

Rheumatoid Arthritis Complicated by Myositis and Vasculitic Neuropathy: A Rare Association

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Abstract

Rheumatoid arthritis (RA) is a multisystem disease with a variety of manifestations. Vasculitis and myositis are two very rare complications of RA. However, the coexistence of both of these complications in the same patient is extremely rare in medical literature. We here present such a rare association of clinical features in a 36 year old male patient with RA. He had RA for around four years before development of these complications almost simultaneously. The patient was treated with rituximab and oral steroids. The myositis component responded promptly but the vasculitic neuropathy was very slow to respond.

Introduction

Rheumatoid arthritis (RA) is a multi-system connective tissue disorder which can have various presentations. Vasculitis in RA is a comparatively rare but potentially serious manifestation¹. Incidence of secondary vasculitis in RA varies from 1–5% with the chief organs affected being the skin and peripheral nerves.¹ However, the 5-year mortality of patients with rheumatoid vasculitis may be as high as 50%. Hence, prompt diagnosis and treatment of the vasculitis is needed.

The association of myositis with RA is even rarer.² Myopathic manifestations may precede or follow the diagnosis of RA. However, the combined occurrence of myositis and vasculitic neuropathy in the same patient of RA is very rarely documented. We here report such a presentation from Eastern India.

The Case Report

A 36 year old man, a known case of rheumatoid arthritis for four years, was admitted with progressive painless proximal weakness of both legs over the last three months. He was a manual labourer who carried a lot of weight every day. But because of this new onset symptom, he had to leave his job. Also, for the last one month, he complained of weakness of small muscles of foot of the right leg. He had difficulty in wearing chappals. There was no significant atrophy of muscles anywhere in the legs. The man was on regular hydroxychloroquine,

methotrexate and leflunomide for his rheumatoid arthritis. Also, occasionally, he used oral steroids (over the counter) for relief of joint pain. At presentation to our institution, the man had no joint pain although the fingers of the hands were deformed. Power of hip flexion was 2/5 bilaterally and power around knee joint was 4/5. There was gross weakness of ankle dorsiflexion and toe flexion on the right side; left side was normal. Although the patient did not complain of any sensory symptoms, sensation to all modalities were reduced on the right side up to mid-calf. On the left side, only an isolated patch of sensory loss around the ankle was found. Knee jerks were normally present bilaterally; ankle jerk was absent on the right side and reduced on the left. There was no muscle tenderness anywhere. There was no weakness in any other muscle, including extra-ocular muscles. Skin rash was absent. Ophthalmoscopy did not reveal any retinal lesions.

Initial laboratory investigations revealed hemoglobin of 8.7 gm/dl, total leukocyte count of 11000/ μ L (neutrophil 80%) and platelet count of 2.5 lakh/ μ L. ESR was 72 mm in the 1st hour and CRP level was 53.8 mg/L (N<6). Serum rheumatoid factor was 88 IU/L (N<20) and anti-CCP level was >200 IU/L (N<5). Anti-nuclear factor, complement

levels, ANCA and cryoglobulin tests were all negative. Serum CPK level was just elevated at 320 IU/L (our institution reference level<150). Blood viral serology for HIV, hepatitis B, C, CMV and blood vitamin B12 levels were normal. Oral glucose tolerance test and kidney function tests were also normal. Anti-Ach-R antibodies were negative. Urine analysis did not show any proteinuria. Nerve conduction velocity study showed axonal type of sensori-motor polyneuropathy in both lower limbs (right>left). Upper limbs were normal. Electromyography revealed a myopathic pattern with polyphasic potentials. Arterial Doppler study did not show any evidence of vasculitis in the large vessels.

After consultation with a multi-disciplinary group, a muscle biopsy was done from the vastus lateralis muscle which showed (Figure 1) partial atrophy of muscle fibres with perifascicular aggregation of inflammatory lymphoplasmacytic cells, suggestive of active inflammation. This biopsy report could explain the proximal weakness of the legs. However, that could not explain the distal sensori-motor symptoms and signs. So, afterwards, a nerve biopsy was also done from the right sural nerve. This showed (Figure 2) intense inflammatory cell infiltration in the nerve fibres around blood vessels with karyorrhexis. Thus, the patient was finally diagnosed to have inflammatory myopathy and also, neuropathy due to small vessel vasculitis. He was given two doses of rituximab (1000 mg, 14 days apart) and oral prednisolone (1 mg/kg). The proximal weakness improved quickly with power 4-/5 around hip after one month. But, the distal weakness and sensory loss persisted at 6 months' follow up. However, after starting

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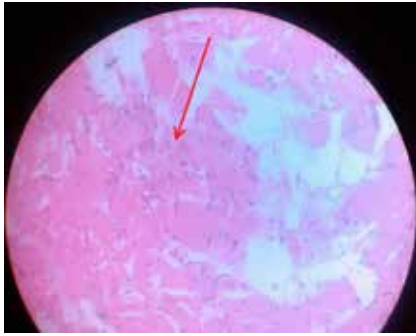


Fig. 1: Muscle biopsy showing inflammatory cells (red arrow) around and inside fascicles

the immunosuppressive regimen, the symptoms/signs of neuropathy have not progressed. Also, he has not developed any new clinical features of vasculitis. The DMARDs for rheumatoid arthritis are being continued as before.

Discussion

Vasculitis in RA can manifest as skin lesions like purpura, pyoderma or ulcers, peripheral nervous system (PNS) involvement like polyneuropathy or Mononeuritis multiplex or it can involve internal organs with potentially more serious consequences.¹ In PNS involvement, nerve biopsy has a very high diagnostic yield. Biopsy usually reveals (as in our case) intense perivascular inflammatory cell aggregation inside the nerve.³ Biopsy is usually diagnostic but sometimes, electrophysiological studies may provide the initial suggestion of vasculitic neuropathy. Electrophysiological studies may show different patterns in RA. A study from Western India have shown that the electrophysiological patterns in RA can be pure sensory or pure motor or mixed and of either axonal or demyelinating variety.⁴ Usually, long duration of RA is associated with the development of vasculitic neuropathy.⁴

Myositis is rare, compared to vasculitis, in RA patients. Like vasculitis, this also occurs in long standing RA cases, but occasionally, myositis can be the presenting feature of RA.⁵ The myositis can involve appendicular muscles, as in our case or exceptionally, it may involve atypical locations like extra-ocular muscles.⁶ The diagnostic approach of myositis in RA is similar to idiopathic polymyositis cases, i.e. EMG study, blood enzyme levels and muscle biopsy, either alone

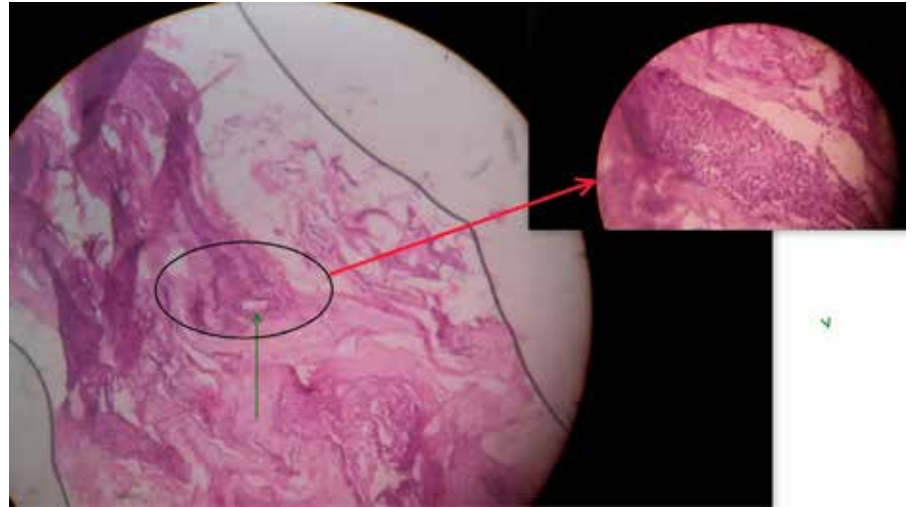


Fig. 2: Nerve biopsy showing a blood vessel (green arrow) surrounded by intense inflammatory cells and nuclear debris

or in combinations.

Vasculitis in RA is treated with steroids, cyclophosphamide or the biological therapies like TNF- α inhibitors.¹ These can be used singly or in combination. But, the treatment response is often variable and unpredictable.¹ Since the treatment is still evolving, different treatment groups have different protocols. In our case, we used rituximab, followed by oral steroids. Our choice of this particular regimen was also prompted by the co-existence of myositis. Since RA myositis is very rare, there is no definitive guideline on its management. But in the reported cases, authors have documented good response with high-dose oral steroids.⁵ In our case too, the proximal muscle weakness improved quickly with steroids. But the neuropathy was very slow to respond.

Now-a-days, anti- TNF- α biologicals are commonly used for RA. There has been some reports of the development of myositis and neuropathy after TNF- α inhibitor use.^{7,8} Hence, if a patient of RA develops such features, prior drug history should always be enquired into to rule out a drug-induced etiology. In our case, there was no history of the use of biologicals.

The co-existence of myositis and vasculitis in RA is very rare in medical literature. There is only one other case similar to ours, reported from the USA.⁹ In that case, a 62 year old man presented with Mononeuritis multiplex and proximal weakness. The joint disease was clinically mild

at the time of presentation, like our case. Final diagnosis in that case was also established by biopsy of muscles and nerves.⁹

Conclusion

Focal weakness in rheumatoid arthritis may be due to serious underlying conditions like vasculitis. Hence, such cases should be thoroughly investigated and treatment initiated promptly for better outcomes.

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