 1984;76:377–84.
- 15 Scott DG, Bacon PA, Tribe CR. Systemic rheumatoid vasculitis: a clinical and laboratory study of 50 cases. *Medicine (Baltimore)* 1981;60:288.
- 16 Laskari K, Ahmadi-Simab K, Lamken M, *et al.* Are anti-cyclic citrullinated peptide autoantibodies seromarkers for rheumatoid vasculitis in a cohort of patients with systemic vasculitis? *Ann Rheum Dis* 2010;69:469–71.
- 17 Franco AE, Schur PH. Hypocomplementemia in rheumatoid arthritis. *Arthritis Rheum* 1971;14:231–8.
- 18 Schneider HA, Yonker RA, Katz P, *et al.* Rheumatoid vasculitis: experience with 13 patients and review of the literature. *Semin Arthritis Rheum* 1985;14:280–6.
- 19 Turesson C, Matteson EL. Management of extraarticular disease manifestations in rheumatoid arthritis. *Curr Opin Rheumatol* 2004;16:206–11.
- 20 Puéchal X, Gottenberg JE, Berthelot JM, *et al.* Rituximab therapy for systemic vasculitis associated with rheumatoid arthritis: results from the AutoImmunity and Rituximab Registry. *Arthritis Care Res (Hoboken)* 2012;64:331–9.
- 21 Voskuyl AE, Zwinderman AH, Westedt ML, *et al.* The mortality of rheumatoid vasculitis compared with rheumatoid arthritis. *Arthritis Rheum* 1996;39:266–71.

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