Case Report

Idiopathic systemic capillary leak syndrome – An often missed diagnosis

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Abstract

Idiopathic systemic capillary leak syndrome (ISCLS) is a potentially fatal disorder characterised by 'attacks' of varying intensity of hypovolemic shock in association with haemoconcentration and hypoalbuminaemia. It is a disease of

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exclusion, and the severity of attacks may mimic sepsis at presentation. We report a case of a lady with recurrent attacks of ISCLS with at least two life-threatening episodes, having been treated elsewhere as a case of steroid insufficiency. The diagnosis is often challenging, and treatment of an acute episode involves the judicious use of fluids and vasopressors, as required. Prophylaxis to prevent further attacks is of varied success.

Keywords
Systemic capillary leak syndrome, episodic hemoconcentration, IVIG, recurrent hypovolumic shock

Case report

A 44-year-old lady presented with complaints of episodic swelling of the body for three years' duration. Each episode, occurring once in five to six days, began with body aches, nausea, fatigue (prodromal phase) and a feeling of sudden weight gain and puffiness of the face (leak phase) with a reduced urine output lasting for a maximum of 48 h, followed by diuresis and resolution of symptoms (recovery phase). On some occasions, the symptoms were severe enough to cause hypotension and breathlessness requiring intensive care. The severity of each episode was dependent on factors such as exposure to hot climates and strenuous activity. She was evaluated elsewhere and was treated with danazol and glucocorticoids considering the possibility of angioneurotic oedema or cortisone deficiency.

On presentation to our centre, we stopped the glucocorticoids and assessed her hypothalamo-pituitary-adrenal axis, which was found to be normal (cortisol 13.5 ug/dL). C3, C4, C1 esterase inhibitor and anti-C1q antibody levels were normal (C3 90 mg/dL (90–180); C4 17 mg/dL (10–40); C1 esterase inhibitor 36 mg/dL (16–36); anti-C1q antibody 5 U/mL (<20). Serum electrophoresis revealed an M band in the γ region (M = 0.4% G). During her in-patient stay, she had an episode, and the parameters are listed in Table 1. It was a mild episode, and she never had a severe attack under our care. However, records from elsewhere (limited data) during a severe attack, when she was admitted with unrecordable blood pressure, showed haemoconcentration, leucocytosis and hypoalbuminaemia (Table 1).

Following literature review, we narrowed the diagnosis to ISCLS based on the following points:

- Recurrent episodes of typical symptoms suggestive of the three phases of ISCLS
- Haemoconcentration and hypoalbuminaemia during the episode
- Presence of monoclonal gammopathy
- No evidence suggestive of infection, drug allergy, anaphylaxis or angioedema

She was started on prophylactic intravenous immunoglobulin (IVIG) (1.5 g/kg/month). Following this, the episodes of capillary leak decreased significantly with no severe episodes thereafter and only mild episodes

Table 1. Lab parameters during the mild attack during hospital stay and limited data during an attack treated elsewhere.

	Mild attack in our care			Severe attack elsewhere	
Parameters	Day 1	Day 2	Day 3	Leak phase	Recovery onset
Haemoglobin (g/dL)	116	160	113	168	110
Total leucocyte count (x10^9/m)	4.4	–	5	53	19.6
Haematocrit (%)	37	54	36	56.6	36.6
Albumin (g/dL)	4.5	3.6	4.2	–	–
Creatinine (umol/L)	70	105	70	203	133
SGOT (U/L)	55	47	–	–	–
SGPT (U/L)	29	24	–	–	–
Sodium (mEq/L)	144	138	139	–	–
Potassium (mEq/L)	3.7	3.8	4	–	–
Creatine phosphokinase (U/L)	–	522	124	–	–
Intake/output (mL)	1700/500	2900/1700	2500/4600	–	–
Weight (kg)	75	76.5	76	–	–

when the immunoglobulin dose was delayed by more than four weeks. She has now received seven doses of immunoglobulin and is being followed up.

Discussion

ISCLS is a rare disorder characterised by episodes of hypotension, hypoalbuminemia and hemoconcentration due to leakage of plasma and proteins into the interstitial compartment.[1] The disease is more common in middle age without any gender predelection.[2] Several hypotheses have been proposed such as the presence of paraproteins, endothelial cell apoptosis and increased interleukin 2 expression.[3–5]

Attacks of ISCLS typically demonstrate three phases: a prodromal, leak and recovery phase. The frequency and severity of attacks vary significantly. The prodromal phase is characterised by symptoms such as fatigue, nausea, myalgia and a sudden increase in body weight. This is followed by a leak phase within one to four days, which is characterised by the triad of hypotension, haemoconcentration and hypoalbuminaemia. A rapid drop in the white blood cell counts from 53 to $19/m^9$ was suggestive of a non-infective aetiology and could be attributed to haemoconcentration. However, we acknowledge that this initial value was recorded elsewhere and not at our centre.

The leak phase is usually followed by a recovery phase during which the extravasated fluid is recruited into the intravascular compartment, and the patient is at an increased risk for volume overload.[6] Our patient had approximately five to six attacks per month with an average of two severe attacks per year.

Various treatment modalities such as corticosteroids have been tried in acute settings without success. Theophylline plus terbutaline has been used with lack of good evidence.[7] We found a good response to IVIG and observed that the attacks resolved almost completely. The mechanism of action of IVIG in preventing ISCLS is unclear, but probably arises through its immunomodulatory effects.[8]

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