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CASE REPORT

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Acute inflammatory myopathy with severe subcutaneous edema, a new variant? Report of two cases and review of the literature

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Abstract Acute inflammatory myopathy with severe subcutaneous edema is extremely rare and has been reported in only a handful of cases. We describe two similar patients presenting with this disorder and generalized rash. Unlike the five previously reported cases, the clinical and histologic features of our two patients are more suggestive of dermatomyositis than polymyositis. Nevertheless, scrutinizing all seven reported patients, a number of specific characteristics could be defined. All patients were adult males. Dysphagia was present in four. In six patients, acute inflammatory myopathy was idiopathic while malignancy was present in one. Two patients died despite intensive therapy, three improved on corticosteroid treatment, and two recovered spontaneously. In all patients, limb involvement with marked subcutaneous edema was present, clinically mimicking deep vein thrombosis in both our patients. The presence of severe subcutaneous edema may be a hallmark of a distinctive variant of acute inflammatory myopathy. More cases are needed to discern subtypes of this general entity and to establish guidelines for treatment and prognosis.

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Introduction

The onset of inflammatory myopathy is typically insidious [1, 2, 3, 4]. Its association with severe subcutaneous edema is extremely rare, having been reported in only five cases with features of acute polymyositis [5, 6, 7]. Etiology and prognosis are not clear. We describe two additional patients who presented simultaneously generalized skin rash and other findings suggestive of dermatomyositis [2, 3, 4, 8]. We review the literature and attempt to define characteristic profiles, which may contribute to future recognition of pathophysiological variants and clinical course.

Case reports

Case 1

A 31-year-old man was admitted because of a 1-week history of high fever, painful mouth ulcers, maculopapular rash, and diffuse muscular weakness and pain. On admission, his temperature was 38°C, pulse was 80/min and regular, and blood pressure was 120/70 mmHg. On physical examination, buccal aphthous ulcers and maculopapular rash over the face, neck, dorsal aspects of hands, feet, and anterior aspect of thighs were noted. Mild proximal muscle weakness and tenderness were evident. The rest of the physical examination was unremarkable. Laboratory evaluation showed: hemoglobin 13.4 g/dl, hematocrit 39%, WBC count 3.9×10^9/l with 60% neutrophils, 21% lymphocytes, and 16% monocytes, platelets 132×10^9/l, ESR 8 mm/h, aspartate aminotransferase (AST) 115 IU/l (normal 5–38 IU/l), alanine aminotransferase (ALT) 43 IU/l (normal 4–41 IU/l), lactate dehydrogenase (LDH) 538 IU/l (normal 230–460 IU/l), and creatine kinase (CK) 2377 IU/l (normal 24–195 IU/l), with an MB isoenzyme fraction of 2.8%. Electro- and echocardiography and chest radiograph were normal. On the following days fever persisted, as did the painful oral ulcers and skin rash. The severity of proximal muscle pain and weakness increased, and the patient was unable to stand or walk. The initial treatment consisted of analgesics and intravenous fluids.

On the ninth hospital day, hemoglobin was 12.4 g/dl, WBC count 3.8×10^9/l and ESR 12 mm/h. Serum levels of AST, LDH, and CK were 1095, 2619, and 26320 IU/l respectively. Thyrotropin (TSH), complement, serum proteins, and immunoglobulins were within normal limits. Serologic tests for antinuclear antibodies (ANA), antineutrophil cytoplasmic autoantibodies (ANCA), rheumatic factor (RF), antistreptolysin O (ASO), cytomegalovirus (CMV), Epstein-Barr virus (EBV), HIV, enteroviruses, hepatitis A, B, and C, influenza A and B, adenovirus, parvovirus, mycoplasma, legionella, chlamydia, toxoplasma, salmonella, brucella, and rickettsia were all negative. Repeated urine and blood cultures were sterile. Electromyogram (EMG) revealed spontaneous activity, small amplitude, and short potentials, and nerve conduction was normal. These findings were compatible with inflammatory muscle disease. Skin biopsy from the thigh region showed lymphocytic and histiocytic infiltration around vessels of the dermis. Biopsy of the left quadriceps muscle was not revealing. On the tenth hospital day, pain and severe edema appeared suddenly in the left forearm. Ultrasonographic and Doppler examinations ruled out deep vein thrombosis. A nonpitting edema extended rapidly to the limbs and trunk within 24 h. Computed tomography of the pelvis and femoral regions showed marked subcutaneous edema. Chest and abdominal CT were unrevealing. The patient was treated with intravenous fluids, sodium bicarbonate, and 300 mg/day of hydrocortisone, which was later increased to 600 mg.

Over the following 2 weeks, the fever gradually subsided, subcutaneous edema improved, and skin rash and ulcerative stomatitis disappeared. However, severe proximal muscle pain and weakness persisted. On day 20, dysphagia appeared. Barium swallow was complicated by aspiration of barium into the bronchial tree. Biopsy of the left deltoid muscle was performed and examined by light and electron microscopy as well as by histochemical and immunohistochemical studies. The findings consisted of necrotic, degenerating, and regenerating muscle fibers with inflammatory infiltrates and microinfarcts, mostly in groups. Intravenous immunoglobulin (IVIg) was administered at 30 g/day for 5 days. The course was complicated by aspiration pneumonia and sepsis, for which piperacillin/tazobactam was added.

During the following 2 weeks, the patient's condition improved gradually. Levels of AST, LDH, and CK dropped to 78, 691, and 1,350 IU/l, respectively. On discharge after 70 hospital days, muscle weakness and pain were minimal, and muscle enzymes and blood count became normal. Repeated serologic tests for CMV, EBV, HIV, influenza virus, parvovirus, and enteroviruses remained negative. We recommended 70 mg/day of prednisone, with gradual tapering. At follow up after 1 year, the patient was completely well on 10 mg/day of prednisone.

Case 2

A 63-year-old, previously healthy man was hospitalized because of a 2-week history of high fever, maculopapular rash, proximal muscle pain, and weakness. On physical examination, his temperature was 38°C, pulse 92/min and regular, and blood pressure 140/80 mmHg. Maculopapular rash was noted over the face, neck, chest, and arms. Submandibular and axillary lymph nodes were enlarged. Marked weakness of the proximal arm muscles was present. The remaining physical examination was normal.

Laboratory findings were: hemoglobin 13.1 g/dl, WBC count $9{,}6\times10^9$/l, platelets 216×10^9/l, ESR 20 mm/h, ALT 150 IU/l, AST 501 IU/l, LDH 1521 IU/l, and CK 14,560 IU/l with normal MB fraction. Electrocardiogram and chest radiograph were normal. The patient was treated with intravenous fluids and sodium bicarbonate.

On the seventh hospital day, pain and severe edema of the left forearm appeared. Deep venous thrombosis was ruled out by ultrasonography and venography. Echocardiogram was normal. Examination by CT showed marked subcutaneous edema of the left forearm (Fig. 1) and unremarkable scans of chest, abdomen, and pelvis. The EMG revealed small amplitudes, short potentials, and spontaneous activity in proximal muscles of the arms, findings compatible with inflammatory muscle disease. Skin biopsy of the left arm showed edema of the dermis and lymphocytic infiltrations around blood vessels. Biopsy of the left triceps muscle revealed predominantly perivascular and interfascicular inflammatory infiltrates, necrosis, phagocytosis, and regeneration of muscle fibers. Axillary lymph node biopsy revealed reactive changes only. Serologic tests for toxoplasmosis, EBV, CMV, HIV, hepatitis A, B, and C viruses, influenza A and B, parvovirus, and enteroviruses were negative. ANA, RF, ANCA, Coomb's test, and cryoglobulins were negative. Serum proteins and immunoglobulins, complement, prostate-specific antigen, and TSH were normal. Blood and urine cultures were sterile. Gastroesophagoscopy and colonoscopy were normal. The patient was treated with intravenous fluids and sodium bicarbonate. On the following days, his condition improved and subcutaneous edema, muscle pain, and weakness diminished. Fever and skin rash disappeared and muscle enzymes returned to normal. He was discharged on the 15th hospital day. One year later, he was in good general condition.

Discussion

Acute polymyositis with severe subcutaneous edema is rare. Reviewing the literature, we have been able to find only five such cases [5, 6, 7]. The clinical, laboratory, and skin histological data of these seven patients are detailed in Table 1. All patients were adult males with a mean age of 53 years (range 31 to 73). This finding is in contrast with the female predominance among patients affected by inflammatory myopathies [3, 4]. Moreover, the clinical presentation in all seven patients consisted of an acute onset with proximal muscle pain and weakness, as opposed to inflammatory myopathy generally characterized by an insidious presentation [1, 2, 3, 4]. Three patients presented with fever, in one case arthralgia was noted, and one patient had ulcerative stomatitis. Serum CK ranged from 448 to 24,600 IU/l. Diagnosis was confirmed in all cases by EMG and muscle biopsy.

Dysphagia developed in four patients. Its appearance was reported in two of them concomitantly with resolution of subcutaneous edema and decline in serum muscle enzyme levels. In one patient, malignancy was eventually diagnosed, whereas in the remaining six no underlying etiology was discovered despite extensive diagnostic efforts.

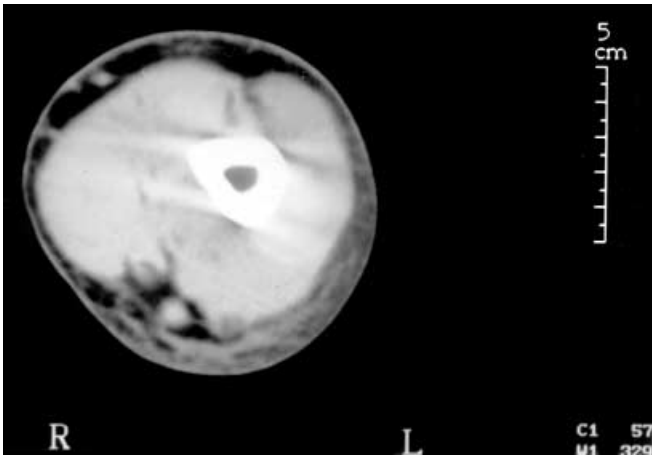

Fig. 1 Severe subcutaneous edema on CT scan of the forearm

Table 1 Characteristics of seven patients with acute inflammatory myopathy and marked subcutaneous edema. *ESR* erythrocyte sedimentation rate, *CK* creatine kinase, *LDH* lactate dehydrogenase, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *IVIg* intravenous immunoglobulin

Reference	Age (years)	Clinical features	Site of subcutaneous edema	ESR and muscle enzyme levels	Skin changes	Skin biopsy findings	Treatment	Fate	Duration of illness (months)
4	73	Proximal limb muscle pain and weakness, fever, dysphagia, respiratory failure	All four limbs	[a]CK 2940	None	Normal	Prednisone and azathioprine	Death	4
	32	Proximal limb, neck, and trunk muscle pain and weakness	Proximal region of four limbs	CK 561	None	Normal	Prednisone alone	Recovery	Not reported
	52	Limb, neck, and trunk muscle pain and weakness, dysphagia, respiratory failure	All four limbs	CK 9000	None	Normal	Prednisone and azathioprine	Death	1.5
5	65	Proximal and distal limb muscle pain and weakness, esophageal carcinoma	Upper limbs	ESR 123, CK 448, [b]LDH 395	None	Not reported	No treatment	Recovery	Not reported
6	56	Proximal limb muscle pain and weakness, arthralgia, dysphagia, aspiration pneumonia	All four limbs and trunk	ESR 35, CK 1300, [c]AST 133, [d]ALT 50	None	Edema of the dermis, small vessel vasculitis	Prednisone alone	Recovery	2
Present case 1	31	Proximal limb muscle pain and weakness, fever, painful oral ulcers, dysphagia, aspiration pneumonia, respiratory failure	All four limbs and trunk	CK 24,600, ALT 1084, AST 1095, LDH 2619	Maculopapular rash over face, neck, hands, and legs	Lymphocytic and histiocytic inflammatory infiltration around vessels of the dermis, edema of the dermis	Hydrocortisone, IVIg and prednisone alone	Recovery	4
Present case 2	63	Proximal limb muscle pain and weakness, fever	Left forearm	CK 14,560, ALT 150, AST 501, LDH 152	Maculopapular rash over face, neck, chest and arms	Edema of the dermis and around the vessels with lymphocytic infiltration	No treatment	Recovery	1

[a]Normal 24–195 IU/l
[b]Normal 230–460 IU/l
[c]Normal 5–38 IU/l
[d]Normal 4–41 IU/l

Two patients recovered with supportive treatment only. Five were treated with corticosteroids. Three of these improved, while the remaining two died of respiratory failure despite addition of azathioprine. In one of our patients, high-dose intravenous immunoglobulin was administered. Duration of illness ranged from 4 to 17 weeks. On long-term follow-up, recovery was complete in all five surviving patients.

The mechanism(s) underlying acute inflammatory myopathy with severe subcutaneous edema is not clear. Inflammation of adjacent muscle tissue or coexistence of vasculitis have been suggested [7]. Yet an additional mechanism could be envisaged, i.e., excessive vascular permeability which may eventually result in severe edema.

The cardinal feature of this entity, severe subcutaneous edema, involved at least one limb in all seven patients. In our two patients, edema appeared abruptly and presented initially at the forearm, mimicking deep vein thrombosis, which was subsequently ruled out. In one of these patients, the subcutaneous edema remained localized while in the second it extended rapidly to the other limbs and trunk. The localized nature of edema, its nonpitting characteristics, and the absence of any clinical or biochemical finding suggestive of cardiac, renal, hepatic, or endocrine disorder ruled out any systemic etiology for the edema. Although all seven patients apparently constitute a homogeneous group, the two cases reported here still differ from the previously described five cases in that a number of features are more suggestive of dermatomyositis. Clinically, both presented with maculopapular rash. Edema of the dermis and perivascular infiltration by lymphocytes and histiocytes were present. Moreover, muscle biopsy findings consisted of necrotic, degenerating, and regenerating alterations of fibers in both, assuming a patchy pattern in one. In the same patient microinfarcts were present. In the other, inflammatory infiltrations were predominantly perivascular and interfascicular. All these findings taken together are much more suggestive of the diagnostic option of dermatomyositis [2, 3, 4, 8]. It thus appears that our two patients represent a variant within the entity of acute inflammatory myopathy with severe subcutaneous edema. Whether this variant shares a similar course and prognosis with the other cases remains to be established. Moreover, additional cases are required to establish guidelines for optimal management.

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