Intensive Care Med (1989) 15:543–548

Intensive Care Medicine

Correspondence

Oesophageal perforation with minitracheostomy

Sir,

In their report of oesophageal perforation with minitracheostomy (Intensive Care Medicine 1989; 15:140–141), Drs. Claffey and Phelan state that despite adherance to the manufacturer's guidelines the tube passed lateral to the trachea to perforate the oesophagus in two patients.

Three simple modifications to technique make this loss of midline orientation less likely. First, stand at the head of the bed not at the side. Second, while infiltrating with local anaesthetic, pass the needle through the cricothryroid membrane aspirating air to identify the trachea and spray local anaesthetic onto the mucosa to reduce coughing and venous bleeding on incision. Finally, when the short, guarded scalpel blade is correctly inserted through the cricothyroid membrane it will usually stand there with a little support from an assistant. The left hand remains splinting the tissues on each side of the blade while the other hand picks up and aligns the introducer. The blade is then lifted clear by the assistant allowing immediate, easy insertion of the introducer.

The use of a Seldinger technique for cricothyrotomy may well prove easier and safer, however, the suggestion to modify the "Minitrach" technique to an open method using a longer blade seems to defeat the object of the procedure and takes us back to the florid description by Chevalier Jackson in 1921 [1].

Yours faithfully,

P.W. Allen and M. Thornton

Reference

1. Jackson C (1921) High tracheostomy and other errors, the chief cause of chronic laryngeal stenosis. Surg Gynecol Obstet 32:392–398

Dr. P.W. Allen, Department of Anaesthesia, Royal Brisbane Hospital, Herston, Qld 4059, Australia

Neutrophil elastase levels and major trauma in man

Neutrophils have been demonstrated to accumulate in the lung parenchyma in the Adult Respiratory Distresss Synchrome (ARDS) where they are capable of releasing proteolytic enzymes, eicosanoids and free oxygen radicals.

Neutrophil elastase (HNE) is a constituent of the primary (azurophil) granules of the human neutrophil and is released as the result of neutrophil activation [1]. In addition to degrading elastin, this protease enzyme acts against a wide range of other substrates including fibrinogen, complement components, fibronectin, plasminogen and immunoglobulins. It is currently believed to be important in the genesis of inflammatory tissue injury. Measurement of released neutrophil elastase provides a sensitive indicator of neutrophil activation. The aim of this study was to investigate whether neutrophil elastase plasma levels were elevated during the trauma process, together with the time course and levels involved.

Eleven patients were studied, 9 males and 2 females, with an age range 19–80 years (mean 43 years). All had sustained injuries as a result of a road traffic accident or a fall from a height. All patients were admitted directly from the scene of the accident to the resuscitation room of the Accident and Emergency Department at the Royal Infirmary of Edinburgh.

Venous blood samples were taken on the patients' admission to the resuscitation room, with the exception of one patient whose first sample was taken the following morning. Six patients had at least one further sample taken during the course of their hospital admission. The blood was centrifuged immediately, the plasma removed and stored at −20 °C. The concentrations of neutrophil elastase in the samples were subsequently measured using a radio-immunoassay technique for human neutrophil elastase similar to that of Plow [2]. The antibody used was produced in-house using rabbit polyclonal antisera. The antigen used was purified from human neutrophils after leucophoresis and was pure by gel electrophoresis. (The antigen was supplied courtesy of Dr. P. Davies, Merck, Sharp and Dome Ltd). The antibody has absolute specificity for neutrophil elastase and does not cross-react with pancreatic or platelet elastases. It detects HNE equally well as the free enzyme or when HNE is complexed with its inhibitors. The coefficient of variation within and between assays was less than 5%.

In the 10 patients who had samples taken within a few minutes of arrival, the initial level was significantly elevated. The range was 34-299 ng/ml, mean 125.5±82.3 ng/ml with 99.9% confidence limits 39.9–211.2 ng/ml (Fig. 1). The normal range was 18.7±10.1 ng/ml with 99.9% confidence limits of 15.1–22.3 ng/ml and $n = 80$ (Fig. 1). Levels fell progressively in those patients who were studied serially.

In order to determine whether there was any relationship between the severity of injury and the maximum concentration of human neutrophil elastase, Injury Severity Scores (ISS) were calculated for each patient using the Abbreviated Injury Scale [3]. The range of scores was 10–75. However, there was no direct correlation between the ISS and the peak level of neutrophil elastase ($r = -0.1928$; $p = 0.57$).

This study demonstrates that traumatised patients have very high levels of human neutrophil elastase detectable within minutes of sustaining their injury. The rapidity of rise in HNE leads to speculation about the mechanism whereby neutrophils are activated during the trauma process.

Previous work on patients with burn injury has indicated that maximal levels of neutrophil activation occur during the first 5 days after injury, while complement activation peaks on post-burn days 6 to 8 or later [4]. This provides strong evidence to support the theory that initial neutrophil activation in injured patients is mediated by mechanisms other than the complement pathway – be it the classic or the alternative one. Davis et al. felt that endotoxin was the most likely candidate and have demonstrated that endotoxin activates neutrophils at concentrations much lower than those required to activate complement [4]. Furthermore, endotoxin is known to be detectable in the circulation shortly after injury [5].

The absence of direct correlation between the severity of injury and HNE plasma levels is difficult to explain. There is a number of possible aetiologies. The lack of correlation between HNE and ISS may reflect an exogenous stimulus being involved. The neutrophil elastase level may reflect the total mass of injured tissue rather than the clinical severity of a particular injury [6]. Or a more general response to trauma that involves not only the size of the injury but

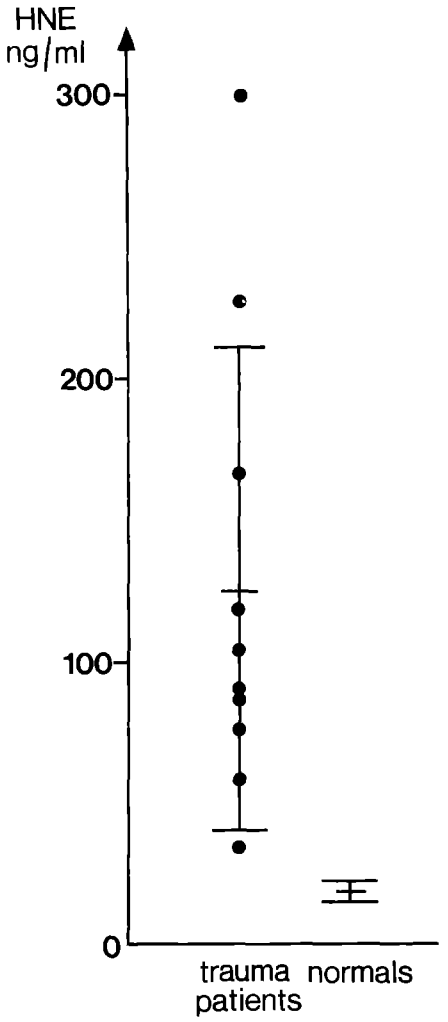

Fig. 1. Neutrophil elastase (*HNE*) levels on arrival in the resuscitation room. Mean and 99.9% confidence limits are indicated

other factors such as pain, fear and the development of clinical shock.

Further studies are underway to delineate the mechanisms involved in early neutrophil activation following trauma. Meanwhile, further investigation is required into the relationship between neutrophil elastase and the development of ARDS and other local tissue complications following trauma.

Yours sincerely,
M.W.G. Gordon, C.E. Robertson and J. Dawes

References

1. Gallin JI (1984) Neutrophil specific granules: a fuse that ignites the inflammatory response. Clin Res 32:320–328
2. Plow EF (1982) Leukocyte elastase release during blood coagulation, a potential mechanism for activation of the alternative fibrinolytic pathway. J Clin Invest 69:564–572
3. American Association of Automotive Medicine (1985) The Abbreviated Injury Scale 1985 Revision AAAM, 2350 East Devon Avenue, Suite 205, Des Planes, Illinois 60018
4. Davis CF, Moore FD, Rodrick ML et al (1987) Neutrophil activation after burn injury: contributions of the classic complement pathway and of endotoxin. Surgery 102:477–484
5. Maejima K, Deitsch EA, Berg R (1984) Promotion by burn stress of the translocation of bacteria from the gastrointestinal tracts of mice. Arch Surg 119:166–172
6. Dittmer H, Jochum M, Fritz H (1986) Freisetzung von granulozytärer Elastase und Plasmaproteinveränderungen nach traumatisch-haemorrhagischem Schock. Unfallchirurg 89: 160–169

Dr. C.E. Robertson
Department of Accident and Emergency Medicine
Royal Infirmary of Edinburgh
Lauriston Place
Edinburgh EH3 9YW, UK

Surgical intervention in hypercalcaemic crisis

Dear Sir,

Acute hypercalcaemia carries a significant mortality [1, 2]. Therapeutic interventions include intravenous fluids (saline), diuresis, steroids, diphosphonates, mithramycin, intravenous phosphate and acute haemodialysis or haemofiltration. Occasionally, despite these measures, the plasma calcium does not fall. We report a case which suggests that urgent surgical exploration of the neck may be indicated in this situation.

A 34-year-old negro male was admitted with a 5 day history of anorexia and weakness, abdominal pain, weight loss and vomiting. On examination, he was pyrexial 38 °C, tachycardic (100/min) and tachypnoeic (30/min). He had epigastric tenderness and a mass on the right side of his neck.

Investigations showed: sodium 132 mmol/l, potassium 2.4 mmol/l, urea 26.7 mmol/l, creatinine 36 umol/l, bicarbonate 29 mmol/l, chloride 90 mmol/l, calcium 5.2 mmol/l, albumin 44 g/l, corrected calcium 4.9 mmol/l, phosphate 1.58 mmol/l, haemoglobin 152 g/l, white blood count 18×10^9 and positive sickle cell trait. Hand, skull X-rays, CXR, and ECG were normal. A differential diagnosis of primary hyperparathyroidism or myeloma was made. Treatment was started with rehydration, potassium replacement, and steroids. The bone marrow result was non-diagnostic.

The patient deteriorated rapidly in the 6 h after admission, becoming unrousable and his respiratory rate increased to 40/min. Arterial blood gases ($FiO_2 = 0.4$) were pH 7.3, PaO_2 6.5 kPa and $PaCO_2$ 4.5 kPa. Central venous pressure and pulmonary capillary wedge pressure measurements were normal (3–9 cms H_2O and 10–14 mmHg). His CXR showed diffuse patchy shadowing.

He was intubated and ventilated, but his condition continued to deteriorate (PaO_2 7.0 kPa, $PaCO_2$ 7.0 kPa, pH 7.22) [($FiO_2 = 0.6$), minute volume of 12 l and 5 cm PEEP]. Despite rehydration, frusemide, hydrocortisone, calcitonin and mithramycin his calcium rose to 5.7 mmol/L. Examination of the neck revealed a mass which was confirmed on ultrasound. The patient proceeded to emergency exploration of the neck but profound hypotension, resistant to massive inotropic support resulted in the patient's death after removal of a 35 g parathyroid adenoma.

In a patient with severe refractory hypercalcaemia, therapeutic measures may be unsucessful. If therapy fails, a parathyroid adenoma should be considered as a possible diagnosis. Early surgical exploration of the neck will not compromise the prognosis if the

hypercalcaemia is associated with a malignancy, but may well save the patient's life if the diagnosis is hypercalcaemic crisis.
Yours sincerely,

K.R. Hughes and R.F. Armstrong

References

1. Schwetzer VG, Thompson NW, Harness JK, Nishiyama RH (1978) Management of severe hypercalcaemia caused by primary hyperparathyroidism. Arch Surg 113:373–381
2. Wang C, Guyton SW (1979) Hyperparathyroid crisis. Ann Surg 90:782–790

Dr. K.R. Hughes
Department of Medicine
5th Floor Jules Thorn Institute
Middlesex Hospital
Mortimer Street
London WIN 8AA
UK

Streptococcus suis meningitis, permanent perceptive deafness and endophthalmitis

Dear Sir,

We wish to report the case of a 43-year-old slaughterhouse worker with meningitis, permanent perceptive deafness and bilateral endophthalmitis due to *Streptococcus suis* type II (group R). This is only the third case of Str. suis infection occurring in our country [1] and to our knowledge only the second case with serious endophthalmitis which has been reported in the literature [2].

The patient was admitted with a two days history of fever, diarrhea and vomiting. He was lethargic but responsive to questioning. Blood pressure was 120–80 mm Hg, pulse rate 100/min and temperature 37.9 °C. Neurologic examination revealed marked nuchal rigidity, symmetric tendon reflexes, plantar reflexes were flexor and the pupils were reactive but slightly unequal. Ocular movements, speech and hearing were normal. No papilledema was seen. Blood examination showed a leucocytosis of 13×10^9/l and a thrombocytopenia of 52×10^9/l. Lumbar puncture yielded turbid cerebrospinal fluid (CSF) containing 2160 WBC/mm^3 (80% neutrophils) and Gram positive cocci (Table 1). Treatment was started with benzylpenicillin 24 million units/day. By the second day there was progressive hearing and visual loss. On audiovestibular examination a total perceptive hearing loss and spontaneous right sided nystagmus were noted. Cold caloric testing with ice-water gave no vestibular reaction in either ear. Ophthalmological examination showed the absence of light perception due to bilateral endophthalmitis. Severe bilateral anterior uveitis and posterior synechiae were found on slit lamp examination. The intraocular pressure was normal. The presence of dense vitreous exudates and membranes made ophthalmoscopic visualisation of the fundus impossible. Ultrasound examination of the eyes demonstrated bilateral extensive retinal detachments combined with dense vitreous echoes. Microscopic examination of the vitreous aspirate revealed some red blood cells and mononuclear cells. Gram stain and culture remained negative. A CT-scan and NMR-scan of the brain did not reveal any evidence of encephalitis. Meanwhile, the first culture of the CSF showed a Str. suis type II, sensitive to penicillin. Blood cultures remained negative. Further treatment with high dose benzylpenicillin resulted in normalisation of the cerebrospinal fluid (Table 1). Several months later there was still a total perceptive hearing loss in both ears and total vestibular areflexia. There was only light perception in the left eye.

Table 1. Cerebrospinal fluid composition

	23/10	25/10	27/10	3/11
WBC (mm^3)	2160	2214	760	25
Neutrophils (%)	80	95	90	–
Monocytes (%)	20	2	10	–
RBC (mm^3)	370	60	500	5
Glucose (mg %)	30	32	41	50
Protein (mg %)	115	113	107	31
Culture	Str. Suis	Negative	Negative	Negative

Str. suis type II is a well recognised cause of septicaemia, meningitis and purulent arthritis in young pigs [3]. Since 1968 more than 70 cases of human infection, mostly after exposure to pig meat, have been reported [3]. In gram-stained smears and even after culture Str. suis frequently is mistaken for a pneumococcus or enterococcus [3, 4]. Damage to the eighth cranial nerve with vertigo and varying degrees of hearing loss are well known [3, 5]. Endophthalmitis has only been reported in one previous case where Str. suis strains were grown from an anterior chamber tap [2]. Because complications of this infection are very severe and bacteriological identification is not always easy, physicians should suspect Str. suis infection in any patient with meningitis who works in the pig meat industry.
Yours sincerely,

L. Coolen, J. Dens, E. Baeck, C. Claes, R.L. Lins, H. Verbraeken and R. Daelemans

References

1. Van Ooteghem Ph, Ceusters W, Vakaet A, Claeys G, Verschraegen J, De Reuck J (1988) Streptococcus suis meningitis. Tijdschr voor Geneesk 44:119–122
2. McLendon BF, Bron AJ, Mitchell CJ (1978) Streptococcus suis type II (group R), as a cause of endophthalmitis. Br J Ophthalmol 62:729–731
3. Arends JP, Zanen HC (1988) Meningitis caused by Streptococcus suis in humans. Rev Infect Dis 10:131–137
4. Chau PY, Huang CY, Kay R (1983) Streptococcus suis meningitis: an important underdiagnosed disease in Hong Kong. Med J Aust 1:414–417
5. Shneerson JM, Chattopadhyay B, Murphy MFG, Fawcett IW (1980) Permanent perceptive deafness due to Streptococcus suis type II infection. J Laryngol Otol 94:425–427

Dr. R. Daelemans
Medical Intensive Therapy Unit
A.Z. Stuivenberg
Lange Beeldekensstraat 267
B-2008 Antwerpen
Belgium

High frequency jet ventilation

In their interesting paper regarding the efficacy of high frequency jet ventilation (HFJV) in dogs with oleic-acid induced pulmonary edema [1] Hachenberg et al. conclude that "both in interstitial and alveolar-edema continuous positive pressure ventilation (CPPV) is more effective than HFJV" and extend their animal model observations to the clinical setting. Since our laboratory and clinical findings in similar pathophysiological states do not completely coincide with their findings, we would like suggest that because of

legitimate but overstated concerns about "auto-PEEP" the authors may have used a less than optimal setting for HFJV, thus prejudicing their results.

The authors compare HFJV utilizing a frequency of 3 Hz and a driving pressure of 1.5 bar, without PEEP, with CPPV utilizing a PEEP of 0.5 kPa. The resultant mean airway pressure was significantly higher in the CPPV mode than for HFJV. The work of Fusciardi et al. [2] and the three other authors quoted by Hachenberg et al. supports the concept that mean airway pressure is a major determinant of gas exchange and oxygenation in diseased lungs. It would appear that HFJV, as utilized in this experiment, was inferior to CPPV. To justify this difference in mean airway pressures the authors refer to four papers showing that HFJV produces hidden "auto-PEEP" which they say may account for more than 0.6 kPa [3–6].

In reviewing these papers we find that Simon [3] and Saari [4] both used a high frequency oscillator and not a jet ventilator. In addition, both authors used frequencies which were for the most part much higher than were utilized in this experiment. Eliasen [5] used a jet ventilator and specifically stated that no "auto-PEEP" was found at frequencies less than 5 Hz. Rouby [6] found that HFJV induced a "PEEP effect" but considered that it was only significant in patients with normal or increased lung compliance and specifically recommended the jet ventilator for "all types of respiratory failure characterized by decreased lung volumes, low pulmonary compliance, or chest wall rigidity", a description that would fit the model utilized by Hachenberg et al. It would therefore appear that none of these papers supports the assumptions about "auto-PEEP" in this model. It is possible that use of HFJV with lower frequency, higher drive pressure and the application of PEEP would have resulted in the authors coming to a different conclusion about the relative value of HFJV and CPPV in the acutely injured lung.

References

1. Hachenberg T, Wendt M, Hermeyer G, Ludwid E, Meyer J, Lawin P (1989) High-frequency jet ventilation during oleic-acid induced pulmonary edema. Intensive Care Med 15:105–110
2. Fusciardi J, Rouby JJ, Benhamau D, Viars P (1984) Hemodynamic consequences of increasing mean airway pressure during high frequency jet ventilation. Chest 86:30–34
3. Simon BA, Weinmann GG, Mitzner W (1984) Mean airway pressure and alveolar pressure during high-frequency ventilation. J Appl Physiol 57:1069–1078
4. Saari AF, Rossing TH, Solway J, Drazen JM (1984) Lung inflation durign high frequency ventilation. Am Rev Respir Dis 129:332–336
5. Eliasen K, Morgensen T, Anderson JB (1986) Peripheral airway pressure during high frequency ventilation. Acta Anaesth Scand 30:97–100
6. Rouby JJ, Simmoneau G, Benhamou D, Sartene R, Sardnal F, Deriaz H, DuRoux P, Viars P (1985) Factors influencing pulmonary volumes and CO_2 elimination during high frequency ventilation. Anesthesiology 63:473–493

J. Gilbert and B. Smith, The University of Texas, Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78284-7838, USA

Hyperlactataemia and increasing metabolic acidosis due to the use of lactate based fluid during haemofiltration

Dear Sir,

The currently commercially available replacement fluids for haemofiltration are acetate or lactate based. Lactate is converted to bicarbonate on an equimolar basis via the Cori cycle. Indeed treatment using large volumes of lactate based fluids in continuous high volume haemofiltration/and or dialysis in patients with adequate hepatic function can result in a metabolic alkalosis [1]. If the rate of administration of lactate exceeds the rate of metabolism, hyperlactataemia occurs. However-previous reports have suggested that hyperlactataemia has no adverse consequences [2, 3]. We report a case in which sequential haemofiltration treatments resulted in increasing hyperlactataemia and acidosis.

A 24-year-old man developed fulminant hepatic failure and oliguric renal failure following paracetamol (acetaminophen) self poisoning. On admission he was in grade 4 hepatic coma and required ventilation. Serum urea 13.4 mmol/l (81 mg/dl), creatinine 787 µmol/l (8.9 mg/dl), alanine transferase 6.071 iu/l (normal <15 iu/l), alkaline phosphatase 12.1 KAu/dl (normal <13), bilirubin 132 µmol/l (normal <15), and prothrombin ratio 8.6 (normal <1.1). Despite volume expansion and dopamine (5 µg/kg/min), he remained oliguric, urine volume less than 5 ml/h. He was therefore treated by daily machine haemofiltration using a polyamide haemofilter (Gambro FH77, Gambro AB, Lund, Sweden), blood pump speed 200 ml/min, transmembrane pressure 200 mmHg, and minimal heparinisation was required. A typical isovolaemic 17 l exchange of fluid was completed in 3.5–3.9 h using a lactate based fluid (Filtrasol 22, containing 45 mmol/l) of a racaemic mixture of D and L lactate).

Arterial blood lactate was measured during each treatment, samples were collected into buffered cetrimide (ICI, Macclesfield, UK) and sodium fluoride, and analysed using an Analox LM2 (Analox, Hammersmith, UK). In addition the arterial hydrogen ion concentration ($[H^+]$) and serum bicarbonate were also measured.

Prior to each treatment, circulating volume was corrected if necessary, and an isovolaemic exchange was undertaken. Mean arterial blood pressure remained in excess of 80 mmHg during all five treatments.

There was a serial increase in the degree of hyperlactataemia during the five haemofiltration treatments (Fig. 1). During the first two treatments the $[H^+]$ decreased and serum bicarbonate increased as expected. Thereafter, $[H^+]$ increased progressively, from 35 to 50 nmol/l (normal range 35–45 nmol/l) during the fifth treatment, and serum bicarbonate fell progressively, from 23.5 mmol/l to

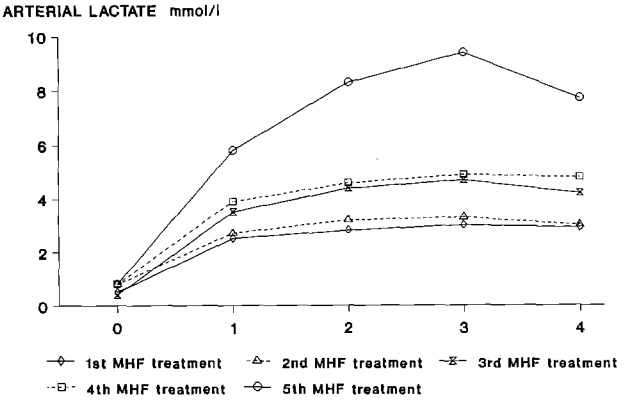

Fig. 1. Increase in lactate during sequential treatments

16.5 mmol/l during the fifth treatment. During this period the serum alanine transferase fell to 150 iu/l and the prothrombin ratio to 1.4 respectively.

One explanation for the paradoxical increases in $[H^+]$ would be that as liver function was severely affected, the rate of conversion of lactate to bicarbonate was less than the rate at which bicarbonate was lost to the ultrafiltrate, and therefore the acidosis was due to bicarbonate loss. However, the absolute bicarbonate loss in the ultrafiltrate was consecutively less with each treatment, being 513 mmol for the first and 342 mmol for the fifth. Thus bicarbonate loss cannot be the explanation. Hyperlactataemia results in the intracellular accumulation of lactate, and in vitro this has been shown to reduce the cytosolic phosphorylation potential and so reduce the amount of ATP available for energy dependent metabolism and cell function [4]. In vivo lactate accumulation has been shown to affect cardiac function by reducing ventricular muscle contraction [5]. It may be that in patients with severe liver failure, who have disturbances of tissue oxygen delivery that hyperlactatemia by affecting cellular energy dependent mechanisms causes a vicious circle to develop, and that bicarbonate based fluids are required in the management of these special cases.

Yours sincerely,

A. Davenport, K. Aulton, R.B. Payne and E.J. Will

References

1. Davenport A, Worth DP, Will EJ (1988) Hypochloraemic alkalosis after high flux continuous haemofiltration and continuous arteriovenous haemofiltration with dialysis. Lancet II:658
2. Glancey GR (1988) Lactate haemodialysis. Artery 4:4–5
3. Cohen RD, Iles RA (1980) Lactic acidosis: diagnosis and treatment. Clin Endocrinol Metab 9:513–527
4. Veitch RL, Lawson JWR, Cornell NW, Krebs HA (1979) Cytosolic phosphoarylation potential. J Biol Chem 254: 6538–6542
5. Saman S, Opie LH (1984) Mechanisms of reduction of action potential duration of ventricular myocardium by exogenous lactate. J Mol Cell Cardiol 10:659–662

Dr. A. Davenport, Department of Renal Medicine, St. James's University Hospital, Beckett Street, Leeds LS 9 7TF, UK

Hemophagocytic syndrome associated with coxsackie virus A 9 infection in a non-immunosuppressed adult

Dear Sir,

Benign histiocytic proliferation with marked hemophagocytosis demonstrated by bone marrow histology has been reported in association with active viral infection and has been named virus associated hemophagocytic syndrome (VAHS) [3]. We report a case of VAHS which was possibly related to Coxsackie virus A 9 infection in a non-immunosuppressed adult who had a systemic illness with comatose encephalitis, acute renal failure and hepatitis.

Case history. A 56-year-old woman, with no past medical history, was admitted to our ICU (D0) from a general hospital where she had been referred with fever (38.7 °C), chills, sweating, diarrhoea, generalized macular rash and diffuse arthritis. On admission, the patient was somnolent and mildly icteric, without fever. Physical examination revealed a left ptosis, liver enlargement, petechial purpura on the legs and hands but no splenomegaly nor lymphadenopathy. Liver cytolysis (SGOT 480 IU/L, SGPT 232/L), non-oliguric acute renal failure (serum creatinine 541 µmol/l) and profound hyponatremia (plasma sodium 112 mmol/l) were noted. The prothrombin time was 67% and the fibrinogen level was 1.6 g/l. 31 h later, she developed seizures, despite a normalized plasma sodium, and required intubation, mechanical ventilation and IV barbiturate therapy. Her CSF was clear and contained 3 mmol/l glucose, 0.68 g/l protein and 40 lymphocytes/ml. Cerebral computed tomography was normal. Simultaneously blood leukopenia and thrombopenia developed (WBC count: 4200/ml, 66% neutrophils at D0 and 1800/ml, 29% neutrophils at D2; platelet count 25000/ml at D0 and 10000/ml at D2). Bone marrow smears demonstrated proliferation of large histiocytes with erythocyte and neutrophil hemophagocytosis, no abnormal cells were seen. From D13, the bone marrow aplasia reversed with a significant reduction of histiocytic proliferation and renal function improved, as did liver function. The conscious level improved slowly allowing spontaneous ventilation via a tracheotomy tube. The seizures persisted and continued IV therapy was required. Septic shock associated with a venous catheter led to death 5 months later.

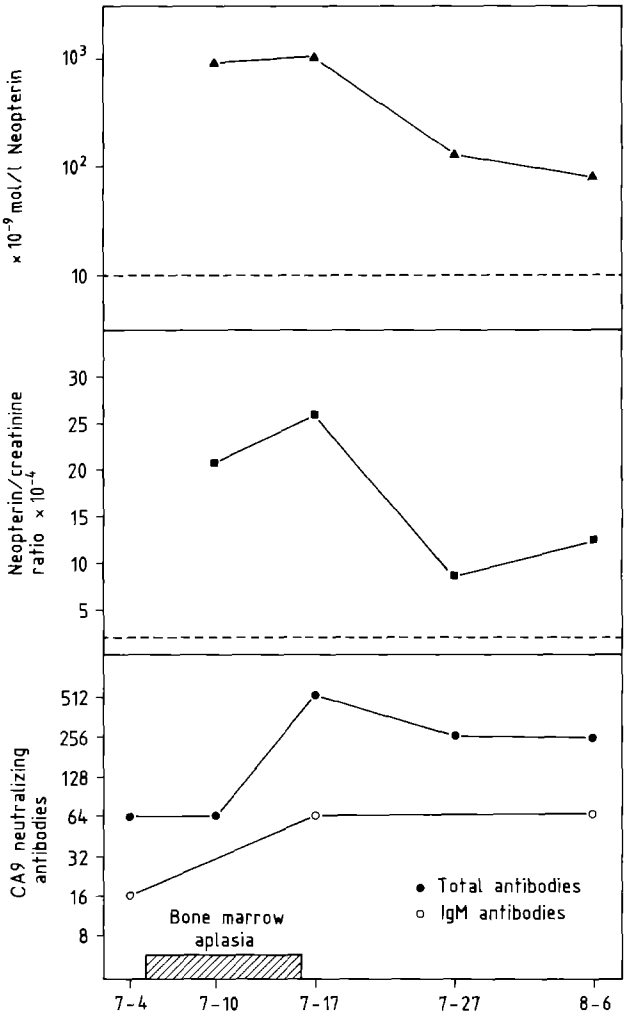

Fig. 1. Evolution of various biological parameters from July 04 (day 1 of ICU admission) to August 06 (day 34). The *dashed lines* represent the top of the normal range. (July 04 = 7–4, August 06 = 8–6 etc.)

Cultures of blood, urine, respiratory secretions, CSF and stools (which were also inoculated into suckling mice) were negative for bacteria, parasites and viruses. Cerebral and hepatic biopsy tissue showed non-specific inflammatory lesions and were sterile on culture. Serological tests for a broad spectrum of agents showed no evidence for infection with the exception of neutralizing antibodies against coxsackie A9 (Fig. 1). Serology was also negative for other enteroviruses (echoviruses 7, 8, 11; coxsackie B 4 and B 5). A part from the serum neopterin and the neopterin/creatinine ratio being 10 times the normal value (Fig. 1), the rest of the immunological workup was normal.

Discussion. Apart from the absence of lymphadenopathy this case closely resembles other reported cases of VAHS [3, 5]. In contrast to the 14 immunosuppressed patients reported in [3], our patient was immunocompetent. Viruses previously implicated in this syndrome are cytomegalovirus, Epstein-Barr virus, varicella-zoster virus and adenoviruses [3, 5]. In another report an enterovirus (coxsackie B 5) infection was suspected in a 12-year-old girl at the onset of Still's disease [2].

The case we have reported is to our knowledge only the second reported case of VAHS related to an enterovirus infection, demonstrated by serological evidence. The high levels of neopterin production related to acute viral infection in renal transplantation [1, 4], is an additional, although non-specific, indication of viral infection in our patient. As the production of neopterin by macrophages is induced by gamma interferon released from activated T lymphocytes, we speculate that this activation of macrophages contributed to the histiocytic proliferation.

Yours sincerely,

C. Guerin, B. Pozzetto and F. Berthoux

References

1. Hacini D, Guerin C, Berthoux P, Ville G, Berthoux F (1987) Monitoring of the serum neopterin/creatinine ratio in renal transplantation. Transplantation Proc 19:2185
2. Heaton DC, Moller PW (1985) Still's disease associated with coxsackie infection and hemophagocytic syndrome. Ann Rheum Dis 44:341
3. Risdall RJ, McKenna RW, Nesbit ME, Krivit W, Balfour HH, Simmons RL, Brunning RD (1979) Virus-associated hemophagocytic syndrome. A benign histiocytic proliferation distinct from malignant histiocytosis. Cancer 44:993
4. Schafer AJ, Daniev V, Dreikorn K, Opelz G (1986) Assessment of plasma neopterin in clinical kidney transplantation. Transplantation 41:454
5. Sullivan JL, Woda BA, Herrod HG, Koh G, Rivara FP, Mulder C (1985) Epstein-Barr virus-associated hemophagocytic syndrome: virological and immunopathological studies. Blood 65:1097

Dr. C. Guerin, Service de Néphrologie, Dialyse et Transplantation, Hôpital Nord, Avenue Albert Raimond, F-42277 Saint-Priest-en-Jarez, France