**Case 7** Acute confusion in an 82-year-old with known type 2 diabetes

Brian, an 82-year-old gentleman with known type 2 diabetes, is brought to A&E with general deterioration and acute confusion.

What differential diagnoses would you consider and what would you do?

Older people commonly present to hospital with acute and subacute confusional states. The differential diagnosis is wide and includes:

- **Infection:**
  - Urinary tract infections (UTIs), which are very common, particularly in women
  - Chest infections
  - Encephalitis and meningitis (rare)
- **Drugs and alcohol**
  - Intoxication (opiates, sedatives, anticholinergics)
  - Withdrawal
- **Hypoxia**
  - Central (sedatives)
  - Pulmonary (infection)
- **Metabolic**
  - Uraemia
  - Liver failure
  - Hypoglycaemia
  - Hypercalcaemia
- **Vascular**
  - Stroke
  - Transient ischaemic attack (TIA)
- **Intracranial lesion:**
  - Raised intracranial pressure (due to a brain tumour for example)
  - Subdural haematoma
- **Epilepsy**
  - Temporal lobe epilepsy
  - Post ictal states

It is not possible to take a history from Brian as he is confused and agitated. Members of his family tell you that they saw Brian a week ago when he was absolutely fine. They stress that he is usually in good health and does his shopping and cooking and has been managing alone for 5 years after the death of his wife. Apart from diabetes and ‘mild’ hypertension, both diagnosed 10 years ago, he has never had any problems with his health. He drinks occasionally (1–4 units/month). His medications include:

- Metformin 850 mg b.d.
- Gliclazide 40 mg b.d.
- Aspirin 75 mg o.d.
- Atorvastatin 10 mg o.d.
- Bendrofluazide 2.5 mg o.d.

**Nutritional deficiencies**

- B12
- Thiamine (particularly in alcoholics)

The first step is to take a proper history to narrow down the differential diagnosis. Questions asked should include:

- **Onset of confusion**
  - Acute
  - Acute on chronic
- **Associated symptoms/previous history**
  - Urinary symptoms or incontinence (UTI)
  - Cough or shortness of breath (chest infection)
  - Weakness in arms or legs or slurred speech (stroke/TIA)
  - Any falls (even mild head bumps may result in a subdural haematoma, particularly in patients treated with warfarin)
- **History of alcohol abuse**
- **Detailed drug history**

Does this help you to rule out any of differential diagnoses mentioned above? What would you do next?

- Although limited, the history from the family estab-
lishes that this is an acute confusional state in an elderly gentleman who is managing to live alone with no apparent problems
• The list of Brian’s medications does not include any sedatives or opiates and his alcohol intake is minimal, ruling out drugs/alcohol as a cause of his confusion. However, he is on gliclazide, which may cause hypoglycaemia. At this stage, an urgent test of capillary glucose is required

What would you do next?
• The patient is hypotensive and tachycardic with a drop in GCS
• He has low-grade temperature
• His oxygen saturation is low
• His capillary glucose is ‘high’ indicating blood sugar probably in excess of 30 mmol/L (most capillary glucose meters fail to accurately measure very high glucose levels and simply refer to these as ‘high’)

As Brian is tachypneic with low oxygen saturation, he should:
• Undergo a full physical examination with special emphasis on the respiratory system
• His arterial blood gases should be checked
• He should also be started on oxygen therapy

On examination, Brian is clinically dehydrated although cardiovascular and abdominal examination are both normal. Chest auscultation indicates decreased percussion note on the right with increased vocal fremitus and bronchial breathing. Neurological examination is difficult as the patient is uncooperative, but it is noted that he is: confused and agitated, moving all four limbs, his pupils are normal in size with a normal light reflex and plantars are down going.

Brian’s arterial blood gas (ABG) analysis showed:
PO₂ 7.1 kPa
PCO₂ 2.3 kPa
HCO₃⁻ 16 mmol/L
pH 7.32

What would you do next?
• The normal heart and abdominal examination make primary pathology in the cardiovascular and gastrointestinal system unlikely, although do not completely rule it out
• Although full neurological examination was difficult, the ‘brief version’ described above indicates that it is unlikely a major neurological pathology is causing the above abnormalities. However, this examination does not conclusively rule out a neurological condition. For example, a subdural haematoma does not necessarily cause any weakness and may manifest as unexplained confusion
• The respiratory examination is consistent with lung consolidation, making a diagnosis of pneumonia a strong possibility
• ABG analysis shows:
  ◦ Hypoxia
  ◦ Mild metabolic acidosis
  ◦ Secondary hypocapnia (trying to correct the metabolic acidosis)

It is essential to test the urine for ketonuria in any diabetes patient with high blood glucose, particularly in the presence of acidosis, to rule out the possibility of diabetic ketoacidosis.

Does Brian have DKA? What other conclusions can be made from the urine dipstick results?
• Brian’s urine dipstick results are not compatible with DKA due to the absence of heavy ketonuria. Mild ketonuria can be frequently seen, particularly in fasted individuals
• The urine dipstick fails to show white cells or nitrates in the urine making a UTI an unlikely diagnosis

What other tests would you request in this patient?
• FBC: looking for raised white cells (infection), anaemia
• Blood cultures: raised temperature, likely chest infection
• U&Es: checking kidney function, particularly in view of the dehydration and acidosis
• Glucose: in view of the history of diabetes and raised capillary glucose
• CXR: in view of the positive findings on examination
• ECG: all acutely unwell individuals, particularly diabetes patients, should have an ECG done to rule out silent myocardial infarction and cardiac arrhythmias
• To complete the confusion screen, the following should be checked:
  ○ LFTs
  ○ Calcium
  ○ B₁₂ plasma levels

What is the diagnosis so far and what would you do while awaiting the results of the above tests?
• In complicated cases, it is advisable to make a list of the abnormalities, which usually helps in organizing further investigations and reaching the correct diagnosis.
  The abnormalities in this case thus far:
  ○ Acute confusion
  ○ Signs of dehydration
  ○ Signs of chest infection
  ○ Hyperglycaemia
  ○ Hypoxia
  ○ Metabolic acidosis (mild, partially compensated)
• Taken together, the most likely diagnosis is pneumonia complicated by hyperglycaemia, dehydration and metabolic acidosis, resulting in confusion and reduced GCS.
• The patient should be started on i.v. fluid (0.9% saline) due to dehydration and low blood pressure, as well as broad spectrum i.v. antibiotics (after taking appropriate cultures) for his chest infection. Oxygen treatment should continue.

What is the anion gap? What are the potential causes of his acidosis?
Anion gap = (sodium + potassium) – (chloride + bicarbonate)
Anion gap = (148 + 4.0) – (111 + 15)
= 26 (normal 12–20)

His anion gap is high. Causes of high anion gap metabolic acidosis are outlined in Case 1.

What is his calculated plasma osmolarity?
Plasma osmolarity can be calculated from the formula:
2 (sodium + potassium) + urea + glucose
2 (148 + 4.0) + 30 + 54 = 388 (normal 285–295)

His calculated plasma osmolarity is greatly increased.

What does his X-ray show? (Fig. 49)
The X-ray shows right middle lobe pneumonia.

What test would you request next?
• Brian has an infection and metabolic acidosis; therefore, lactic acid levels should be requested. Metformin can also cause lactic acidosis particularly in the presence of renal failure and this is another reason to check lactate levels.

Brian’s lactic acid levels are 5.8 mmol/L (1.0–2.4).

What are the diagnoses?
• Chest infection associated with hypoxia and hypotension
• Hyperosmolar non-ketotic hyperglycaemia resulting in dehydration and contributing to low blood pressure
• Metabolic acidosis due to:
  ○ Raised lactic acid (secondary to infection, hypoxia and possibly metformin treatment)
  ○ Deranged renal function may have also contributed to the metabolic acidosis

How would you treat Brian?
Brian requires treatment for:
• Chest infection
• Hyperosmolar non-ketotic hyperglycaemia
  Treatment of the infection and normalization of renal function will correct Brian’s metabolic acidosis.
What is the prognosis in this case?
- The prognosis of hyperosmolar non-ketotic hyperglycaemia is unfortunately poor
  - More than a third of patients die, commonly from thromboembolic disease

Brian is treated with i.v. antibiotics, fluid and insulin and makes a very good recovery, with all his blood parameters returning to normal 48 h after admission. However, 60 h after his admission, he complains of sudden onset shortness of breath. He denies chest pain.

What is the most likely differential diagnosis?
The most likely differential diagnosis here is:
- Pulmonary embolism
- Relapsed/partially treated chest infection
- Myocardial infarction

What would you do?
- A physical examination, concentrating on the cardiovascular and respiratory system
- ECG
- CXR
- Routine bloods

Box 23 Treatment of hyperosmolar non-ketotic hyperglycaemia
- Intravenous administration of broad spectrum antibiotics
- Respiratory support as necessary
- Bicarbonate: This is not needed in uncomplicated hyperosmolar hyperglycaemia as the patient is not usually acidic
- Monitoring: This should be done regularly with blood samples taken every 2 h in the first 6–8 h to assess response to treatment

On examination, blood pressure is 110/65 (145/85 earlier that day), pulse 104 beats/min regular, O2 saturation 90% (98% earlier in the day) and respiratory rate 32 breaths/min. Cardiovascular auscultation reveals an additional S3 gallop heart sound. Chest auscultation shows bilateral basal crepitations.

Are these findings compatible with a pulmonary embolus (PE) and why?
- Although PE is a strong possibility, the clinical findings do not fit this diagnosis. In large PE, S3, due to right ventricular dysfunction, may be heard but bilateral basal crepitations are not a feature and these are usually found in left ventricular failure.

Box 22 Treatment of chest infection
- Intravenous administration of broad spectrum antibiotics
- Respiratory support as necessary
- Precipitating cause(s): Infection is the most common precipitating cause and, therefore, antibiotic cover must be started after appropriate cultures
- Other measures: Due to high osmolarity and dehydration, thrombotic disease is very common in these patients and, therefore, all should be covered with prophylactic unfractionated heparin (unless haemorrhage is suspected)
- Monitoring: This should be done regularly with blood samples taken every 2 h in the first 6–8 h to assess response to treatment
The most likely diagnosis here is left ventricular dysfunction resulting in pulmonary oedema.

*Brian’s ECG on admission did not show major abnormalities, his repeat ECG is shown in Fig. 50.*

**What does the repeat ECG show?**
The ECG shows ST elevation in V1-V4 indicating acute anterior-septal myocardial infarction.

### Table 31 Main features and management of hyperosmolar non-ketotic hyperglycaemic (HONK)

<table>
<thead>
<tr>
<th>Age group affected</th>
<th>Older people with or without a history of diabetes (this could be the first presentation of diabetes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>Usually very high (30–80 mmol/L)</td>
</tr>
<tr>
<td>Acidosis</td>
<td>Not a feature unless complicated by metabolic acidosis due to other causes (i.e. infection or myocardial infarction)</td>
</tr>
<tr>
<td>Serum osmolarity</td>
<td>Very high (&gt;350 mmol)</td>
</tr>
<tr>
<td>Ketonuria</td>
<td>There is an absence of severe ketonuria but mild to moderate ketonuria is common (starvation/vomiting)</td>
</tr>
<tr>
<td>Precipitating factor</td>
<td>Common: suspect an infection or a vascular event</td>
</tr>
<tr>
<td>Management</td>
<td>Gentle i.v. fluid</td>
</tr>
<tr>
<td></td>
<td>Gentle i.v. insulin</td>
</tr>
<tr>
<td></td>
<td>Prophylactic heparin is mandatory (unless a bleed is suspected)</td>
</tr>
<tr>
<td></td>
<td>Aggressive use of i.v. antibiotics is encouraged</td>
</tr>
</tbody>
</table>

- The most likely diagnosis here is left ventricular dysfunction resulting in pulmonary oedema.

**What is the diagnosis? How would you explain the absence of chest pain?**
- The diagnosis is acute myocardial infarction causing left ventricular dysfunction.
- Silent MI (no chest pain) is common in diabetes patients, and this should be taken into account when assessing these individuals.

The main features of hyperosmolar non-ketotic hyperglycaemia are summarized in Table 31.

**CASE REVIEW**

Brian is an older gentleman who is brought into hospital with general deterioration and acute confusion, a common clinical presentation in this age group. The differential diagnosis is wide and includes infection, intoxication with drugs or alcohol, hypoxia, vascular event, intracranial lesion or metabolic/nutritional derangements. An appropriate history, taken usually from relatives or friends, is important to give some clues to the cause of the confusion. Physical examination in this gentleman is consistent with dehydration and chest infection. Subsequent
tests show biochemical evidence of dehydration with raised glucose, together with hypoxia and lactic acidosis secondary to chest infection. The diagnosis is hyperosmolar non-ketotic hyperglycaemia precipitated by a chest infection. Brian is treated with intravenous antibiotics, fluid and low-dose insulin, subsequently making a good recovery. However, 2 days later he complains of sudden onset breathlessness without chest pain, which was due to heart failure secondary to silent myocardial infarction. The latter is common in patients with diabetes and should be considered in those with recent history of shortness of breath.

**KEY POINTS**

- Hyperosmolar non-ketotic hyperglycaemia (HONK) is a rare complication of type 2 diabetes and usually affects the older patient
- HONK carries a poor prognosis as mortality rates can be as high as 50%
- In more than half the cases, HONK occurs in patients who are not known to have diabetes
- HONK is frequently precipitated by an infection or vascular event and patients are severely dehydrated with impaired kidney function and very high plasma glucose levels
- Acidosis is not a feature of HONK, unless it is due to the associated condition, and there is no heavy ketonuria (mild ketonuria may be present due to starvation)
- Patients with HONK should be treated with intravenous:
  - Fluid (careful not to overload and precipitate heart failure)
  - Insulin (only small doses are required)
  - Antibiotics after appropriate cultures (infection is a common precipitating cause)
  - Prophylactic heparin (vascular thrombosis is a common cause of death in patients)