Comment

This demonstration of "pseudonormonatremia" may be relevant to the interpretation of electrolyte concentrations in patients with severe lipaemia or paraproteinaemia. Hypernatraemic states are associated with a high mortality,² and it is important that they should not be missed or underestimated.

¹ Halter, J B, *et al*, *Journal of Clinical Endocrinology and Metabolism*, 1977, **44**, 609.

² Daggett, P, *et al*, *British Medical Journal*, 1979, **1**, 1177.

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Waterhouse-Friderichsen syndrome caused by *Haemophilus influenzae* type b

The Waterhouse-Friderichsen syndrome describes a clinicopathological correlation between a catastrophic illness in childhood and bilateral adrenal haemorrhages found at necropsy. The clinical features include rapid onset and progression to shock and cyanosis with a petechial rash. Death follows rapidly, often within 24 hours of the first symptoms. The syndrome is often associated with meningococcal septicaemia, although it may occur with pneumococcal or staphylococcal sepsis. There are a few reports of an association with other septicaemic illnesses, some in immunologically compromised children. We report a case of the Waterhouse-Friderichsen syndrome associated with *Haemophilus influenzae* type b septicaemia.

Case report

A 9-month-old Caucasian girl presented with a four-hour history of listlessness, vomiting, and grunting respirations. The onset had been acute with a brief convulsion. She had been healthy until two weeks before admission, when she had received a seven-day course of penicillin for otitis media with complete recovery. She was pale and listless with grunting respiration and tachypnoea. The rectal temperature was 39°C and the heart rate 200 beats/min. There were no localising physical signs in any system. The white blood cell count was reduced at $4.6 \times 10^9/l$ ($4600/mm^3$), of which 28% were neutrophils. Plasma urea and electrolyte concentrations were normal. Lumbar puncture yielded clear CSF at normal pressure containing 3×10^6 white blood cells/l ($3/mm^3$) and 15×10^6 red blood cells/l ($15/mm^3$). The CSF protein and glucose were normal. A Gram-stained smear of a centrifuged deposit of the CSF showed no organisms. A septicaemic illness was suspected and treatment begun with intravenous penicillin and gentamicin. Five hours later the child collapsed with severe peripheral vasoconstriction and cyanosis. Despite vigorous resuscitation there was relentless clinical deterioration.

Ten hours after admission a few colonies of *H influenzae* were isolated from the CSF. Counter immunoelectrophoresis at this time showed *H influenzae* antigen in the blood culture, from which *H influenzae* was isolated the next day. Chloramphenicol was then added to the antibiotic regimen. Scattered petechiae appeared on the skin: coagulation studies suggested disseminated intravascular coagulation. The child died 15 hours after admission. CSF obtained immediately after death yielded a few

colonies of *H influenzae* on culture after three days' incubation, but blood obtained simultaneously was sterile. *H influenzae* was not isolated from throat swabs from the child's family. Necropsy showed bilateral haemorrhagic adrenal infarction, but there was no focus of infection and no evidence of meningitis. Immunoglobulin concentrations assayed on a blood sample taken during resuscitation were all decreased: IgM 0.21 g/l, IgA 0.10 g/l, and IgG 2.50 g/l. There was, however, no confirmatory evidence of immune deficiency. Lymph node and thymus morphology was normal. The other members of the family had normal immunoglobulins and isohaemagglutinin titres.

Comment

H influenzae type b causes a septicaemic illness in young children, usually with a focus of infection in the meninges, epiglottis, or bones. Although the illness is often severe, with endotoxic shock, the Waterhouse-Friderichsen syndrome is rare. We have found only five reported cases where clinical details were given (table) and a further three probable cases in which clinical details were not reported.¹ In all cases where clinical details were available purulent meningitis was a presenting feature. Our case, however, shows that *H influenzae* type b may closely mimic the meningococcus in causing an overwhelming septicaemic illness with a normal cell count in the CSF.

We thank Dr Hugh Johnson for reporting on the necropsy.

¹ Harms, D, Pape, G R, and Bohle, A, *Deutsche medizinische Wochenschrift*, 1973, **98**, 542.

² Lindsay, J W, *et al*, *American Journal of the Medical Sciences*, 1941, **201**, 263.

³ Ginandes, G T, and Howard, J E, *Journal of the Mount Sinai Hospital*, 1947, **14**, 778.

⁴ Cavinato, G, and Rude, L, *Pediatrics (Napoli)*, 1969, **77**, 452.

⁵ Fox, B, *Archives of Disease in Childhood*, 1971, **46**, 680.

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Complication of mebendazole treatment for hydatid disease

Mebendazole may shrink or kill hydatid cysts, thus avoiding the need for operation.¹ Although the drug is used in high doses, few side effects or complications have been recorded. We describe two patients who became feverish during treatment, possibly as a response to drug-induced tissue necrosis.

Case reports

Case 1—A 11-year-old Libyan girl had progressive abdominal distension due to multiple hydatid cysts, which had been found at a laparotomy one year before. Her haemoglobin concentration was 10.1 g/dl and erythrocyte sedimentation rate over 100 mm in first hour. Blood urea, blood sugar, and plasma bilirubin concentrations were normal, as were serum alkaline phosphatase and serum aspartate aminotransferase activities. Serum albumin

Previously reported cases of *H influenzae* causing Waterhouse-Friderichsen syndrome

Author	Age (months)	Duration of illness (hours)	CSF white cell count ($\times 10^6/l$)	Cultures		Necropsy
				Blood	CSF	
Lindsay <i>et al</i> ²	36	48	1420	<i>H influenzae</i>	<i>H influenzae</i>	Purulent meningitis, bilateral adrenal haemorrhage
Lindsay <i>et al</i> ²	6	13	986	<i>H influenzae</i>	<i>H influenzae</i>	Meningeal oedema and exudates, bilateral adrenal haemorrhage
Ginandes and Howard ³	48	48	"Cloudy"	<i>H influenzae</i> type b	<i>H influenzae</i> type b	Focal adrenal haemorrhage. Brain not studied
Cavinato and Rude ⁴	24	36	400	—	<i>H influenzae</i>	Purulent meningitis, bilateral adrenal haemorrhage
Fox ⁵	7	33	"Purulent"	—	<i>H influenzae</i>	Purulent meningitis, bilateral adrenal haemorrhage

concentration was 22 g/l, total protein 94 g/l, IgG 5.5 g/l, IgA 3.1 g/l, and IgM 5.6 g/l. Abdominal computed tomography (CT) showed multiple cysts in the liver 2-3 cm diameter and cysts in the spleen and posterior abdominal wall. Pulmonary cysts were seen on chest radiography. She began treatment with mebendazole, the dose increasing to 250 mg thrice daily. On the tenth day she became unwell, with a swinging fever and pleuritic left upper-quadrant abdominal pain. This area was acutely tender to palpation. Mebendazole was stopped and the pain and fever gradually settled over 10 days without antibiotics. Extensive laboratory investigations failed to uncover any infective cause and there was no change in renal or hepatic function. Mebendazole was reinstituted for a further four weeks without mishap in a dose of 20 mg/kg daily. At follow-up three months after the course of mebendazole the abdominal distension was greatly reduced and the liver smaller and softer than before.

Case 2—A 35-year-old Saudi woman had a long history of abdominal distension, which had recently become more severe. Extensive hydatid disease had been found at laparotomy in Saudi Arabia. Examination in London showed enormous abdominal distension with numerous palpable cystic lumps. The laparotomy wound was incompletely healed and extruded small hydatid cysts. Her haemoglobin concentration was 12.1 g/dl and erythrocyte sedimentation rate 87 mm in first hour. Blood urea, blood glucose, and plasma bilirubin concentrations were normal, as were serum alkaline phosphatase and serum aspartate aminotransferase activities. Serum albumin concentration was 33 g/l and total protein 91 g/l. Abdominal CT showed multiple hydatid cysts in the liver, spleen, and peritoneal cavity. Mebendazole was given in increasing doses, and after four days' treatment she developed a swinging fever, which persisted after the drug was stopped (figure). Extensive laboratory investigations failed to uncover

Case 2. Swinging fever noted during treatment with mebendazole.

any infective cause. The abdominal wound, however, discharged several small cysts, which showed extensive degenerative changes histologically. Despite the fever mebendazole was reinstituted for a further four weeks in a dose of 26 mg/kg daily. At the end of this time she was afebrile and there was considerable reduction in abdominal size.

Comment

In mice with hydatid disease,² mebendazole may almost completely destroy the germinal membrane of cysts, and from clinical and ultrasound evidence in man cysts may shrink and even disappear.¹ The fever in our two cases may have been a reaction to drug-induced tissue necrosis in the cysts. Certainly in both cases abdominal girth decreased strikingly, presumably owing to shrinkage of the cysts, and in the second case the small cysts extruding through the wound sinus were found to be degenerate histologically. In neither case was there any evidence of an infective cause for the fever, and in both patients the fever persisted for more than a week after the drug was stopped.

¹ Bekhti, A, *et al*, *British Medical Journal*, 1977, **2**, 1047.

² Heath, D D, Christie, M J, and Chevis, R A F, *Parasitology*, 1975, **70**, 273.

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New cannula for intermittent and continuous venous sampling without heparinisation

Multiple intermittent venous samples required for many clinical investigations are usually obtained through a heparinised indwelling cannula. This may be inconvenient and invariably leads to contamination of samples with heparin, which interferes with some biochemical investigations and also delays clotting. Heparin bonding to plastic cannulae has been described,^{1,2} but these cannulae are not commercially available. Silicone elastomer central venous cannulae have been available for many years³ and are less likely than plastic catheters to cause thrombophlebitis and thrombosis.^{4,5} A short 5.1-cm silicone elastomer cannula (figure) for peripheral infusions may soon be available in the UK (Visis catheter manufactured by VICRA, Division of Travenol Laboratories). We have therefore carried out a

Silicone elastomer cannula for venous sampling.

pilot study to see whether it might be useful for intermittent and continuous venous sampling in man without the need for heparinisation.

Patients, methods, and results

Twenty patients who required intermittent venous sampling for basal prolactin followed by combined TRH and LHRH tests took part in the study. Preliminary attempts to withdraw venous blood through a 20G gauge cannula were unsuccessful so a 18G gauge cannula was used in all patients. It was placed in the median cubital vein of the forearm using the technique suggested by the manufacturer, after which an empty 2-ml syringe was placed into the cannula and secured to the forearm. A resting period was then allowed, usually one to two hours, after which blood was withdrawn for estimating basal hormone concentrations. A standard combined TRH-LHRH stimulation test was then performed taking venous samples after 20 and 60 minutes. The cannula was then removed and examined for thrombus within the lumen. In all 20 subjects the cannula remained patent for at least three hours without heparinisation. Examination of the cannulae after removal confirmed that there was no appreciable thrombus formation within the lumen. Samples clotted promptly with good clot retraction, allowing rapid separation of serum. We also used the cannula for continuous overnight venous sampling in two children. The cannula was placed in the median cubital vein. The connecting tubing from the cannula to the pump and sample collector was heparinised but the cannula itself was not. Splinting of the arm was not required owing to the flexibility of the cannula. During the 12-hour sampling period the cannulae remained patent and were free of thrombus at the end of the investigation.

Comment

This preliminary study shows that short (5.1 cm) 18G silicone elastomer cannulae are suitable for intermittent and continuous peripheral venous sampling and remain patent without heparinisation. Silicone elastomer cannulae are more expensive than their plastic counterparts and they are unlikely immediately to replace existing techniques for short sampling periods. Nevertheless, they have a clear advantage when heparin-free samples are required and for prolonged venous sampling, since a large peripheral vein such as the median cubital can be used without restricting movement of the elbow joint because of the flexibility of the cannula. During the period of the study no thrombus formed within the lumen of this silicone elastomer cannula. That was consistent with reports of the low thrombogenicity of this material.

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