Systemic capillary leak syndrome: a case-report

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ABSTRACT

We report a case of a patient presenting with episodic hypotension, tachycardia and oedema, with an elevated serum IgG kappa paraprotein level. She was diagnosed as having systemic capillary leak syndrome and upon commencing oral theophylline has had no further presentations. The patient has since progressed to multiple myeloma.

Case Description

A 53-year-old woman was first admitted with a 5-day history of upper respiratory tract symptoms and a 1-day history of diarrhoea. At presentation she was alert and oriented with a pulse rate of 120 per minute and a systolic blood pressure of 85 mmHg. She developed progressive oedema to her mid-calves. The haemoglobin was 182 g/L with a haematocrit of 0.53. Initially her serum albumin was 37 g/L but fell over 2 days to 22 g/L. Her troponin was negative, ECG normal and echocardiogram revealed normal left ventricular function. The CRP was 15 mg/L and screen for sepsis was negative. Her serum creatinine was 225 µmol/L and she had 1+ protein in her urine with large numbers of hyaline casts. She had a low urine output. She was given 16 L of intravenous crystalloid solution over a period of 4 days with slowly improving blood pressure and urine output. She made a full recovery and was discharged 6 days after admission. No specific diagnosis was established.

Over the next 7 years the patient had 3 further admissions with profound hypotension, tachycardia and oedema, usually following trivial infections. The last of these admissions required a prolonged stay in the intensive care unit with intubation, ventilator and inotropic support, and transient dialysis. During each admission she was haemoconcentrated, hypoalbuminaemic and with evidence of pre-renal acute kidney injury. There was never any evidence of acute sepsis contributing to these events. Adrenal function was normal. Repeated echocardiograms showed normal systolic function. Serum protein electrophoresis showed the presence of an IgG kappa paraprotein with an estimated density of 3 g/L.

Based on the clinical features of the patients repeated presentations, a diagnosis of systemic capillary leak syndrome was made and the patient was commenced on oral theophylline. Over the subsequent 3 years she has had no further presentations with this disorder but has progressed to having multiple myeloma.

Discussion

Systemic capillary leak syndrome (SCLS) is due to recurrent episodes of generalised increased capillary permeability. This results in the rapid accumulation of fluids and proteins into the extravascular space, causing a rapid fall in blood pressure and subsequent hypovolemic shock. Episodes of SCLS are characterised by generalised
oedema associated with an elevated haemotocrit (haemoconcentration) and hypoalbuminaemia, usually in the absence of albuminuria.2

The progression of a typical episode of SCLS can be divided into three phases: prodromal, acute leak and late post-leak phases.3 During the prodromal phase, individuals often complain of weakness, malaise, myalgias and abdominal pain, which can last hours to days. This is followed by the leak phase, during which marked hypoperfusion, hypotension and oedema occur as a result of extravasation of fluid and protein. This typically lasts several days. The post leak phase occurs after the repair of capillary barrier function and involves the restoration of intravascular volume via reabsorption of extravasated fluids and proteins, and subsequent diuresis.3

Capillary permeability is normal during quiescent periods.4 Although the precise mechanism behind the increased capillary permeability has not yet been established, several hypotheses have been proposed. These include activation of the classical complement pathway, endothelial damage due to cytokines such as interleukins 2 and 6, interferon gamma and tumour necrosis factor alpha and raised plasma concentrations of vascular endothelial growth factor.4

SCLS is a clinical diagnosis and requires the exclusion of other conditions that can result in increased capillary permeability, such as sepsis. The majority of patients with SCLS also have a monoclonal gammapathy present and testing for this can be useful when the condition is suspected. During quiescent periods this is generally the only notable laboratory abnormality.5 The class of this paraproteinaemia is predominantly IgG with either kappa or gamma light chains.

During an acute episode, careful use of intravenous fluid support is recommended to maintain adequate perfusion of the kidneys, brain, and other vital organs. However sufficient fluids to normalise blood pressure often exacerbates the oedema and can predispose the patient to pulmonary oedema.4 During the post-leak phase there is mass reabsorption of extravasated fluids and proteins. This can result in acute intravascular fluid overload if the patient's kidneys are unable to compensate via diuresis. Therefore it is important that clinicians recognise the switch from the leak phase to the post-leak phase so they may alter patient management accordingly. This can been achieved with the use of loop diuretics if renal function is intact, otherwise haemodialysis or haemofiltration can be utilised.4

While no curative treatment exists for SCLS, several therapies have shown some success. Treatment with selective β2 stimulants (terbutaline) has been shown to inhibit the histamine and bradykinin-dependent macromolecular capillary leakage during acute episodes.6 In addition, combination treatment with theophylline and terbutaline reduces the incidence of, or completely abates, acute episodes of SCLS. More recently treatment with intravenous immunoglobulins has been used successfully as a prophylactic treatment.7 Several cases of SCLS-diagnosed patients progressing to multiple myeloma, as seen in our patient, have been described and therefore referral to a haematologist for surveillance is advised.8
CLINICAL CORRESPONDENCE

Competing interests: Nil

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