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CASE REPORT

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A case of eosinophilic myositis associated with orbital myositis

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Abstract A 29-year-old woman was admitted to our hospital because of fever, myalgia, and ocular pain. She had been given norgesterone and ethinylestradiol orally. Laboratory data indicated the presence of systemic inflammation together with elevated levels of muscle enzymes. Magnetic resonance imaging revealed inflammatory lesions in skeletal and extraocular muscles. The diagnosis of eosinophilic myositis was based on histopathological examination of the deltoid muscle, which showed infiltration of eosinophils into the tissue with necrotizing muscle fibers. Prednisolone treatment resulted in marked clinical improvement. This is the first case report of eosinophilic myositis in which the extraocular muscles were affected.

Key words Eosinophilic myositis · Estradiol · Orbital myositis

Introduction

Eosinophilic myositis is an inflammatory muscle disease characterized by the infiltration of eosinophils into the muscle tissue.[1,2] Eosinophilic myositis is common in the field of veterinary medicine; however, it has rarely been found in human cases. Orbital myositis is also an inflammatory disease that involves the extraocular muscles.[3,4] Orbital myositis sometimes develops in association with systemic autoimmune diseases such as systemic lupus erythematosus and giant cell myositis.[5,6] However, no case of orbital myositis complicated with eosinophilic myositis has been reported. In the present case report, we show a patient with both diseases occurring during sex steroid replacement therapy who responded well to corticosteroid treatment.

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Case report

A 29-year-old woman was admitted to our hospital because of fever, generalized skeletal myalgia, and ocular pain. She had a history of atypical genital bleeding and had received treatment with norgesteron, 0.5 mg/day, and ethinylestradiol, 0.05 mg/day. Twenty days later, fever and acute onset of severe thigh pain developed so that she could not easily stand up or walk; in addition, she suffered from ocular pain and limitation of ocular movement without exophthalmos or the loss of visual acuity. The laboratory data on admission revealed hemoglobin at 11.1 g/dl and white cell count at 4010/μl with 80% neutrophils, 9% lymphocytes, 8% monocytes, and 3% eosinophils. Systemic inflammation was manifested by elevated levels of erythrocyte sedimentation rate, 86 mm/h, and C-reactive protein, 33.8 mg/dl. Serum levels of creatinine kinase and aldolase were markedly increased, to 6296 IU/l and 65.6 IU/l, respectively. Tests for autoantibodies such as antinuclear antibody, anti-DNA antibody, anti-nRNP, antibody and anti-Jo-1 antibody were negative (Table 1). Thyroid function tests were normal, and studies using the Holter electrocardiogram and echocardiogram showed no abnormalities in cardiac function. In contrast, magnetic resonance imaging (MRI) demonstrated the presence of inflammatory lesions, manifested by high-intensity signals on the T_2-weighted image, in deltoid muscles and quadriceps, particularly in areas of vastus medialis and vastus intermedialis (Fig. 1).

Similar inflammatory lesions were also found in both orbital medial rectus muscles (Fig. 2). To clarify the cause of

Table 1. Laboratory data

WBC	4010/μl
St	62%
Seg	26%
Lym	4%
Eo	5%
Mo	1%
RBC	371×10^4/ul
Hb	11.1 g/dl
Ht	32.9%
Plt	25.4×10^4/μl
T.P.	5.5 mg/dl
Alb.	2.2 mg/dl
γ-gl	26.7%
T.B.	0.7 mg/dl
GOT	302 IU/l
GPT	155 IU/l
LDH	747 IU/l
γ-GTP	29 IU/l
CPK	6296 IU/l
BB	0%
MB	1%
MM	99%
Aldorase	65.6 U/l
Myoglobin	97.6 mEq/l
T.chol	78 mg/dl
Amy	15 IU/l
BUN	16.1 mg/dl
Cr	0.4 mg/dl
CRP	33.8 mg/dl
ESR	86 mm/h
IgG	2650 mg/dl
IgA	219 mg/dl
IgM	250 mg/dl
IgE	490.8 IU/ml
ANA	(–)
Anti-ssDNA Ab	(–)
Anti-dsDNA Ab	(–)
Anti-RNP Ab	(–)
Anti-Jo-1 Ab	(–)
P-ANCA	(–)

myositis, a muscle biopsy was performed from the right deltoid muscle. Histopathological examination showed intense infiltration of eosinophils into the muscle tissue together with necrotizing muscle fibers (Fig. 3). Eosinophils were partially infiltrated into perivascular areas, but neither vasculitis nor dermatitis could be detected on the biopsy specimen. Based on these results, the diagnosis of eosinophilic myositis that probably involved extraocular muscles was made and treatment with prednisolone (PSL), at 40 mg/day, was started. Soon after beginning PSL treatment, her symptoms and signs, including ocular pain and diplopia, were resolved in parallel with a marked improvement of laboratory abnormalities. The MRI findings following 3-month PSL treatment revealed the disappearance of inflammatory lesions in upper and lower extremities (Fig. 1) as well as in the extraocular muscles (Fig. 2). Therefore, PSL was tapered off. During the 1-year follow-up period, no recurrence of myositis was observed.

Discussion

We have shown a case of eosinophilic myositis associated with orbital myositis. Eosinophilic myositis, similar to polymyositis and dermatomyositis, involves skeletal muscles and causes myalgia and muscle weakness. However, eosinophilic myositis is believed to be classified into a disease entity differing from other inflammatory myopathies, because the histopathological findings of eosinophilic myositis are characterized by a marked infiltration of eosinophils into the muscle tissue.[1] Muscular degeneration is also found, irrespective of the perimysial destruction. Eosinophilic myositis occurs clinically in acute or subacute forms,

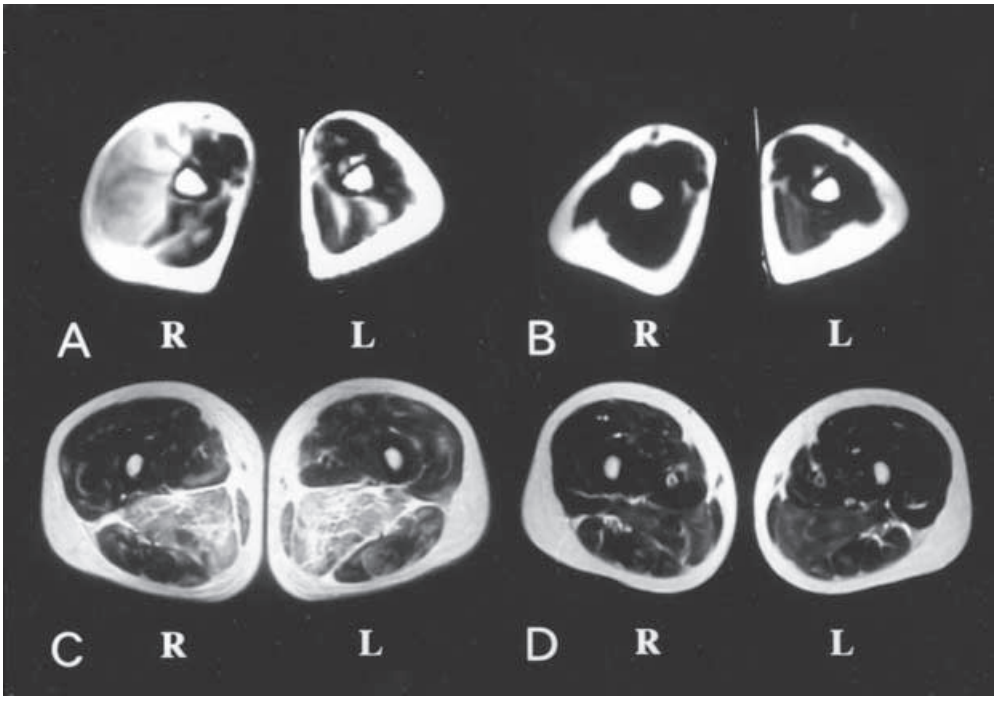

Fig. 1. Magnetic resonance imaging (MRI) of upper arms and midthighs shows inflammatory lesions with increased T_2 signals in deltoid muscles (**A**) and quadriceps (**C**). In contrast, MRI following 3-month prednisolone treatment shows no inflammatory lesions in either extremity (**B** and **D**, respectively)

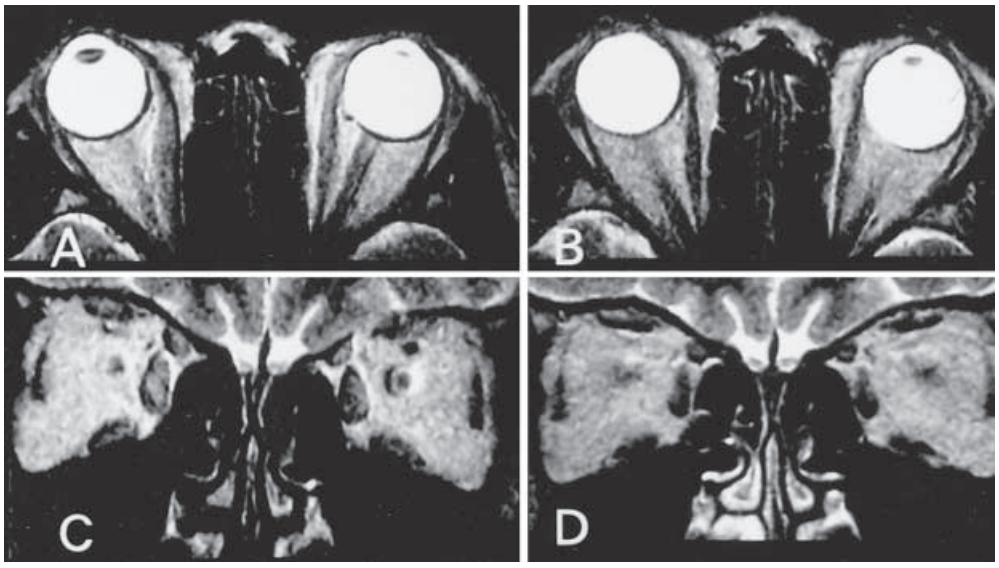

Fig. 2. MRI of both eyes shows swelling (**A**) and inflammation with increased T_2 signals (**C**) in bilateral medial rectus muscles. In contrast, MRI following 3-month predonisolone treatment shows no inflammatory changes in extraocular muscles (**B**, **D**)

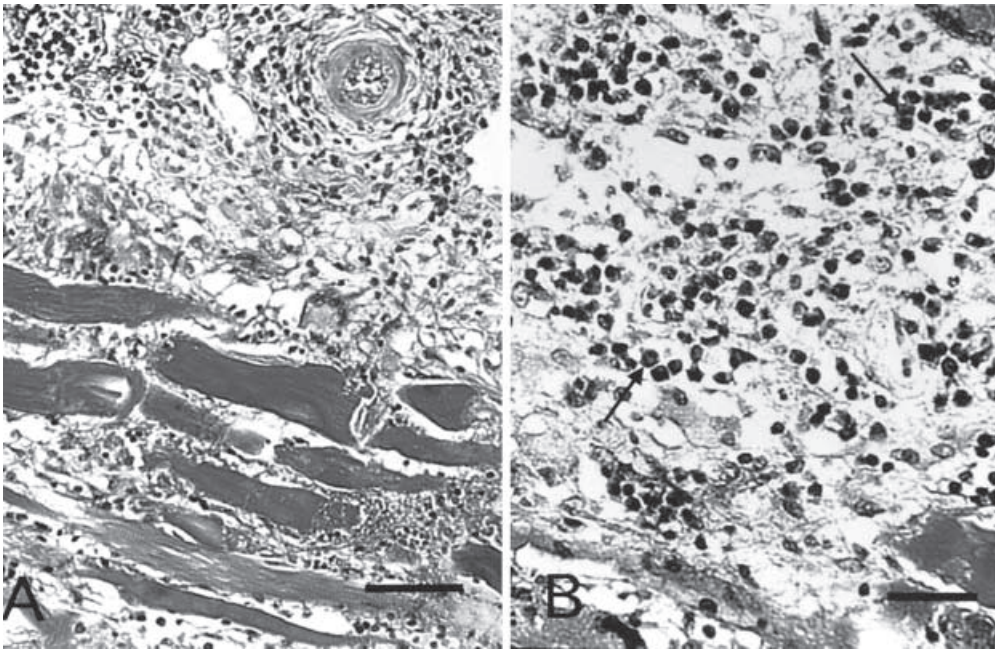

Fig. 3. Histopathological findings of the deltoid muscle biopsy specimen. **A** Degenerated muscle fibers are surrounded by eosinophils, which are partially infiltrated into perivascular areas, but vasculitis is not observed. *Bar* 200 μm. **B** Infiltrated cells mainly consist of eosinophils as indicated by *arrows*. *Bar* 100 μm

whereas polymyositis or dermatomyositis progresses gradually, and the clinical symptoms and laboratory abnormalities in eosinophilic myositis rapidly respond to corticosteroid therapy, which are consistent with our patient.[1,2,7] The number of eosinophils in the peripheral blood increase in many patients with eosinophilic myositis, but eosinophilia is not essential to the disease, as found in this patient. Eosinophilic myositis with eosinophilia sometimes resembles hypereosinophilic syndrome (HES), which is defined as the disease manifested by a sustained eosinophilia in association with multiorgan involvement in the absence of known causes of eosinophilia.[8] In HES, the cardiac muscle is a target organ and skeletal muscles are rarely affected. In our case, the patient had a normal number of peripheral blood eosinophils during the clinical course of her illness. In addition, she had no abnormalities in cardiac function. Accordingly, skeletal muscle involvement with eosinophilic infiltration in our patient was not likely to have developed as a part of HES.

The pathogenesis of eosinophilic myositis is not fully understood. Eosinophils contain cytotoxic protein granules such as major basic protein (MBP), eosinophil peroxidase, and eosinophil cationic protein. In these granules, MBP is thought to be a major candidate for muscle destruction induced by infiltrated eosinophils. In fact, MBP is present in the core of granules in eosinophils and is released as a toxic agent to both parasites and host cells. Moreover, MBP is shown to be cytotoxic to heart muscle cells.[9–11] Consistent with these findings, extracellular deposition of MBP in the affected skeletal muscle tissues of patients with eosinophilic

myositis was reported by Kaufman et al., indicating that MBP is a key factor in the process of the disease.[1]

In the current case report, the patient had eye symptoms such as ocular pain and limited eyeball movement although her visual acuity was normal. MRI showed inflammatory lesions in bilateral extraocular muscles. Orbital myositis, a subtype of nonspecific inflammation in the orbital regions primarily affecting extraocular muscles, involves both eyes, where the medial rectus is most frequently affected.[3,4] Patients with orbital myositis dramatically response to corticosteroid treatment. The clinical course and symptoms of our patient were consistent with these findings. Several investigators have shown that orbital myositis is sometimes complicated with systemic lupus erythematosus or giant cell myositis[5,6]; however, there is no case report describing the association of orbital myositis with eosinophilic myositis. Eosinophilic infiltration into the extraocular muscles is detected in some patients with orbital myositis[12]; therefore, it is conceivable that our patient had both diseases, resulting in a prompt and complete remission by PSL treatment.

Recent studies have shown the role of estradiol in eosinophilic infiltration into the uterine cervix.[13] Furthermore, Hamano et al. have reported that estradiol facilitates the adhesion of eosinophils to human mucosal microvascular endothelial cells and that a coadministration of estradiol and progesterone stimulates the degranulation and release of cytotoxic protein granules from eosinophils.[14] To our knowledge, only one case of drug-induced eosinophilic myositis has been reported; however, these findings suggest a possible link between the use of sex steroids, such as norgesterone and ethinylestradiol, and the development of eosinophilic myositis in our patient.

We showed here a first case report of eosinophilic myositis associated with orbital myositis. Sex steroids may contribute to the process of eosinophilic infiltration, although further studies are required for understanding the mechanisms accounting for disease development and progression.

References

1. Kaufman LD, Kephart GM, Seidman RJ, Buhner D, Qvarfordt I, Nassberger L, et al. The spectrum of eosinophilic myositis. Arthritis Rheum 1993;36:1014–24.
2. Pickering MC, Walport MJ. Eosinophilic myopathic syndromes. Curr Opin Rheumatol 1998;10:504–10.
3. Scott IU, Siatkowski RM. Idiopathic orbital myositis. Curr Opin Rheumatol 1997;9:504–12.
4. Mannor GE, Rose GE, Moseley IF, Wright JE. Outcome of orbital myositis. Ophthalmology 1997;104:409–14.
5. Grimson BS, Simons KB. Orbital inflammation, myositis, and systemic lupus erythematosus. Arch Ophthalmol 1983;101:736–9.
6. Kattah JC, Zimmerman LE, Kolsky MP, Chrousos G, Chavis R, Jaffe G, et al. Bilateral orbital involvement in fatal giant cell polymyositis. Ophthalmology 1990;97:520–5.
7. Kumamoto T, Ueyama H, Fujimoto S, Nagao S, Tsuda T. Clinicopathologic characteristics of polymyositis patients with numerous tissue eosinophils. Acta Neurol Scand 1996;94:110–4.
8. Fauci AS, Harley JB, Roberts WC, Ferrans VJ, Gralnick HR, Bjornson BH. The idiopathic hypereosinophilic syndrome: clinical, pathophysiologic, and therapeutic considerations. Ann Intern Med 1982;97:78–92.
9. Tai PC, Hayes DJ, Clark JB, Spry CJ. Toxic effects of human eosinophil products on isolated rat heart cells in vitro. Biochem J 1982;204:75–80.
10. Tai PC, Ackerman SJ, Spry CJ, Dunnette S, Oslen EG, Gleich GL. Deposits of eosinophil granules in cardiac tissues of patients with eosinophilic endomyocardial disease. Lancet 1987;8534:643–7.
11. deMello DE, Liapis H, Jureidini S, Nouri S, Kephart GM, Gleich GL. Cardiac localization of eosinophil-granule major basic protein in acute necrotizing myocarditis. N Engl J Med 1990;323:1542–5.
12. Jakobiec FA. Non-infectious orbital inflammation. In: Spencer WH, editor. An atlas and textbook. 4th ed. Philadelphia: WB Saunders; 1996. p. 2810–59.
13. Ramos LJG, Varayoud J, Kass L, Rodriguez H, Munoz de Toro M, Montes GS, et al. Estrogen and progesterone modulation of eosinophilic infiltration of the rat uterine cervix. Steroids 2000;65:409–14.
14. Hamano N, Terada N, Maesako K, Numata T, Konno A. Effect of sex hormones on eosinophilic inflammation in nasal mucosa. Allergy Asthma Proc 1998;19:263–9.