Case report

Recurrent focal myositis developing into a generalised idiopathic inflammatory myopathy with anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase autoantibodies

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SUMMARY

We present the case of a 43-year-old woman with generalised idiopathic inflammatory myopathy (IIM) with anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) autoantibodies (Abs) that developed following recurrent focal myositis. Anti-HMGCR Abs are myositis-specific Abs that are associated with immune-mediated necrotising myopathy, a subtype of IIM that is characterised by relatively prominent and severe muscle involvement, generally necessitating multimodal immunosuppressant treatment. While earlier reports have described patients developing polymyositis following focal myositis, this is the first report to describe a patient developing IIM with anti-HMGCR Abs following focal myositis. Thus, clinicians should be aware of the possibility that focal myositis may develop into a generalised IIM and should instruct the patient and monitor the patient accordingly.

femoris muscle. Muscle biopsy of the right vastus lateralis muscle showed variation in muscle fibre diameter, focal increase in connective tissue and muscle fibre regeneration (CD56+), no necrosis, focal infiltration of macrophages (CD68+) and lymphocytes (CD3+ and CD20+), no clear major histocompatibility complex-I upregulation and perimysial positivity of alkaline phosphatase. Serological evaluation was not performed considering the focal nature of the abnormalities.

DIFFERENTIAL DIAGNOSIS

Considering the absence of any signs of infection, structural abnormalities or other underlying etiologies on clinical and ancillary investigations, we diagnosed our patient with focal myositis (Focal Myositis Simple Score (FMSS) of 3)).⁴ The main differential diagnosis was generalised IIM, which may initially mimic focal myositis.^{5–8}

BACKGROUND

While focal myositis is considered to be a relatively benign disease in which glucocorticoid monotherapy generally suffices, generalised idiopathic inflammatory myopathy (IIM) often necessitates multimodal immunosuppressant treatment.^{1–3} Timely recognition of generalised IIM developing following focal myositis may prompt the clinician to prescribe adequate treatment and thereby prevent damage and disability caused by the disease.³

CASE PRESENTATION

A 43-year-old-patient without a history of statin-use presented with pain in the right upper leg which began 4 months earlier. There was some swelling and redness on the right leg which subsided before she was evaluated. There was no relevant medical history and the patient had used ibuprofen and tramadol because of the pain. Neurological examination showed mild weakness of the right iliopsoas and quadriceps femoris muscles.

INVESTIGATIONS

Ancillary investigations showed a normal serum creatine kinase (CK) activity, and normal electromyography. T2-weighted MRI with fat suppression showed muscle oedema in the right quadriceps

TREATMENT

We started our patient on 40 mg oral prednisolone once daily.

OUTCOME AND FOLLOW-UP

Three months later the symptoms resolved completely and repeated neurological examination showed no muscle weakness, after which prednisolone was tapered slowly and subsequently discontinued.

However, the patient presented 4 years later again with pain, swelling and muscle weakness of the left forearm. Evaluation by a rheumatologist showed no signs of an underlying autoimmune disease. Repeated ancillary investigations showed normal serum CK activity and muscle oedema in the muscles of the left forearm on MRI. An ultrasound-guided muscle biopsy was performed but showed no abnormalities on histopathology nor immunohistochemistry, possibly due to sampling error. Serological evaluation showed neither myositis-specific autoantibodies (Abs) (MSAs) including anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) Abs nor myositis-associated Abs. She was diagnosed with recurrent focal myositis (FMSS of 2). She was again treated with 40 mg oral prednisolone once daily on suspicion of a relapse of her

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Figure 1 T2-weighted axial MRI with fat suppression showing muscle oedema (white arrows). Muscle oedema was initially solely present in the right thigh (figure 1A), but progressed to more generalised muscle oedema showing abnormalities of the thighs bilaterally (figure 1B) and focally in the upper (figure 1C,1D) and lower arms (figure 1E, 1F).

focal myositis. This led to complete resolution of complaints in 2 months.

During tapering in the following 6 months, at a daily dose of 5 mg prednisolone, the patient developed pain in all the extremities. There was no muscle weakness on clinical investigation. Serum CK activity was not elevated. Repeated muscle MRI showed diffuse muscle oedema (figure 1(A–F)). Serological evaluation was repeated and this time, anti-HMGCR Abs turned out to be positive with a titre of 34 U/mL (Euroimmun, Lubeck, Germany; ref: <20 U/mL). The earlier diagnosis of focal myositis was discarded based on an FMSS of 0 and a diagnosis of generalised IIM with anti-HMGCR Abs was considered, although a formal diagnosis of immune-mediated necrotising myopathy (IMNM) could not be established due to the lack of pathological confirmation. Consequently, prednisolone treatment was intensified to 20 mg once daily and methotrexate 25 mg was added once weekly. Symptoms resolved within a month following the intensified treatment regimen.

DISCUSSION

Focal myositis is an inflammatory disorder restricted to one (or more adjacent) skeletal muscle(s) with a benign, that is, mostly self-limiting disease course.^{1 2 8} In contrast, generalised IIM—of which IMNM/IIM with anti-HMGCR Abs is a subset—are characterised by proximal (axial and limb-girdle) muscle weakness and often require multimodal immunosuppressive treatment.^{3 9 10}

Learning points

- ▶ Generalised idiopathic inflammatory myopathy (IIM) may develop following focal myositis.
- ▶ A majority of patients with generalised IIM require multimodal treatment, while glucocorticoid therapy generally suffices for focal myositis.
- ▶ Prompt recognition of generalised IIM following focal myositis may allow for adequate treatment and subsequently, prevent damage caused by the disease.

Thus, it is important to distinguish focal myositis from generalised IIM to prevent both undertreatment and overtreatment.

However, it seems there is pathophysiological and clinical overlap between focal myositis and generalised IIM, as illustrated by reports of patients who developed generalised polymyositis (PM) following focal myositis.¹¹ A variety of biomarkers may aid the clinician in distinguishing focal myositis from generalised IIM and identifying patients with focal myositis at risk of developing a generalised IIM.^{1 2} First, conventional laboratory markers such as serum CK activity, erythrocyte sedimentation rate (ESR) and C-reactive protein are atypical for focal myositis; indeed, earlier reports described a higher risk of development of generalised IIM in patients with focal myositis who also had abnormal serum CK activity or ESR. Furthermore, muscle MRI may indicate the extent of the disease, thus distinguishing focal myositis from generalised IIM. Histopathology and immunohistochemistry on muscle biopsy cannot accurately distinguish between focal myositis and generalised IIM. More recently, serological testing—based on the detection of MSAs that are not found in focal myositis as seen at the first stage of the disease in the case presented here has helped clinicians in diagnosing and characterising generalised IIM according to distinct clinico-serological profiles.^{1 2 9 12} Indeed, it has been found that PM—the patients who developed generalised IIM following focal myositis described earlier were diagnosed with PM—is a rather heterogeneous group of diseases, encompassing a variety of distinct IIM subtypes (IMNM, antisynthetase syndrome, non-specific myositis/overlap myositis) and even untreatable muscle diseases such as inclusion body myositis and muscular dystrophies.^{13 14} Accordingly, the detection of anti-HMGCR Abs by the highly specific (sensitivity and specificity 44.9% and 99.7%, respectively for IMNM) and commercially available contributed to classifying the disease in our patient.¹⁵ Therefore, a more specific description based on innovative ancillary investigations, such as testing of MSAs, is needed to accurately identify patients who are at risk of developing a generalised IIM following focal myositis.

To our knowledge, this is the first report of a patient who developed a generalised IIM with anti-HMGCR Abs following focal myositis. As such, multimodal immunosuppressive treatment was prescribed with favourable results. Our case report illustrates the importance of (serial) muscle imaging and repeated testing of MSAs for correct diagnosis of generalised IIM possibly developing from a focal myositis.

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