CASE REPORTS

Spontaneous fulminant gas gangrene
M S Delbridge, E P L Turton, R C Kester

Gas gangrene is a rare condition, usually associated with contaminated traumatic injuries. It carries a high rate of mortality and morbidity. A number of studies have implicated non-traumatic gas gangrene and colonic neoplasia. This paper reports a patient who presented spontaneously with *Clostridium septicum* gas gangrene and an occult caecal carcinoma.

A previously healthy, non-diabetic, 82 year old man was admitted to York District Hospital complaining of pain and swelling of the right arm. He attributed this to a trivial injury sustained to his arm on a supermarket shelf earlier that day. At approximately 6:30 pm on the same day his wife noticed what appeared to be a bruise over the upper arm with small areas of blistering. He was admitted to York District Hospital later that evening by which time the entire right upper limb had become tense and swollen up to the level of the neck; the skin was dusky purple and cyanosed, and there were a number of haemorrhagic bullae.

On examination he appeared pale and distressed but was alert and cooperative. Inspection of the upper limb revealed diffuse crepitation and absent distal pulses, both on palpation and Doppler. Vital signs were as follows: pulse 100 per minute, blood pressure (BP) 100/60 mm Hg, temperature 36.7 °C. Abnormal laboratory results included low plasma sodium levels (127 mmol/l; hyponatraemia), raised urea and creatinine (7.3 mmol/l and 186 μmol/l, respectively) and raised plasma glucose level (24.6 mmol/l; hyperglycaemia). A chest x-ray confirmed the presence of diffuse surgical emphysema (fig 1).

The patient was catheterised and given 1.5 g cefuroxime, 500 mg metronidazole, and 600 mg benzylpenicillin; in addition he received opiate analgesia and 1 l of succinylated gelatin (Gelofusine; B Braun Medical, UK).

Early next morning he was transferred to St James University Hospital. On arrival at 8:15 am he remained afebrile and was still cardiovascularly stable. However, it was clear that he had deteriorated severely—he was confused, agitated, and tachypnoeic. The blistering and discoloration had spread across his chest wall, neck, back, and abdomen. His vital signs at this point were as follows: urine output 30 ml/h, pulse 100 per minute, BP 120/70 mm Hg and temperature 36 °C. Additional laboratory results demonstrated metabolic acidosis (HCO₃⁻ 16.3 mmol/l and pH 7.28).

We sought advice about management of the patient from both a microbiologist and a plastic surgeon, but it was deemed that radical debridement would be of little use at this stage and any treatment would be palliative. At 9 am he was intubated and ventilated and an internal jugular central line inserted. He was given 100 ml 20% mannitol, 50 ml 8.4% HCO₃⁻ and 1 l 0.9% NaCl; in addition we carried out multiple fasciotomies in an attempt to improve circulation in the upper limb (fig 2).

The patient had a cardiac arrest at 9:30 am and was successfully revived, but unfortunately he had a second arrest and resuscitation was unsuccessful. He was declared dead at 10:50 am.

A diagnosis of arterial vascular occlusion secondary to gas gangrene was made which was confirmed by post mortem. Microbiological examination revealed Gram-positive bacilli and culture demonstrated profuse *C. septicum* infection. The post mortem declared the cause of death to be acute myocardial ischaemia, but a major contributing factor was the gross infection of the upper limb; an additional finding...
was a small caecal carcinoma with a 4 cm metastatic deposit in the right lobe of the liver.

DISCUSSION

Gas gangrene is a condition of rapidly developing and spreading infection mediated by toxins released by the bacteria Clostridium spp. It is most often associated with traumatic injuries. C. perfringens is the commonest species, followed by C. novyi. C. septicum is relatively uncommon, and it is estimated to be the cause of only 1.3% of all clostridial infections.\(^1\)\(^,\)\(^2\)\(^,\)\(^3\)\(^,\)\(^4\) C. septicum represents a novel subtype among clostridial species, with several notable differences. It is able to cause devastating tissue necrosis in the absence of prior trauma,\(^5\)\(^,\)\(^6\) and is able to present distant from the presumed portal of entry resulting in metastatic myonecrosis.\(^5\)\(^,\)\(^6\)

Clostridial infections are believed to have a greater prevalence among individuals who have malignant disease.\(^1\)\(^,\)\(^2\) Larson et al, in a series of 241 patients with clostridial infection, found 10% had an associated malignancy.\(^1\) However, when C. septicum infections were considered alone the incidence of associated malignancy was 52.6%.\(^7\) In a further study of patients with C. septicum infection, conducted between 1966 and 1993, 50% had a primary malignancy, 75% of which were colonic, of these 40% were caecal.\(^1\)

Few patients presenting with C. septicum infection have a history of prior trauma.\(^1\)\(^,\)\(^2\)\(^,\)\(^5\)\(^,\)\(^6\) Several papers have suggested that mucosal ulceration of the tumour surface and haemorrhage.\(^5\) However, when clostridial infection, found 10% had an associated malignancy.\(^6\) In a series of 241 patients with C. septicum infection, conducted between 1966 and 1993, 50% had a primary malignancy, 75% of which were colonic, of these 40% were caecal.\(^1\)

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Our case illustrates the fulminant nature of gas gangrene and although it is an uncommon diagnosis, it is essential that the management be initiated early. This should include aggressive resuscitation, early antibiotics, hyperbaric oxygen therapy (although this has never been subjected to a controlled trial and unless it is readily available it would seem to present a potentially fatal delay), and radical surgical debridement.

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the patient remained on the intensive care unit (ICU) where he developed a left sided pneumonia and signs consistent with adult respiratory distress syndrome. A transthoracic echocardiogram at this time was reported as normal. The patient gradually deteriorated and by day 10 he had developed florid pulmonary oedema and haemoptysis. In addition, a new systolic murmur was reported. Repeat transthoracic echocardiography showed significant mitral regurgitation with a subaortic ventricular septal defect (VSD).

Following transfer to the St Thomas’ Hospital Cardiothoracic Centre, an emergency transoesophageal echocardiogram showed a tear in the anterior leaflet of the mitral valve, with severe regurgitation, and confirmed the VSD (fig 1). The patient was taken directly to the operating theatre where cardiopulmonary bypass was established, and the mitral valve was exposed through a Guiraudon incision which passed through the right atrium and across the atrial septum to enter the left atrium. The knife had entered the right ventricular wall, penetrated the ventricular septum (causing the VSD) and had lacerated the anterior mitral valve leaflet. The middle scallop of the anterior leaflet of the mitral valve was found to be detached (fig 2). The valve was repaired with interrupted 2-O Ethibond sutures and the insertion of a 28 mm Cosgrove-Edwards annuloplasty band. The subvalvar VSD beneath the right coronary cusp of the aortic valve was repaired using interrupted Ethibond sutures.

The patient was discharged from the ITU after one day, was successfully rehabilitated, and was discharged from hospital after three weeks. Postoperative transthoracic echocardiography, done immediately before discharge from hospital, showed only mild transvalvar mitral regurgitation and no residual flow at the site of the VSD repair.

DISCUSSION

There are examples of traumatic ventricular septal defects with associated mitral valve damage in the medical literature but they are uncommon. The rate of cardiac stabbings is increasing in the United Kingdom, so awareness of this condition is becoming more important. The importance of this case is that the full extent of the cardiac injury was not revealed until late. Initial echocardiographic findings were normal, but repeated investigations showed gross pathology. Similar findings have been described by Thandroyen and Mattison, who proposed that penetrating cardiac injury creates an intracardiac fistula which enlarges over time. In addition, it is postulated that thrombus formation or muscular spasm may initially seal small cardiac wounds. Such a mechanism may explain the delayed presentation which occurred in this case.

There are many published reports of traumatic VSDs but fewer reports of VSDs with associated mitral leaflet damage as a result of trauma, particularly stabbing. Even in the absence of cardiac tamponade, significant intracardiac trauma may have occurred. In the management of penetrating thoracic injuries it is important not to underestimate the full extent of potential injuries, which may often be greater than the inlet and exit injuries suggest. Careful consideration of the likely anatomical pathway, in accordance with the length of stabbing implement, aided by directed echocardiography are essential features of the management of such injuries. A high index of suspicion and repeated re-examination of the patient are important, and early liaison with a cardiothoracic centre is recommended.

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Rectus sheath haematoma: ‘a diagnostic dilemma?’

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Rectus Sheath Haematoma is a relatively rare presentation in the context of acute Accident and Emergency presentations. Correct diagnosis and subsequent management depend on sound clinical acumen and history taking with appropriate use of diagnostic aids in order to avoid prolonged and inappropriate management of such cases. We present an interesting case of a young fit male whose history alone suggested the diagnosis despite an initial diagnostic dilemma.

CASE REPORT
A fit 18 year old male rugby player presented to Accident and Emergency Department with a 4 hour history of acute onset progressive right lower quadrant abdominal pain. Such pain, described as sharp in nature and exacerbated by pelvic movement and coughing, was initially noticed during a rigorous exercise programme on a rowing machine. He was normotensive, afibrile with a pulse rate of 86 bpm (average). Examination revealed quite a marked degree of abdominal guarding and rigidity particularly in the right lower quadrant. Nothing else remarkable was in evidence on further examination. Subsequent investigation revealed normal Fbc, Bioprofile, and plain radiographic studies of the abdomen. The patient remained in extremis and treated accordingly with incremental doses of intravenous opiate analgesia. A provisional diagnosis of acute appendicitis was made and admission arranged for surgical management.

Despite refractory presentation a decision was made to continue with supportive symptomatic management. The patient showed symptomatic improvement with conservative management (intravenous fluids and analgesia).

‘Next-day’ ultrasound abdomen revealed a large Rectus Sheath Haematoma. The patient quickly improved and was discharged the following day on oral analgesia as required.

Appropriate advice was issued regarding sports, exercise, and training.

DISCUSSION
Rectus Sheath Haematoma, as an acute abdominal presentation,1 is relatively uncommon. Reported rates vary,2 but current literature suggests a female: male preponderance of 2:3:1 in the 50 to 60 year old age group (however, equal distribution in the younger age groups is noted despite different aetiology). Overall incidence is not quantified owing to rarity of presentation.

Rectus Sheath Haematoma is an accumulation of blood in the anterior Rectus abdominis muscle. Primary causation is due to either epigastric vessel rupture or muscle body tear. This may occur in any abdominal quadrant but typically sub-umbilical due to Rectus Abdominis posterior wall supportive defect below the level of the linea semilunaris (weak transversalis fascia and peritoneum being the essential supportive framework for Rectus Abdominis) and relative infrastructural rigidity (firm adherence of inferior epigastric penetration arteries to rectus abdominis). As in our case, intense, perhaps unaccustomed, muscular exertion induced labile contractile muscle lengths and shear forces in a plane opposite to epigastric penetration vessels resulting in immediate haematoma formation.

Predisposing factors associated with Rectus Sheath Haematoma formation are varied and include hypertension, arteriosclerosis, old age, obesity, direct abdominal trauma, anticoagulant therapy, previous abdominal surgery, pregnancy and acute intra-abdominal pressure fluctuations (straining, coughing, exertion) – the latter illustrating male predominance, as in our index case.

Interestingly, one series reported a case related to intramuscular administration of low molecular weight subcutaneous heparin.3

Clinical presentation is often non-specific4 – pain and swelling/mass in any one of the four abdominal quadrants (left upper quadrant being the site of least frequency in reported series) – typically the lower quadrants being the sites of most frequent occurrence.4 Pain, often in isolation of mass/swelling, is usually of acute onset, of moderate severity with signs suggestive of peritoneal irritation. The presence of an associated mass is often highly suggestive, particularly if right sided and is considered diagnostic if extends to midline. Some series have quoted associated signs – notably Fothergill’s Grey Turner’s, Cullen’s, and dysuria/urinary frequency – depending on breach of peritoneum but these are typically associated with delayed presentation beyond 48 hours.

Supportive data may occasionally include a mild leucocytosis, a low grade pyrexia or a corroborative drop in haemoglobin (clearly extent related), however, these are considered unusual.

Diagnostic conclusion is usually successful with a combination of clinical awareness and radiographic imaging – Ultrasound or Computed Tomography. Ultrasound is usually the investigation of choice due to high sensitivity rates (approaching 100% in most series), time/cost efficacy and radiation safety protocol. Classical ultrasonographic appearances range from sonoluent (early stage) to sonodense (late stage) appearance with time from initial injury.

Computed Tomography is considered more sensitive an investigation and useful in cases of inconclusive ultrasound but due to issues relating to time/resource management is less commonly employed. Magnetic Resonance Imaging has been less employed and is considered as sensitive as the aforementioned. Should the diagnosis continue to prove elusive, more invasive methods such as diagnostic needle aspiration and laparotomy have been suggested, however, the former has not received much acclaim due to reasons relating to sepsis propagation.6

A conservative non interventional approach to diagnosis/management has received acceptance most recently. Such approach, of course, advocates analgesia, serial clinical assessment, bedrest, haematoma compression, icepack application, and managing the predisposing cause. Clearly, haemodynamic compromise necessitates operative intervention - clot evacuation and vessel ligation via laparotomy or laparoscopic7 approach is usual. Levy et al6 reported successful interventional outcome with Gelfoam embolization however this method has not received much acclaim.
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Accidental human poisoning with a veterinary tranquiliser

F H Cummins

Detomidine is an alpha-2 adrenoceptor agonist drug, which is used in veterinary medicine for sedation of large animals. It is highly potent and has sedative and analgesic properties. This paper reports a case of accidental human poisoning with this drug.

CASE REPORT

A 35 year old farmer was preparing to sedate a bull in order to pare its hooves. No vet was present. The farmer had 5 ml of Domosedan (detomidine hydrochloride 10 mg/ml) in a 5 ml syringe with a 21G x 1.5” (0.8 x 40 mm) needle attached. The bull moved as the farmer was about to give this medication and he injected himself in the thenar eminence of his left hand. He later said that he had been holding the syringe by the barrel rather than the plunger and he did not think he had injected a significant volume of the drug. He claimed that he could not recall how he came to possess the drug. He had no relevant medical history, was on no medication, and had last drunk alcohol 4 days previously.

Within 10 minutes of this accident, the farmer began to feel drowsy, dizzy, and relaxed. His companions noted that he was not performing his tasks normally. When questioned, he responded in a slurred and drunken manner. His gait became unsteady. He was carried to a vehicle and taken to the emergency department.

On arrival he was noted to be drowsy, with slurred speech, and a passively euphoric state, but his Glasgow Coma Score (GCS) was 15. His heart rate was 44 beats/min and his blood pressure 106/48 mmHg. A small superficial puncture wound was noted on the left thenar eminence. No other abnormality was apparent on examination. His ECG showed a sinus bradycardia with no evidence of heart block or ischaemia.

Peripheral intravenous access was obtained and an infusion of 0.9% sodium chloride was started. Two boluses of atropine 500 µg were given. Within minutes, a sustained rise in heart rate and blood pressure was noted, but the patient remained significantly drowsy. He was given 2 litres of intravenous saline over 2 hours. TOXBASE (an online poisons database; www.spib.axl.co.uk) was consulted. The patient was observed overnight with cardiac monitoring but received no further medications. Over the next 16 hours he regained full consciousness and his pulse and blood pressure remained normal. He was discharged home.

DISCUSSION

Detomidine (trade names Domosedan and Dormosedan) is used for sedating horses and other animals to facilitate examination and surgical procedures. Detomidine causes a bradycardia with blood pressure initially raised and then normal or low, reduced cardiac output, and slowing of intracardiac conduction with partial sinoatrial and atrioventricular block. Respiratory depression and diuresis may occur. Detomidine potentiates the actions of other sedative and analgesic drugs. It has similar effects to clonidine.

TOXBASE (www.spib.axl.co.uk/toxbase/poisons%20information/d/detomidine.htm) mentions that a dog that chewed a vial of detomidine had salivation, sedation, collapse, hypotension, bradycardia, arrhythmias, and coma, which lasted for 18 hours. The treatment advised by TOXBASE in human poisoning is supportive, with observation for at least 4 hours, or longer if symptomatic, and monitoring of blood pressure and cardiac rhythm. Hypotension should be corrected by raising the foot of the bed and by giving intravenous fluids, and vasopressors should be considered in severe cases. Bradycardia may require treatment with atropine and rarely with cardiac pacing. Severe and persistent hypertension may be treated with phenolamine.

The only previous report of detomidine poisoning in humans is a single case of deliberate injection of detomidine 50 mg and butorphanol 100 mg in a 36 year old man. Butorphanol is an opioid drug for which the antidote is naloxone. The patient presented with a GCS of 6 and required a continuous infusion of naloxone, but his heart rate never fell below 70 beats/min and his blood pressure never below 110/80 mmHg. He made a full recovery.
Unusual abdominal complication of rib fracture: a case report and review of literature

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Rib fracture is known to cause a variety of intrathoracic and intra-abdominal injuries. It is associated with intra-abdominal solid organ injuries, but rarely is itself a cause of hollow viscus perforation. We report a case of a woman who sustained a blunt injury during which a segment of fractured rib penetrated through the diaphragm and perforated the stomach.

CASE REPORT
A 33 year old woman was brought to the accident and emergency department at West Cumberland Hospital following an accident in which she was crushed by a grabber from behind, sustaining blunt injuries to the chest and abdomen. She complained of pain in the chest and abdomen and vomited once. She denied any respiratory, cardiovascular, or gastrointestinal symptoms. She was conscious, coherent, and haemodynamically stable, with normal pulse and blood pressure. Her Glasgow coma score was 15. Examination revealed tenderness and subcutaneous emphysema in the left lower chest with good air entry bilaterally. Examination of the abdomen revealed a laceration measuring 5 cm in length, with tenderness and guarding in the left upper quadrant.

Dipstix examination of the urine showed moderate amounts of blood. Full blood count and serum biochemistry was normal. Chest x ray showed fractures of the eighth and ninth ribs on the left side, and confirmed local subcutaneous emphysema in the soft tissues overlying the fractures. There was no evidence of pneumo/hemothorax or pneumoperitoneum. A computerised tomography (CT) scan of the abdomen was performed, which showed normal solid abdominal viscera with intact spleen and well perfused kidneys. There was some free intraperitoneal gas and fluid. The CT scan again confirmed rib fractures and local emphysema close to the splenic flexure, suggesting colonic perforation. The stomach was distended and appeared intact. Major vessels were intact. Minor posterior atelectasis was noted at the base of the lungs, but there was no pneumothorax or significant pleural effusion. CT scan also showed a fracture of the left transverse process of L4 vertebrae with intact vertebral body and psoas swelling.

In the light of the CT scan, exploratory laparotomy was performed, which revealed copious amounts of bilious free fluid in the abdomen. Two perforations close together were noted in the posterior wall of the body of the stomach. A large piece of the fractured rib, which had penetrated the diaphragm, was seen protruding through the retroperitoneum below the spleen. There was a 3 cm tear in the transverse mesocolon, and a breach in the peritoneum overlying the left lumbar transverse process close to the ureter. A laceration in the left psoas muscle was noted. The remaining intra-abdominal viscera, including the small and large bowel, liver, spleen, pancreas, kidneys, and ureter, were normal. The area with the perforations in the posterior wall of the stomach was excised, and the stomach closed with linear stapler. The peritoneal cavity was lavaged with copious amounts of normal saline, and the abdomen was closed using the mass closure technique after placing drains in the left subphrenic space and pelvis. The laceration over the abdomen was closed with interrupted nylon sutures. A prophylactic chest drain was inserted in the left fifth intercostal space in the mid-axillary line.
The patient had an uneventful recovery from surgery. The chest drain was removed with no further complications. The fracture of the lumbar transverse process was managed conservatively with analgesics, physiotherapy, and mobilisation. She was symptom free at follow up.

**DISCUSSION**

Fracture of the ribs can cause a variety of intrathoracic and intra-abdominal complications. Apart from the usual complications of surgical emphysema and pneumothorax, it has also been reported to cause mediastinal emphysema and pneumopericardium. During blunt injuries, lower rib fractures are associated with intra-abdominal, solid organ injury, in particular to the liver and spleen, but the fractured segment itself is rarely a cause of intra-abdominal hollow viscus injury. Gastric perforation is an interesting and a rare complication of fractured rib, and to our knowledge, has not previously been reported in the English language literature, although a similar case with multiple rib fractures that resulted in a segment of the fractured rib penetrating through the diaphragm to the stomach was reported in the Japanese literature.

Imaging investigations can at times be misleading, as in our present case. The initial chest x-ray did not reveal either pneumothorax or pneumoperitoneum. The CT scan did not show pneumothorax; it suggested a colonic rather than gastric perforation due to a presumed intact and distended stomach and the proximity of rib fractures to this splenic flexure. In our case, a segment of fractured rib had penetrated through the diaphragm and perforated the stomach.

**CONCLUSION**

Gastric perforation is an interesting and a rare complication of rib fracture. As the clinical examination and investigations can be misleading, there should be a high index of suspicion of intra-abdominal organ injury, particularly in patients with lower rib fractures. This case emphasises the importance of thorough exploration of all intra-abdominal organs during laparotomy, and the physician should not be falsely reassured by the imaging investigations.

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the atlas without a posterior tubercle and ruled out a fracture or any other structural injury (fig 2). Laboratory investigations, including haemoglobin electrophoresis and blood smear revealed the following results (laboratory reference values in parenthesis): haemoglobin 9.8 mg/dl (14.0–18.0); MCH 29 pg (29.0–34.0); MCV 85 fl (86.0–100.0); serum iron 130 μg/dl (40–130); HbA₂ 6.3% (2–3%); HbF 3.1% (0.8–2%); HbA₁ 90.6% (95–98%). Thus the presence of a hypochromic, microcytic anaemia led to a diagnosis of β-thalassaemia.

DISCUSSION
Perichondral ossification of the posterior arch of the first vertebral body starts from two centres in the lateral masses and proceeds to the midline. Fusion normally occurs at three to five years of age, and incomplete fusion persists in 3–5%. Occasionally, ossification starts from a separate posterior centre, fusing with the lateral masses to form the posterior arch and leading to the development of a posterior tubercle. Larger defects of the posterior arch are rare; some authors have reported an incidence of less than 1%. The underlying embryological basis is commonly believed to be a local mesenchymal defect leading to lack of chondrification. Currarino et al proposed an anatomical classification of the defects of the posterior atlas, modified from Von Torklus and Gehle:

- Type A—failure of the posterior midline fusion of the two hemiarches
- Type B—unilateral cleft
- Type C—bilateral clefts
- Type D—total absence of the posterior arch with a persistent posterior tubercle
- Type E—total absence of the posterior arch with missing posterior tubercle.

According to this classification, the present patient has a rare type E abnormality. A hypertrophic spinous process of the axis (C2) is described occasionally in type E abnormalities. Our patient also had this (fig 1).

Hereditary factors may contribute to these anomalies, but the frequency of heredity is not known. Motatenau et al reported an affected mother and daughter, and mother and son, respectively. Our patient’s father had thalassaemia minor as well as the patient herself, but we were unable to obtain informed consent for further x ray examination of the cervical spine or laboratory examination. In most reports, the lesion was discovered incidentally in asymptomatic patients. In other patients, the patients had complained of neck discomfort and x ray examination of the cervical spine had revealed incomplete arches. Sporadic neurological deficits have been described. To our knowledge, however, no permanent neurological deficits such as paralysis have been reported. Richardson et al reported a patient with an incomplete absence of the posterior arch who had intermittent quadriparesis after hitting his head against a car door, and who recovered completely with resolution of any neurological symptoms. Thalassaemia major (Cooley’s anaemia) sometimes leads to bony abnormalities such as “hair on end” appearance of the skull bone, but no cervical spine abnormalities have been reported so far.

CONCLUSION
It is essential to be aware of both conditions—deficiency of the posterior arch of the atlas and thalassaemia minor—as both anomalies may lead to false diagnosis, especially in trauma victims. Of course, the aetiopathogenetic relation cannot be proved in this case. When treating trauma victims it is important to have both abnormalities in mind, in order not to mistake slightly injured for severely injured patients.

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Primary gradient defect distal renal tubular acidosis presenting as hypokalaemic periodic paralysis

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A 45 year old man presented with recurrent hypokalaemic paralysis. Laboratory investigations revealed renal tubular acidosis as the cause of the hypokalaemia, and dynamic tubular studies suggested a gradient defect as the underlying cause. The patient had associated dextrocardia. To our knowledge, this is the first report of this condition.

One of the important presentations of distal renal tubular acidosis (DRTA) is recurrent hypokalaemic weakness, which can be life threatening. DRTA has been reported to cause periodic hypokalaemic paralysis, and the defect is usually secretory, characterised by an inability of the tubular cells to secrete $\text{H}^+$ ions, resulting in acidosis and alkaline urine. However, amphotericin B has been known to cause DRTA due to a permeability defect, where the inability to lower urinary pH despite unimpaired $\text{H}^+$ secretion is attributable to $\text{H}^+$ leakback, which is more evident when the tubular urine is acidic.

One study reported an infant with a spontaneous metabolic acidosis induced by a gradient defect; however, to our knowledge, no case of hypokalaemic periodic paralysis caused by a gradient defect DRTA has been reported previously. We report a case of hypokalaemic periodic paralysis in which the renal tubular defect was subsequently found to be due to an underlying gradient defect.

**CASE REPORT**

A 45 year old man was admitted with a 1-day history of lower limb weakness that had progressed slowly to involve his upper limbs over a period of 12 hours. He had received an insect bite on his right thigh 4 days previously, which had resulted in local cellulitis for which he was receiving cefuroxime and nimuselide. There was no history of intake of any diuretics, excessive sweating, gastrointestinal illness, or exposure to excessive cold or heat. The patient denied any tingling, paresthesia, weakness of the cranial nerves or respiratory muscles, or any sphincteric disturbance. He had experienced three similar episodes in the past, each being managed in the hospital by oral potassium chloride.

Clinical examination revealed a pulse rate of 96 beats/min, a blood pressure of 130/80 mmHg, a respiratory rate of 23 breaths/min, and temperature of 37.5°C, with grade 3 motor weakness of the upper limbs and grade 0–1 weakness of the lower limbs. Reflex, sensation, and sphincter responses were normal. The patient had no localisation of the cardiac impulse, cardiac dullness from the right third space in the midclavicular line to the midsternal line, but stronger heart sounds on the right side of the chest (findings consistent with dextrocardia). He had resolving cellulitis of the left inguinal region, and the rest of the general and systemic examination was normal.

Haemoglobin was 132 g/l, leucocytes 5.3 x 10^9/l with a normal differential, platelet count 157 x 10^9/l, serum urea nitrogen 6.33 mmol/l, creatinine 70.7 mmol/l, glucose 4.77 mmol/l, proteins 78 g/l, and albumin 40 g/l. Serum alanine transfrase was 86 IU/l (normal 0–40), aspartate transfrase 75 IU/l (normal 0–35), creatinine kinase 1941 IU/l (normal 50–195), lactate dehydrogenase 555 U/l (normal 250–450), sodium 130 mmol/l (normal 135–145), potassium 2.9 mmol/l (normal 3.5–5.5), and chloride 112 mmol/l (normal 98–108). Arterial pH was 7.41 (normal 7.38–7.44), $\text{PCO}_2$ 26.5 mmHg (normal 35–45), and bicarbonate 15.3 mmol/l (normal 22–28). Chest radiograph and electrocardiogram were consistent with dextrocardia. The patient was started on potassium chloride and recovered over a period of 24 hours.

**Dynamic tubular function testing**

Urinary pH was 7.0. In order to test renal acidification after induced academia, ammonium chloride (0.1 g/kg body weight) was administered, during which the blood pH increased to 7.30 but the urinary pH continued alkaline (pH>6.5), suggesting a defect in distal tubular acidification. Serum osmolality was 286 mOsmol/kg and urinary osmolality 379 mOsmol/kg; the osmolality did not change after administration of pitressin, suggesting hyposthenuria.

A bicarbonate infusion was administered at the rate of 3 ml/min/kg. At an induced blood pH of 7.76, urinary (U)
Ultrasound examination of the abdomen and intravenous urogram was normal. Serum antibodies to nuclear antigen, latent agglutination test, and antibodies to smooth muscle, parietal cell, and mitochondrial antigen were not detected. Serum levels of copper, caeruloplasmin, rennin, and aldosterone were normal, as was urinary excretion of calcium, phosphate, urate, protein, and aminoacids. An upper gastrointestinal tract endoscopy for dyspeptic symptoms revealed anatomy consistent with situs inversus. All family members of the patient denied a similar history and tested negative for any urinary acidification defect.

DISCUSSION

Gradient defect was for many years postulated to be the primary mechanism underlying DRTA. However, an inability to increase urinary pCO₂ was subsequently demonstrated, implying a defect in proton secretion. A reliable measure of this was found to be the difference in urinary and blood pCO₂ (urine minus blood levels); in DRTA the value is low. However, in DRTA induced by amphotericin B, there is a typical gradient defect, characterised by the ability of the tubule to increase urinary pCO₂ after maximum alkalinisation.

The diagnosis of DRTA in our patient was made from his inability to acidify urine in the face of metabolic acidosis. Various mechanisms underlying the common forms of DRTA are shown in fig 1. Ability to increase urinary pCO₂ after maximum alkalinisation and to decrease urinary pH after giving furosemide strongly argue in favour of a gradient defect in our patient, rather than a primary H⁺ ion defect, where there is an inability to increase urinary pCO₂ following alkalinisation of urine. Such a gradient defect is similar to that induced by amphotericin B. Associated hypokalaemia in our case suggested a generalised permeability defect involving both intercalated and principal cells, as is typically seen with patients receiving amphotericin B. One previously described case of gradient DRTA did not have accompanying hypokalaemia, but hypokalaemia induced paralysis was the primary presentation in our case. We are unaware of a similar report in the literature.

Recent insights into the molecular understanding of DRTA have unravelled certain genetic mutations associated with the condition, including mutations in the chloride-bicarbonate anion exchanger 1 (AE1) seen in autosomal dominantly transmitted DRTA, ATPB1 in autosomal recessive DRTA associated with sensorineural deafness, and H-ATPase in patients with autosomal disease without sensorineural deafness. An increase in U–B pCO₂ has also been postulated to arise from a misdirection of AE1 to the apical membrane of type A intercalated cells in a patient with Southeast Asian ovalocytosis who presented with hypokalaemia, but on dynamic tubular testing was found to have high urinary CO₂ tension with an inability to lower pH with furosemide.

Our patient illustrates that a gradient defect might be the underlying defect in patients with DRTA. Investigating patients with RTA with dynamic tubular studies could unravel the defect in more cases.

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