Microalbuminuria following anaphylaxis with general anaesthesia

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Microalbuminuria is increasingly recognized as a marker of pathologies that cause acute systemic capillary leak. We report a case of an anaphylactic reaction to general anaesthesia involving cardiac arrest. In this case the urinary excretion of albumin following resuscitation suggests that severe anaphylaxis is another condition for which microalbuminuria is a sensitive monitor.

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Microalbuminuria secondary to systemic capillary leak is increasingly recognized in association with a number of acute medical and surgical conditions. We present a case of drug-induced anaphylaxis in which serial measurement of urinary albumin was made during resuscitation and subsequent intensive care. The potential role of microalbuminuria as a sensitive monitor of the systemic inflammatory response is discussed.

Case report

A 14-yr-old male, weighing 62 kg presented for surgery to release axillary contractures. Fourteen months previously the patient had sustained a 58% body surface area electrical burn and prior to this procedure he had already received 15 general anaesthetics, involving the uneventful administration of atracurium and morphine (both 11 times) and ondansetron (four times). Physically he was left with a

![Fig 1 Urine albumin excretion and haemoglobin following anaphylaxis and resuscitation. The fluid resuscitation block indicates volume loading with crystalloid and colloid in addition to normal maintenance requirements.](https://academic.oup.com/bja/article-abstract/84/6/808/343477)
Microalbuminuria following anaphylaxis with general anaesthesia below knee amputation and upper body contractures, but was otherwise well. On admission to hospital, physical examination of his airway and cardio-respiratory system were unremarkable. Arterial pressure and heart rate (sinus rhythm) were both within normal limits. Preoperative serum electrolyte and urea concentrations were normal (potassium 4.1 mmol litre\(^{-1}\)) and haemoglobin concentration was 13.8 g dl\(^{-1}\) (haematocrit 41%). He was not taking any medication. Unmedicated induction of anaesthesia occurred with up to 8% sevoflurane and 40% nitrous oxide in oxygen, during which oxygen saturation and ECG were monitored. After loss of consciousness an i.v. cannula was inserted and ondansetron 4 mg, morphine 3 mg and atracurium 30 mg given in sequence and flushed with normal saline. An initial brief period of resistance to hand ventilation with a bag and mask was immediately followed by rapid arterial oxygen desaturation, from 97% to 75% with an associated sinus bradycardia of 50 beat min\(^{-1}\). The trachea was intubated immediately and hand ventilation continued with 100% oxygen, while glycopyrrolate 0.2 mg was administered i.v. In spite of these measures the patient became pulseless, and external chest compression was started.

After a 20-min period of resuscitation involving the administration of 2 litres of normal saline, epinephrine 3 mg (three bolus injections of 1 mg) and atropine 3.6 mg (0.6 mg + one 3 mg bolus), a sinus tachycardia (160 beat min\(^{-1}\)) rhythm was restored with an arterial pressure of 100/60 mm Hg. Arterial blood-gas analysis immediately post-resuscitation revealed H\(^+\) 73.8 nmol litre\(^{-1}\), \(P_{\text{ACO}_2}\) 5.14 kPa and \(P_{\text{AO}_2}\) 62.3 kPa with a base excess of –16 mmol litre\(^{-1}\). The haemoglobin had risen to 18.1 g dl\(^{-1}\) (haematocrit 53%).

The patient was sedated with propofol and transferred to the intensive care unit (ITU) for mechanical ventilation and stabilization of his condition. On admission to ITU, arterial blood-gas analysis revealed a metabolic acidosis, H\(^+\) 67.3 nmol litre\(^{-1}\), \(P_{\text{ACO}_2}\) 5.19 kPa and \(P_{\text{AO}_2}\) 65.24 kPa with a base excess of –14.5 mmol litre\(^{-1}\) and a chest x-ray showed evidence of pulmonary oedema but was otherwise normal. At this time the patient was noted to have a pink rash, and serial blood and urine samples were taken to investigate the cause of his collapse.

Serum tryptase activities (reference range 4–14 \(\mu\)g litre\(^{-1}\)) immediately after the cardiac arrest, and 3 and 24 h later were >200, 151 and 39.5 \(\mu\)g litre\(^{-1}\), respectively. Hourly capillary permeability was assessed by urine albumin excretion rates (reference range <9.1 \(\mu\)g min\(^{-1}\)), which 1 h post-arrest, and after 3 and 15 h, respectively were 563, 1006 and 6.1 \(\mu\)g min\(^{-1}\) (Fig. 1). The immediate post-resuscitation haemoglobin of 18.1 g dl\(^{-1}\) (a finding consistent with an initial shift of protein and water into the interstitial space) had fallen to 11.0 g dl\(^{-1}\) 5 h later after further fluid resuscitation (Fig. 1). The patient’s lungs were ventilated for 3 days during which the only biochemical abnormality was a slowly resolving metabolic acidosis. All sedation was then discontinued until he could be extubated safely. His Glasgow Coma Score was 9 on discharge from the ITU, and a computerized tomographic scan of his brain performed 6 days post-arrest was reported as normal although electroencephalograms performed at 6 and 16 days post-incident demonstrated changes consistent with global cerebral hypoxia.

One month after discharge from ITU in vivo allergy tests to skin prick and intradermal injection were performed to identify sensitivity to a range of other neuromuscular blockers. The patient was subsequently issued with a medical alert bracelet and a ‘statement of clinical events’, including a list of the drugs involved in this incident and the results of the in vivo tests. He was discharged to neurological follow up and at the time of writing has made a substantial neurological recovery.

**Discussion**

This patient’s clinical presentation, response to treatment and the subsequent serum tryptase analysis strongly support a diagnosis of anaphylaxis from a type 1 hypersensitivity reaction. The tryptase levels documented in this patient are rarely seen without anaphylaxis,\(^1\) and furthermore the time course of the decline in the serum tryptase is also consistent with systemic mast cell degranulation at the time of cardiovascular collapse.\(^2\)

Mast cell degranulation does occur as a direct pharmacological action of narcotics, especially morphine. However, in such cases the serum tryptase is only moderately elevated. Type I hypersensitivity to morphine may also occur and the possibility of this ‘dual’ histamine release makes the interpretation of subsequent intradermal testing problematic. Hypersensitivity to ondansetron is relatively rare,\(^3\) and to our knowledge there are still no reports of suspected anaphylaxis to inhalation agents.

Anaphylaxis from neuromuscular blocking drugs is responsible for the majority of anaesthesia-related reactions,\(^4\) and cross-sensitivity between neuromuscular blocking drugs occurs in up to 60% of patients\(^5\) so that determination of safe drugs for future anaesthesia is a priority in the investigation of the patient. The subsequent investigation of our patient followed published guidelines\(^6\) in an effort to determine safe alternatives to atracurium.

The systemic inflammatory response syndrome (SIRS) is recognized as a non-specific and generalized response to a variety of traumatic and infective pathologies. Studies in trauma and burn patients have demonstrated that the severity of injury and subsequent development of SIRS correlates positively with an increase in urine albumin excretion (microalbuminuria),\(^7\)\(^8\) detectable only by sensitive immunoassay. Microalbuminuria is defined as a spot urinary albumin concentration of 30–200 mg litre\(^{-1}\), or alternatively as an excretion rate greater than 9.1 \(\mu\)g min\(^{-1}\).\(^9\) It is a feature of such diverse conditions as elective aortic aneurysm surgery, pancreatitis, bacterial meningitis and myocardial infarction.\(^10\) The underlying mechanism is loss of capillary
membrane integrity which permits generalized protein leak. What is not certain is the extent to which the degree of albuminuria may be predictive of the subsequent clinical course in different conditions.

Urine albumin excretion has been measured in 20 previously healthy individuals following bee or wasp stings. Abnormal values were recorded in three patients, whereas normal values were obtained in three other patients who were hospitalized with hypotension, respiratory problems and generalized urticaria, although the severity of their anaphylaxis is not stated. Urine was collected the morning after admission so it is possible that post-anaphylaxis microalbuminuria had resolved.

In contrast, our patient was monitored continuously for the first 20 h following anaphylaxis, during the first 5 h of which he developed clinical albuminuria (Fig. 1).

The albumin excretion we measured mirrored the elevation and decline in serum tryptase activity during the period of maximum capillary leak, and we believe that anaphylaxis may be another pathology in which microalbuminuria may serve as a non-specific but sensitive marker of the acute inflammatory response. Microalbuminuria cannot, in isolation, confirm a diagnosis of anaphylaxis but it may have prognostic value. Confirmation of this possibility in other cases of anaphylaxis would be dependent on albumin excretion being measured as near as possible from the time of onset, up to 12 h later.

References


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