

SELF ASSESSMENT ANSWERS

A case of reduced consciousness and hypoventilation

Q1: What is the diagnosis on admission? What other electrolyte result is essential in management of this condition?

The patient has metabolic alkalosis. Serum chloride is essential for further management. The chloride was measured at <70 mmol/l, the lowest point at which the assay is accurate and was probably considerably lower than this.

Q2: Explain the effect of supplemental oxygen on the arterial blood gas result (point A to point B; see fig 1 on p 242)

Increasing the inspired oxygen has improved the oxygenation; however, the carbon dioxide and bicarbonate have risen further. This is because compensation for metabolic alkalosis involves hypoventilation, leading to respiratory acidosis. The degree of hypoventilation is limited by hypoxia and by providing a higher inspiratory concentration of oxygen a further decrease in minute ventilation has occurred. This has resulted in a rise in carbon dioxide.

Q3: Explain the action of saline (point B to point C) and acetazolamide (point C onwards; see fig 1 on p 242)?

This patient's alkalosis is due to a loss in hydrochloric acid from the gut during the severe and protracted vomiting. For every hydrogen ion secreted into the gut a bicarbonate ion is released into the serum. Potassium chloride is also lost into the gut. The resulting dehydration and hypokalaemia leads to increased sodium reabsorption from the kidney. Unfortunately there is no chloride available to accompany the sodium, therefore to maintain electrochemical neutrality hydrogen ions and potassium ions are lost from the kidney. This continued loss of hydrogen ions maintains the alkalosis. Saline provides rehydration and chloride ions, which enable the kidney to conserve hydrogen, thereby improving the alkalosis.

Acetazolamide acts by inhibiting carbonic anhydrase in the kidney, thereby promoting bicarbonate loss.

Q4: What is the cause of her hypoxia at point D (see fig 1 on p 242)? How could this have occurred?

The chest radiograph (see fig 2 on p 242) shows a collapsed left lung, probably caused by hypoventilation and subsequent mucus plugging.

Discussion

Metabolic alkalosis develops when a net acid loss or net base gain is associated with a failure of excretion of bicarbonate by the kidney. The condition has three phases: generation, maintenance, and correction.

The generation of metabolic alkalosis occurs in one of two ways. Firstly, loss of acid, for example in gastric fluid and urine or because of acid shift into cells. Second, serum bicarbonate can rise inappropriately, for example with exogenous bicarbonate administration or in post-hypercapnic states when continued reabsorption of bicarbonate can occur for some days.

Maintenance of the alkalosis may be by the same or a different mechanism, common causes being volume depletion, hypokalaemia, mineralocorticoid excess, hypochloraemia, and a reduced glomerular filtration rate.

Clinically the condition is grouped into a chloride responsive type and a chloride resistant type. The chloride responsive type is associated with volume depletion and may be due to persistent loss of gastric acid, diuretic use, diarrhoea, high doses of penicillin, or in post-hypercapnic states. The chloride resistant type is associated with a normal or expanded extracellular fluid volume, may be due to hyperaldosteronism, excess alkali intake, or hypoproteinaemia.

Clinically the patient may exhibit confusion, apathy, and stupor. Rarely generalised twitching, tetany, and coma are seen. There may be hypoventilation with reduced respiratory rate and depth. Cardiac dysrhythmias may occur. Serious ventricular dysrhythmias may appear if the pH is >7.5 and are related to severe hypokalaemia. Features of volume contraction may be prominent and investigations may show an increase in urea, creatinine, and packed cell volume. Abdominal distension may occur secondary to ileus.

The symptoms of metabolic alkalosis *per se* are difficult to separate from those of chloride, volume, or potassium depletion. Compensatory hypoventilation may cause hypoxia and contribute to pulmonary infection in critically ill patients. Blood gas measurements provide the definitive diagnosis.

Management of the alkalosis depends on the cause. If the dehydration is the primary mechanism it should be corrected, along with potassium and magnesium deficits. Primary mineralocorticoids excess may be treated with spironolactone before definitive therapy. In patients with post-hypercapnic metabolic alkalosis acetazolamide will result in a prompt bicarbonate diuresis. Ammonium chloride or arginine hydrochloride infusion into large vein over 18–24 hours may be useful in resistant cases. Finally, in patients with renal failure or precarious fluid status haemodialysis allows precise control of fluid regulation.

Final diagnosis

Metabolic alkalosis.

Further reading

- 1 Galla J. Metabolic alkalosis. *J Am Soc Nephrol* 2000;11:369–75.
- 2 Webster NR, Kulkarni V. Metabolic alkalosis in the critically ill. *Critical Reviews in Clinical Laboratory Sciences* 1999;36:497–510.
- 3 Khanna A, Kurtzman NA. Metabolic alkalosis. *Respiratory Care* 2001;46:354–65.
- 4 Pochet JM, Laterre PF, Jadoul M, *et al.* Metabolic alkalosis in the intensive care unit. *Acta Clin Belg* 2001;56:2–9.

Dyspnoea and a subcutaneous swelling

Q1: What does the initial radiograph show (see p 243)?

The initial radiograph shows a homogenous opacity the left hemithorax with a concave upper border, slightly higher laterally, and obscuring the diaphragm and underlying lung.

Q2: What does the radiograph after the chest drain demonstrate (see p 243)?

There is marked pleural thickening on the lateral borders of the left hemithorax.

Q3: What is its significance?

Pleural thickening can be due to previous pulmonary infection, infarction, lipoma, lymphoma, tumour, or previous asbestos exposure. More extensive unilateral pleural thickening is usually the result of tuberculous pleuritis, mesothelioma, previous thoracotomy, or pleural effusion.

Q4: What is shown on the chest photograph (see p 243)?

There is small round to oval lump in the region of chest drain.

Q5: What is the unifying diagnosis?

Malignant mesothelioma.

Discussion

Mesothelioma may affect pleura, peritoneum or pericardium, the last two sites being less commonly affected than pleura. Malignant mesothelioma is usually due to prolonged exposure to asbestos dust, particularly crocidolite. The tumour characteristically affects 20–40 years after exposure to asbestos. The first symptoms are those associated with worsening dyspnoea, pleural effusions, chest pain, and weight loss. The usual appearance is nodular pleural thickening around all or part of lung. A haemorrhagic pleural effusion may be present but the lung changes of asbestos may be absent. The effusion may obscure the pleural masses. Often the mediastinum is central despite the presence of a large effusion, and this is thought to result from volume loss of the underlying lung secondary to either ventilatory restriction by the surrounding tumour, or bronchial stenosis by tumour compression at the hilum.¹ Rib involvement may occur with malignant mesothelioma. In the advanced stages of disease, patients will gradually become weaker and cachectic as the tumour bulk increases. Eventually, they will develop unremitting chest pain secondary to the invasion of the chest wall and intercostal nerves. Dyspnoea will worsen due to restriction of lung and chest expansion. Palpable tumour masses may be present at this stage.

Differential diagnosis includes tuberculous pleural disease and secondary pleural carcinoma, the later usually bilateral except when due to bronchial or breast carcinoma.

Histology alone cannot differentiate malignant mesothelioma from other pleural cancers and further immunohistochemistry and or electron microscopy are mainstays of definitive diagnosis. If the diagnosis cannot be made from examination of pleural fluid and if the needle biopsy specimen was insufficient, under these circumstances, evidence of pleural tumour, consistent with the diagnosis is sufficient to exclude a treatable cause of pleural disease and is also adequate evidence in UK for industrial injuries benefit to be paid.² The trimodality therapy, consisting of an extrapleural pneumonectomy, 4–6 week cycles of chemotherapy, and radiation therapy, has the best results for palliation and longer disease-free survival.

Occasionally malignant mesothelioma is complicated by tumour seeding along biopsy or drainage tracts. It has been suggested that one should avoid repeating such procedures in patients with suspected mesothelioma.³

The occurrence of such skin deposits however, appears to have little clinical consequence because they are not painful and cause no other morbidity.⁴

Death usually occurs in 4–12 months due to complications of pneumonia or respiratory failure.³

Final diagnosis

Malignant mesothelioma.

References

- 1 **Sutton D.** *Text book of radiology and imaging.* Vol 1. Oxford: Churchill-Livingstone, 1999: 396.
- 2 **Seaton A,** Seaton D, Late Leitch AG. *Crofton and Douglas text book of respiratory diseases.* Vol 2. Oxford: Blackwell Sciences, 2000: 1175.
- 3 **Elmes PC,** Simpson MJC. The clinical aspects of mesothelioma *Q J Med* 1976;**179**:427–49.
- 4 **Law MR,** Hodson ME, Turner-Warwick M. Malignant mesothelioma of pleura: clinical aspects and symptomatic treatment. *Eur J Respir Dis* 1984;**65**:162–8.

Recurrent gastrointestinal bleed**Q1: What is the endoscopic diagnosis (see fig 1 on p 243)?**

Haemobilia. Bile and blood are seen trickling through the end-on ampulla. Upper gastrointestinal endoscopy was done twice, within 24 hours of the first and the second bleed, and was normal on both occasions, thereby indicating intermittent bleed from the biliary tract.

Q2: What is the procedure and what does it show (see fig 2 on p 244)?

The procedure is hepatic angiography and shows two large lobulated pseudoaneurysms in the right lobe of the liver supplied by a single branch of the right hepatic artery (fig 2A). Superselective catheterisation of the feeding branch and embolisation were done using two coils (3 cm × 4 mm). Postembolisation angiography shows complete cut off of the pseudoaneurysm with block of the feeding artery (fig 2B). The patient was asymptomatic after the procedure.

Discussion

Sandblom and Mirkovitch described hepatic artery pseudoaneurysm formation as a complication after blunt or a penetrating trauma to the liver or after a percutaneous diagnostic or therapeutic procedure performed on the hepatobiliary system and presenting as haemobilia.¹ A meta-analysis on a Medline search showed that two thirds of cases of haemobilia were iatrogenic, while accidental trauma accounted for 5% of the cases.² Croce *et al* reviewed surgery details of 482 patients with hepatic injury.³ Six developed haemobilia, three were due to blunt trauma (1.2%). Based on the hepatic injury scale the present case had grade III type of hepatic artery injury.⁴

The formation of intrahepatic cavity of blood and bile after blunt injury to the liver can predispose the patient to develop hepatic artery aneurysm.¹

In an experimental study, Sandblom and Mirkovitch showed that bile retards liver healing and causes lysis of clotted blood.¹ This could result in an unrecognised arterial injury leading to a pseudoaneurysm; infection contributes further to its development. As the cavity expands due to continued bleeding at arterial pressure, progressive pressure necrosis develops around the margin. Also the poor contractility of the vessels results in a persistent haemorrhage into the cavity. The cavity eventually erodes into a major branch of the biliary tree, which is already damaged by

either the initial injury or the interventional procedure, thus resulting in haemobilia.

Diagnosis of haemobilia is based on the Quincke's triad: jaundice (51%), colicky abdominal pain (80%), and blood in either vomitus or stool (62%). The bleed may be a major one and life threatening or minor. It can present several weeks after injury. Duodenoscopy can image blood oozing from the papilla of Vater as was possible in our case. Endoscopic retrograde cholangiopancreatography may show biliary tracts filled with blood clots. Ultrasound can detect intrahepatic haematomas and arterial aneurysms. Both these procedures were useful in diagnosis in the present case. Abdominal computed tomography and selective visceral angiography, apart from showing the site of bleed, can also help in detecting arterial variations.⁵ Long standing haemobilia is associated with rapidly developing intrahepatic collaterals. Superselective catheterisation may be necessary.

Management is aimed at tackling the pseudoaneurysm, the intrahepatic cavity,³ and relieving the biliary obstruction. Selective arterial embolisation of the pseudoaneurysm is the procedure of choice. Surgery is reserved for those refractory to embolisation. Green *et al* managed 43% of patients with haemobilia conservatively and 36% by transarterial embolisation.² The mortality rate was 5%. Large cavities (8 cm and above) after blunt trauma would require debridement since they act as sources of infection. Occasionally, the debridement can stop the bleed and also result in regression of small hepatic cavity (2 × 2 cm).³

The clinical presentation of haemobilia, which was distinct in the present case, was confirmed at duodenoscopy. Transarterial embolisation controlled the bleed.

Final diagnosis

Haemobilia caused by blunt trauma.

References

- 1 **Sandblom P,** Mirkovitch V. Haemobilia: some salient features and their causes. *Surg Clin North Am* 1977;**57**:397–408.
- 2 **Green MHA,** Duell RM, Johnson CD, *et al.* Haemobilia. *Br J Surg* 2001;**88**:773.
- 3 **Croce MA,** Fabian TC, Spiers JP, *et al.* Traumatic hepatic artery pseudoaneurysm with haemobilia. *Am J Surg* 1994;**168**:235–8.
- 4 **Moore EE,** Shackford SR, Pachter HL, *et al.* Organ injury scaling: spleen, liver and kidney. *J Trauma* 1989;**29**:1664–6.
- 5 **Samek P,** Bober J, Vrzgula A, *et al.* Traumatic haemobilia caused by false aneurysm of replaced right hepatic artery: case report and review. *J Trauma* 2001;**51**:153–8.

Acute severe anaemia in an elderly patient with hereditary spherocytosis**Q1: Was does the bone marrow biopsy show?**

The bone marrow smear shows a giant pronormoblast with cytoplasmic vacuolisation and large eosinophilic nuclear inclusion bodies characterising infected human erythroid cells.

Q2: What is the most likely diagnosis?

In patients with congenital haemolytic anaemia, such as hereditary spherocytosis, life threatening transient aplastic crisis may occur due to parvovirus B19 infection.

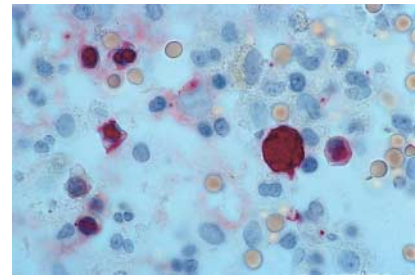


Figure 1 Strong immunoreactivity of erythroid precursor cells (including one giant pronormoblast) with monoclonal antibodies against the capsid proteins of parvovirus B19 (original magnification × 400).

Q3: Which investigations would you perform to confirm the diagnosis?**(A) Serology for parvovirus B19 in serum**

In our patient, ELISA was positive for anti-B19 IgM and anti-B19 IgG antibodies (IgM: 1:16 on day 5, 1:512 on day 11, and 1:256 on day 20; IgG 1:<64 on day 5; 1:512 on day 11, and 1:2048 on day 20), findings consistent with acute parvovirus B19 infection.

(B) Immunohistochemical detection of parvovirus B19 in the infected cell

The giant pronormoblast showed strong immunoreactivity with a monoclonal antibody against VP1 and VP2 capsid proteins of parvovirus B19 (fig 1).

(C) Polymerase chain reaction (PCR) for parvovirus B19 in the bone marrow

The PCR was not done in our patient, but it is an accurate and reliable method to diagnose an aplastic crisis due to parvovirus B19 in patients with congenital haemolytic anaemia or HIV infection.¹

Outcome

Twelve days after admission, numerous cohorts of early erythroid cells were present in the bone marrow. For support, the transfusion of nine units of packed red blood cells was required during hospitalisation.

Discussion

Parvovirus B19, a small non-enveloped DNA virus first described in 1975,² is the only pathogenic member of the family parvoviridae found in humans and is associated with a wide range of disease manifestations. Approximately 50% of children age 15 are seropositive, and the prevalence rises to more than 90% in the elderly. Most infections are asymptomatic or unrecognised. Frequent clinical manifestations include erythema infectiosum (fifth disease or slapped cheek disease) in children, polyarthralgia syndrome mimicking rheumatoid arthritis in adults, miscarriage or hydrops fetalis and eventually congenital anaemia of the newborn in pregnant women, or transient aplastic crisis in patients with underlying haemolytic disorders and chronic bone marrow failure in immunocompromised individuals.¹ Pathophysiologically, the virus selectively targets human erythroid cells for propagation. In human erythroid cells derived from bone marrow, susceptibility to parvovirus B19 increases with differentiation; the pluripotent stem cell appears to be spared, and the main target cells are erythroid progenitors. Erythroid specificity results as the virus uses the blood group P antigen,³ found only on

erythroid progenitors, erythroblasts, megakaryocytes, and endothelial cells, to gain entry into the cell. For this reason, individuals genetically lacking P antigen on erythrocytes are resistant to B19 infection.⁴ Expression of viral structural proteins results in cytotoxicity and transient erythropoietic maturation arrest. Unnoticed in normal individuals, it may become a crisis in patients with underlying haemolytic disorders or in immunocompromised patients where the virus can not be eliminated.

Due to the widespread presence of the virus worldwide, most cases of aplastic crisis associated with parvovirus B19 have been reported in children and adolescents. Nevertheless, crisis may occur in adults,⁵ and occasionally in the elderly, as shown in the present case. In our patient, hereditary spherocytosis has been diagnosed previously but remained largely asymptomatic until aplastic crisis developed. In contrast, aplastic crisis may be the initial manifestation unmasking the underlying haemolytic disorder.⁶

Diagnosis of acute parvovirus B19 infection is based on examination of bone marrow smears and virological studies—that is, the detection of IgM and IgG antibodies or transient viraemia. In immunocompetent patients, infection is self limited requiring only supportive therapy and blood transfusion in severe cases, whereas in immuno-

compromised individuals, infection may persist; these patients may benefit from administration of immunoglobulins, but relapses may occur necessitating careful monitoring.¹

Final diagnosis

Parvovirus B19 associated aplastic crisis in a patient with hereditary spherocytosis.

References

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- 2 **Cossart YE**, Field AM, Cant B, *et al*. Parvovirus-like particles in human sera. *Lancet* 1975;*i*:72–3.
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Learning points

- Parvovirus B19 causes widespread infections, with more than 90% of the elderly being seropositive.
- Although most infections are asymptomatic, healthy individuals may present with erythema infectiosum or polyarthropathy syndrome, and infection and in pregnant women may result in miscarriage, hydrops fetalis, or congenital anaemia in pregnant women.
- Due to erythroid tropism, acute parvovirus infection may result in aplastic crisis in patients with haemolytic disorders or chronic bone marrow failure in immunocompromised individuals.
- Aplastic crisis due to parvovirus B19 infection must be considered in patients with haemolytic disease presenting with severe anaemia, even in the elderly.
- Infection is self limiting in immunocompetent individuals requiring only supportive therapy, but may persist in immunocompromised individuals.

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