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CASE REPORT

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Severe subcutaneous generalized edema in a patient with dermatomyositis

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Abstract Subcutaneous generalized edema associated with dermatomyositis (DM)/polymyositis (PM) is extremely rare. Herein we report a case of severe subcutaneous generalized edema complicating DM. A 78-year-old woman was hospitalized in our department because of massive edema in the four limbs. Elevated muscle enzymes, heliotrope rash, results of electromyography, and muscle biopsy confirmed the diagnosis of DM. The absence of other diseases that could cause the symptoms indicated that massive edema was correlated with the pathophysiology of DM. Although myopathy and edema responded well to oral prednisolone, dysphagia persisted. We conclude that subcutaneous generalized edema can occur during the course of DM/PM, and subcutaneous vasculopathy may be involved in the pathogenesis of DM/PM.

Key words Dermatomyositis · Polymyositis · Subcutaneous generalized edema

Introduction

Idiopathic inflammatory myopathy (IIM) is considered a heterogeneous category with common features including symmetrical proximal muscle weakness, myalgia, and elevated serum skeletal muscle enzymes such as creatine kinase (CK) and aldolase (ALD). Dermatomyositis (DM), polymyositis (PM), and inclusion body myositis are well-known subtypes of IIM.

Massive subcutaneous generalized edema associated with DM/PM is extremely rare. To the best of our knowledge, this is the 12th reported case of generalized edema due to DM/PM, and the sixth in patients with DM reported in the literature.[1–8] The etiology and prognosis of DM/PM with generalized edema are still unknown. We report a 78-year-old woman who presented with severe subcutaneous edema in her upper and lower extremities as an initial clinical manifestation of DM.

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Case report

A 78-year-old woman presented with a 10-day history of tenderness and edema in her left upper limb and consulted a local hospital. Her serum creatinine kinase (CK) level was 2520 IU/l. Because of the unilateral manifestation, local inflammation or vascular occlusive disease such as venous thrombosis were suspected. Venography of her arms and computed tomography of the chest was conducted, revealing normal results. Over the next 7 days, her body weight increased by 5 kg to 51 kg, and she developed a heliotrope rash and massive pitting edema in both the upper and lower extremities (Fig. 1a). She was admitted to our hospital on August 22, 30 days after onset. On admission, weakness of the proximal muscles of both the upper and lower extremities and dysphagia were noted. Electromyogram revealed small amplitudes and short potentials, and nerve conduction was normal. These findings were compatible with inflammatory muscle disease. Muscle biopsy indicated myopathic change with perifascicular atrophy, muscle fibers with various sizes and degenerating fibers (Fig. 1b). Laboratory data on admission were as follows: white blood cell count, 4900/mm^3; platelet count, prothrombin time, and partial thromboplastin time, all normal; lupus anticoagulant and anticardiolipin antibodies, negative; C-reactive protein, 0.67 mg/dl; serum levels of creatinine, blood urea nitrogen, albumin, 0.5 mg/dl, 13 mg/dl, and 2.8 g/dl, respectively; serum CK level, 1390 IU/l; serum ALD level, 8.5 IU/l; creatinine-clearance, 58 ml/min; thyroid-stimulating hormone, free T3, free T4, within normal limits; antinuclear antibody, anti-SS-A/Ro, anti-SS-B/La, and anti-centromere antibodies, all positive; anti-aminoacyl tRNA synthetase antibodies including anti-Jo-1 antibodies, negative based on

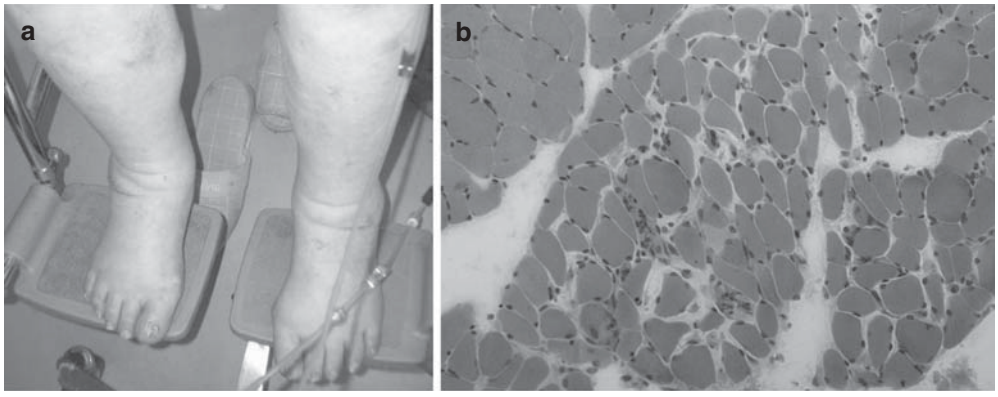

Fig. 1. **a** Pitting edema presented on the lower limbs. **b** A muscle biopsy specimen. Various sizes of muscle fibers were noted. A few degenerating fibers with mononuclear cell infiltration are also shown, consistent with DM (H&E stain, ×200)

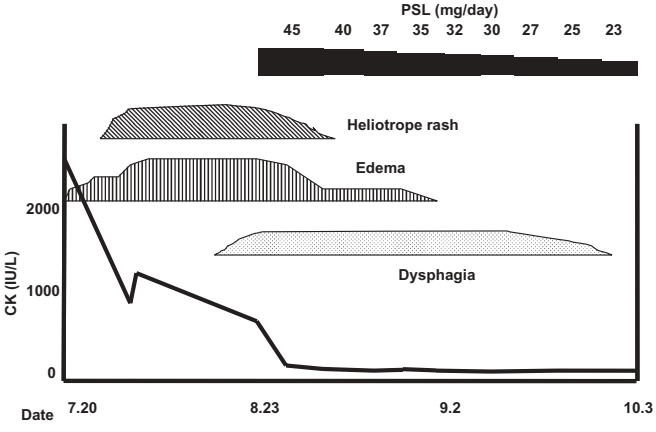

Fig. 2. Clinical course. *PSL*, prednisolone; *CK*, creatinine kinase

RNA immunoprecipitation assay. Echocardiography was almost normal, with only mild tricuspid regurgitation. Investigation of malignancy including ultrasonography and a computed tomographic scan of the abdomen and pelvis were normal. Her daily urine volume was normal. She was diagnosed as DM and given 45 mg/day of intravenous prednisolone (PSL) (Fig. 2). During treatment with PSL, she developed aspiration pneumonia because of severe dysphagia. Creatinine kinase decreased to a normal level in 5 days with PSL. Then, PSL was gradually tapered by less than 10% of the former dose over 1–2 weeks. Ten milligrams of oral PSL was maintained and her CK level did not increase again. Subcutaneous edema in her extremities also rapidly improved without any diuretics and her body weight reduced to 46 kg in 7 days. Although her proximal muscle strength gradually recovered, dysphagia persisted and she required intravenous hyperalimentation therapy for 40 days. Interstitial lung disease was not observed during the whole observation period.

Discussion

Symmetrical proximal muscle weakness, heliotrope rash, increased serum muscle enzymes, and typical findings of electromyogram and muscle biopsy in this case were compatible with DM. The absence of other diseases that might be associated with peripheral edema such as deep vein thrombosis, nephrotic syndrome, hypothyroidism, cardiac failure, liver disease, and malignancy strongly suggested that the edema had a close relation to the pathophysiology of DM. The patient did not take any drugs which could induce generalized edema. Rapid improvement of edema over the course of prednisolone treatment without diuretics or anticoagulation also strongly supported this speculation. Hypoalbuminemia followed peripheral edema and seemed to be caused by insufficiency of oral intake due to dysphagia, making it unlikely as a cause of edema.

The mechanisms underlying DM/PM with severe subcutaneous generalized edema are unknown. Protein-losing gastroenteropathy is known as a cause of abrupt peripheral edema in patients with systemic lupus erythematosus (SLE). Lupus-associated protein-losing enteropathy is characterized by the onset of edema and hypoalbuminemia, which, in many cases, is the first obvious manifestation of SLE. Dermatomyositis/polymyositis cases associated with protein-losing enteropathy have not been reported. In the present case, a normal level of serum albumin at the onset of edema and absence of diarrhea during the whole observation period makes the presence of protein-losing enteropathy unlikely. It is reported that serum concentrations of vascular endothelial growth factor (VEGF) are elevated in patients with remitting seronegative symmetrical synovitis with pitting edema, and VEGF could contribute to their increased vascular permeability and subcutaneous edema.[9] In the present case, VEGF in sera before treatment was 239 pg/ml by the enzyme-linked immunosorbent assay (SRL, Tokyo, Japan), which is within the normal range. We suspect that inflammation of adjacent muscle tissue or excessive vascular permeability in muscle and subcutaneous tissue as a result of immune complex-mediated vasculopathy may result in severe subcutaneous edema,[3,5,6,8] as suggested by the presence of vasculitis of small blood vessels and edema of the dermis in skin biopsy.[3] However, no vascular inflammation was observed on muscle biopsy of the present case.

Reviewing the literature, massive subcutaneous edema is associated with both adult DM and PM cases, without significant differences in their clinical characteristics (Table 1.).[1–8] Adult males are more frequently subjected to this

Table 1. Characteristics of 12 adult patients with edema associated with DM/PM

First author[Ref.]	Sex	Age (years)	Diagnosis	Site of edema	Dysphasia	Treatment	Outcome
Venables[1]	M	73	PM	Upper-lower limbs	+	Prednisolone, azathioprine	Dead
Venables[1]	M	32	PM	Upper-lower limbs	–	Prednisolone	Recovered
Venables[1]	M	52	PM	Upper-lower limbs	+	Prednisolone, azathioprine	Dead
Lyon-Caen[2]	M	65	PM	Upper limbs	–	No specific treatment	Recovered
Andonopoulos[3]	M	56	PM	Upper-lower limbs, trunk	+	Prednisolone	Recovered
Nitshe[4]	F	62	DM	Upper limbs, trunk	+	Prednisolone	Recovered
Smyth[5]	F	27	DM	Forearms	–	Prednisolone, azathioprine	Recovered
Gorelik[6]	M	31	DM	Upper-lower limbs	+	Hydrocortisone, immunoglobulin	Recovered
Gorelik[6]	M	63	DM	Left arm	–	No specific treatment	Recovered
Mroue[7]	F	78	DM	Upper limbs	–	Prednisolone	Recovered
Werner de Castro[8]	M	40	DM	Upper-lower limbs, trunk	+	Prednisolone, immunoglobulin	Dead
Present case	F	78	DM	Upper-lower limbs	+	Prednisolone	Recovered

PM, polymyositis; DM, dermatomyositis

condition than adult females, in spite of the female predominance in adult patients with DM/PM.[1–8] Cases of juvenile DM with anasarca were also reported.[10–13] In most cases, edema begins with the initial manifestation of myopathy, whereas edema can also be observed with the recurrence of myopathy.[1–8] Dysphagia or esophageal involvement is another characteristic of this entity, which often appears concomitantly with the resolution of edema and decline in serum muscle enzyme levels.[1,3,4,6,8] The presence of antinuclear antibody is described in some cases,[6,7] whereas myositis-specific or myositis-associated autoantibodies have not been investigated. Optimal treatment or prognosis of this myopathy has not yet been elucidated with analysis of additional cases; however, its prognosis seems to be relatively good.[8] Most edema symptoms resolve after the administration of prednisolone.[1,3,4,7] However, three patients died despite treatment with corticosteroids in combination with azathioprine or immunoglobulin,[1,8] whereas two patients recovered without any treatment.[2,6]

The frequency of severe generalized subcutaneous edema associated with DM/PM seems very low. Within 32 DM and 51 PM patients who consulted our department in Kyoto University Hospital from May 2001 to 2006, only the present patient manifested severe generalized subcutaneous edema.

Our patient responded well to prednisolone, and the serum muscle enzyme level rapidly decreased to the normal limit. In contrast to previous reports, the appearance of dysphagia was before the resolution of edema, and dysphagia continued despite the recovery of proximal muscle strength. Dysphagia was the final symptom of this patient that needed clinical intervention. Although recurrent cases have not been reported with long-term observation, close follow-up is essential in the present case.

In conclusion, subcutaneous generalized edema is a very rare manifestation that can occur as the initial symptom of DM. Additional cases are needed to establish guidelines for treatment and to clarify the pathogenetic mechanism of peripheral edema with DM/PM.

References

1. Venables GS, Bates D, Cartlidge NE, Hudgson P. Acute PM with subcutaneous oedema. J Neurol Sci 1982;55:161–4.
2. Lyon-Caen O, Bouche P, Chaunu MP, Duyckaerts C, Vitoux JF. Acute PM with spontaneously regressive subcutaneous edema. Rev Neurol (Paris) 1985;141:749–52.
3. Andonopoulos AP, Gogos CA, Tzanakakis G. Subcutaneous edema: "unrecognized" feature of acute PM. Rheumatol Int 1993;13:159–61.
4. Nitsche A. Edema de tronco y de pared abdominal en DM. Medicina (B Aires) 2000;48:331–2.
5. Smyth AE, Bell AL. Acute oedematous DM. Ann Rheum Dis 2000;59:575.
6. Gorelik O, Almoznino-Saraflan D, Alon I, Rapoport MJ, Goltsman G, Herbert M, et al. Acute inflammatory myopathy with severe subcutaneous edema, a new variant? Report of two cases and review of the literature. Rheumatol Int 2001;20:163–6.
7. Mroue KH, Sharara NH, Rbeiz JG, Arayssi TK. A case of edematous DM. J Rheumatol 2003;30:2722–3.
8. Werner de Castro GR, Appenzeller S, Bertolo MB, Costallat LTL. Acute DM with subcutaneous generalized edema. Clin Rheumatol 2006;25:898–900.
9. Arima K, Origuchi T, Tamai M, Iwanaga N, Izumi Y, Huang M, et al. RS3PE syndrome presenting as vascular endothelial growth factor associated disorder. Ann Rheum Dis 2005;64:1653–5.
10. Karabiber H, Aslan M, Alkan A, Yakinci C. A rare complication of generalized edema in juvenile DM: a report of one case. Brain Dev 2004;26:269–72.
11. Kimball AB, Summers RM, Turner M, Dugan EM, Hicks J, et al. Magnetic resonance imaging detection of occult skin and subcutaneous abnormalities in juvenile DM. Implications for diagnosis and therapy. Arthritis Rheum 2000;43:1866–73.
12. Mehndiratta S, Banerjee P. Juvenile DM presenting with anasarca. Indian Pediatr 2004;41:752–3.
13. Mitbell JP, Dennis GJ, Rider LG. Juvenile DM presenting with anasarca: a possible indicator of severe disease activity. J Pediatr 2001;138:942–5.