RHEUMATOLOGY

Letter to the Editor (Case Report)

doi:10.1093/rheumatology/kex262

Life-threatening systemic capillary leak syndrome in juvenile dermatomyositis

Rheumatology key message

- Systemic capillary leak syndrome should be suspected in JDM patients with unexplained onset of oedema, myalgia, hypotension and rhabdomyolysis.

Sir, JDM is a rare disease characterized by chronic inflammation of muscle and skin. Herein, we describe three cases of JDM complicated by systemic capillary leak syndrome (SCLS), a rare, life-threatening disorder characterized by severe hypotension, hypoalbuminaemia and haemoconcentration [1].

Case 1: a 7-year-old boy presented with a 3-week history of skin rash associated with progressive fatigue. Physical examination revealed symmetrical proximal muscle weakness, heliotrope rash and Gottron's papules. On admission, laboratory tests showed elevation of all the muscle enzymes (Table 1). MRI showed spotty oedema of pelvic, gluteal and posterior thigh muscle groups consistent with inflammatory oedema. A diagnosis of JDM was made, and treatment with i.v. methylprednisolone pulses (30 mg/kg/day for 3 days) followed by prednisone (2 mg/kg/day) was promptly started. A week after admission, the patient presented with acute respiratory distress, dysphagia, sudden s.c. oedema of the neck and upper limbs, myalgia, oliguria and hypotension. Laboratory investigations showed worsening of all muscle enzymes, neutrophilic leucocytosis and a significant reduction of sodium and albumin (Table 1). The patient's general condition rapidly deteriorated, and he needed admission into the paediatric intensive care unit (PICU), where albumin infusion, diuretics and total parenteral nutrition were administered. As SCLS was suspected, IVIG therapy (400 mg/kg/day for 5 days) was started. The patient was discharged 1 month after admission on oral prednisone (1 mg/kg/day), MTX (15 mg/m^2/week) and monthly IVIG infusions (400 mg/kg/dose).

Case 2: a 13-year-old boy presented at our Unit with heliotrope rash, Gottron's papules over the elbows and generalized weakness (Childhood Myositis Assessment Scale [2] 15/51). MRI showed diffuse hyper-intense signals involving the thigh and pelvic muscles, with oedematous thickening of the s.c. tissues and diffuse perifascial oedema. Laboratory tests and muscle biopsy findings were consistent with inflammatory myopathy (Table 1). A diagnosis of JDM was made, and pulsed high-dose i.v. methylprednisolone therapy was started. In the following days, the patient presented with acute-onset generalized oedema, myalgia, dysphagia, respiratory distress, oliguria, hypotension and tachycardia. Blood tests worsened (Table 1). SCLS was suspected, and the patient was closely monitored by the PICU team and immediately treated with IVIG (400 mg/kg/day for 5 days). Weekly MTX s.c. injections (15 mg/m^2/week) were also started. Therapy was stopped after 2 years, and at the time of writing the patient is still in clinical remission off medication.

Case 3: a 3-year-old boy was admitted to a regional hospital because of progressive gait impairment, fatigue and muscle weakness. Laboratory tests were consistent with inflammatory myopathy (Table 1); therefore, three consecutive i.v. methylprednisolone pulses were administered. In the following days, the patient suddenly presented with oedema of the face and neck associated with oliguria. Blood tests rapidly worsened (Table 1). As the patient's clinical condition deteriorated, with anasarca, acute kidney and respiratory failure, he was transferred to the PICU of a tertiary referral Hospital, where mechanical respiratory assistance and aggressive immunosuppressive treatment with i.v. methylprednisolone pulses, CYC and plasmapheresis was adopted. Owing to the development of acute compartment syndrome in the upper extremities, an emergency fasciotomy was undertaken. The patient was discharged after 4 months' hospitalization with no defined diagnosis, unable to walk and with a severe bilateral visual impairment. Two months later, the patient presented eyelid and erythematous rash over the IP joints, face and ears. He was referred to our Unit, where physical examination revealed mild heliotrope rash, flexion contractures of knees and elbows, with diffuse muscle atrophy and weakness (Childhood Myositis Assessment Scale 15/52). MRI showed evidence of muscular oedema at the anterior compartment of both thighs and the pelvic girdle, with mild atrophy of the adductor muscles. Signs of calcinosis of the thighs were also present. A muscle biopsy was consistent with inflammatory myopathy; therefore, therapy with MTX (15 mg/m^2/week s.c.) and oral prednisone (1 mg/kg/day) together with an intensive physiotherapy programme were started. On the basis of his past medical history and the suspicion of previous SCLS, monthly IVIG infusions for 18 months were administered. Two years after the disease onset, the patient's muscle strength is normal, but the severe central visual impairment persists.

To the best of our knowledge, this is the first case series of JDM complicated by life-threatening SCLS. Only one case of DM complicated by fulminant capillary leak syndrome attributable to C1 inhibitor deficiency has been reported in an adult patient to date [3]. Interestingly, our patients developed SCLS while on

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Table 1 Laboratory changes during the systemic capillary leak syndrome in JDM

	Case 1		Case 2		Case 3	
	On admission	Systemic capillary leak syndrome	On admission	Systemic capillary leak syndrome	On admission	Systemic capillary leak syndrome
Creatine kinase, U/l	2291	32 407	17 744	18 900	1022	11 360
Aspartate transaminase, U/l	214	1500	561	822	1039	603
Alanine transaminase, U/l	95	570	165	112	487	108
Albumin, g/l	36	22	32	21	38	20
Haematocrit, %	38.5	54.7	40.2	48.2	35	47.6
White blood cells, /mm^3	9250	46 250	13 210	22 560	8810	29 010
Neutrophils, /mm^3	5490	40 240	10 410	18 533	5250	20 307
Sodium, mmol/l	140	122	136	125	138	123

high-dose methylprednisolone therapy, confirming that CSs cannot prevent this complication [4].

SCLS is a rare condition characterized by recurrent episodes of fluid and protein leakage in the interstitial compartment leading, in some cases, to hypovolaemic shock and death. Plasma leakage into muscle and fascia can cause increased intracompartmental pressure, inducing muscle damage, rhabdomyolysis and compartment syndrome [5]. The pathogenesis of this disorder seems to be related to abnormalities in VEGF, endothelial cell apoptosis and increased expression of pro-inflammatory molecules. More recently, SCLS has been reported in association with various autoimmune diseases [6]. A confirmation of the possible immunological pathogenesis of this complication is the reported efficacy of the IVIG treatment [7], clearly shown also in two cases of ours in which SCLS was promptly diagnosed. Given that generalized oedema, at JDM onset, is an indicator of severe disease course [8], a close monitoring of this subgroup of patients at high risk of developing SCLS is mandatory.

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

Disclosure statement: The authors have declared no conflicts of interest.

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Revised version accepted 6 June 2017

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