CASE FIVE

Short case number: 3_3_5
Category: Gastrointestinal and Hepatobiliary systems
Discipline: Medicine
Setting: Emergency Department_rural
Topic: Acute and Chronic Pancreatitis

Case

Lenny Deighton, a 45 year old cattle farmer, presents to the emergency department, with worsening epigastric pain, nausea and vomiting. The nursing staff have called you in because he looks unwell.

On review, Lenny is in obvious pain, he is pale & diaphoretic.
Afebrile, BP 100/60; HR 95 bpm, Regular, RR 23/min. SaO_2 – 95 [room air]

You know that Lenny has had a previous episode of pancreatitis and you are concerned that he is suffering again with this.

Questions

1. What are key features of the history in the assessment of the possible cause of Lenny's problem?
2. What are the key features of the physical examination, in particular the clinical signs that suggest severe illness?
3. Outline the possible complications of acute pancreatitis in relation to time after presentation and correlate these with the underlying pathophysiology.
4. What investigations would you recommend in your assessment of Lenny? Describe the findings that support a diagnosis of acute pancreatitis.
5. Lenny is diagnosed with acute pancreatitis and is admitted to the ward; outline the management of Lenny's pain and fluid balance.
6. Four [4] hours later you are called to see him again as he has deteriorated further. In a table detail the factors during the first 48 hours that indicate severe pancreatitis.
7. Lenny deteriorates further and needs treatment in an intensive care unit, this requires you to organise a retrieval team. Summarise the process for organising an intensive care bed and retrieval from a rural town. *[this will require some research beyond the textbooks]*
8. Lenny returns to see you a few months later; he has now developed chronic pancreatitis. Describe the pathogenesis of chronic pancreatitis and outline how it differs from acute pancreatitis.

Suggested reading:

1. Kumar P, Clark ML, editors. Kumar & Clark's Clinical Medicine. 8th edition. Edinburgh: Saunders Elsevier; 2012. Chapter 7.

2. Bromley J, Pavli P, Disorders of the pancreas, How to treat; Australian doctor, http://search.ebscohost.com.ipacez.nd.edu.au/login.aspx?direct=true&db=anh&AN=22940789&site=ehost-live&scope=site

ANSWERS

1. In the Western world gallstones and alcohol account for the vast majority of cases. A drinking history needs to be taken. Pain associated with fatty or fried foods may indicate the presence of gallstones. If neither of these factors are relevant then rarer causes need to be considered e.g. trauma, recent introduction of drugs e.g. corticosteroids or the presence of hyperlipidaemia. In 10 % of cases the cause is unknown i.e. idiopathic pancreatitis.

The cardinal symptom of acute pancreatitis is abdominal pain which is dull, boring and steady. Usually the pain is sudden in onset and gradually intensifies in severity until reaching a constant ache. Most often it is located in the upper abdomen, usually the epigastrium but may be perceived more on the left or right side, depending on which portion of the pancreas is involved. The pain radiates directly through to the back in 50% of cases. Nausea and vomiting are often present along with anorexia.

In Lenny's case depending on the validity of the previous diagnosis of pancreatitis, how the diagnosis was made etc. then it is reasonable to ask the patient whether his current symptoms are similar or differ in important aspects.

2. Physical examination at the time of presentation may show little more than a patient in pain with some upper abdominal tenderness but no systemic abnormalities.
In more severe disease the patient may be febrile (75%), have a tachycardia (65%), be hypotensive and oliguric. Muscle guarding and distension are observed in most. A minority exhibit jaundice and approximately 10% will experience dyspnoea/ tachypnoea (irritation of the diaphragm, pleural effusion).

In severe cases haemodynamic instability is evident. In addition they are often pale, diaphoretic and listless. Hypovolaemia results from inflammation and 'third spacing' of fluid in the abdomen.
A few uncommon physical signs are associated with severe necrotizing pancreatitis:
- Cullen's sign is a bluish discolouration around the umbilicus resulting from haemoperitoneum.
- Grey-Turner sign is a reddish-brown discolouration along the flanks resulting from retroperitoneal blood dissecting along tissue planes.
- Erythematous skin nodules may result from focal subcutaneous fat necrosis.

3. Within the first seven days the morbidity and mortality of acute pancreatitis depends on the degree of inflammation, patient's physiological reserve and degree of fluid and electrolyte imbalance/ metabolic disturbance. Large volume intravascular fluid depletion and significant metabolic disturbance can result in multi organ failure. Edema of tissues from a systemic inflammatory response syndrome (SIRS) can result in pulmonary edema and pleural effusions. Renal impairment, respiratory compromise, haemodynamic compromise and bone marrow suppression may result. (Students should read further on SIRS)
After the initial period the prognosis is most closely related to the extent of pancreatic necrosis. Extensive necrosis (> 50% of the pancreas) is associated with high risk of complications e.g. infection.

Pancreatic necrosis may become secondarily infected. Seeding from intestinal bacteria are the predominant source. The usual suspects (in decreasing prevalence) are E.Coli, Pseudomonas, anaerobes, Staphylococcus, Klebsiella, Proteus, Streptococcus, Enterobacter.
Patients who are febrile with raised or increasing WCC/CRP in whom other sources of infection have been excluded (chest, urine, intravenous access lines) should have a CT scan of the abdomen to assess for pancreatic necrosis and possible secondary infection.
Treatment is with IV antibiotics (e.g. meropenem) and percutaneous (CT guided) aspiration and drainage if technically feasible. The sample should be sent to microbiology for M,C and S.
Rarely these days, surgical intervention in the form of pancreatic necrosectomy is required.

Peri- pancreatic edema or inflammatory fluid may be seen early in pancreatitis.
Over time, the fluid may accumulate and develop a capsule- a pancreatic pseudocyst. These by definition are not found until 6 weeks after the onset of the illness. The smaller pseudocysts (< 6 cms in diameter) frequently resolve on their own but others may persist in the long term, giving rise to potential complications such as infection and intra-peritoneal bleeding.
Pseudocysts that are sterile (not infected) may require drainage if they are causing mass effect e.g. gastric outlet obstruction presenting with nausea, early satiety and vomiting/poor oral intake +/- abdominal bloating/pain.
Drainage may be percutaneous or endoscopic or by surgical intervention.

Patients with severe acute pancreatitis or recurrent pancreatitis may develop a chronic pancreatitis. This manifests as pancreatic exocrine insufficiency (malabsorption + steatorrhea) and endocrine insufficiency (diabetes).

4. Serum lipase level is the standard laboratory test carried out to confirm the diagnosis made on history and examination. If this is measured within 24 hours of the onset of pain and elevated to three or more times the upper limit of normal, it is diagnostic.
Other baseline investigations include a full blood count and CRP, urea and electrolytes, blood glucose, liver function tests, plasma calcium and arterial blood gas. These are documented at presentation and then repeated at 24 and 48 hours and provide a basis for assessing the severity of an attack.
An erect chest X-ray is mandatory to exclude gastro-duodenal perforation, which also raises the serum lipase.
An upper abdominal U/S is used as a screening test to identify a possible biliary (gallstone) cause of pancreatitis. The U/S may also demonstrate pancreatic swelling and necrosis as well as peripancreatic fluid collections if present.
(If the patient deteriorates a contrast-enhanced CT scan should be carried out within 2 – 3 days of presentation to assess the extent of pancreatic necrosis. This provides very valuable prognostic information.)
After the diagnosis has been made, determining the severity of the episode is the most important issue. Overall about 10% of cases are classified as severe; these have a mortality rate of about 20 – 30%

5. The initial management of acute pancreatitis is similar, whatever the cause.
Patient is kept nil by mouth (NBM) and intravenous fluid hydration therapy is commenced.
Especially in the early phase of the illness, aggressive fluid resuscitation is critical. Resuscitation should be enough to maintain normal circulatory parameters (heart rate, BP, urine output).

Fluid balance charts are mandatory and assessment for fluid overload (pulmonary and peripheral edema) as well as hypoxia should be part of regular clinical assessment.

Analgesics are used to control which is essential for quality care. Paracetamol alone or in combination with opiates / patient controlled analgesia, tramadol may be used depending on the severity of the pain.

Acute pancreatitis is associated with severe pain usually requiring opioid analgesia. Patient-controlled analgesia supervised by an acute pain team may be appropriate if repeated doses of parenteral opioid are required. There is no evidence that morphine worsens pancreatitis or that pethidine should be used in preference to morphine.
(Analgesic requirements differ enormously depending on many factors such as age, sex, body mass and previous exposure to opioids.)

6. Factors during the first 48 hours that indicate severe pancreatitis and a poor prognosis (three or more factors present predict a severe episode).

Ranson/Imrie prognostic criteria for acute pancreatitis
On admission or diagnosis age > 55 years
White cell count > 15.0 x10^9 /L
Hyperglycaemia > 10 mmol/L
Plasma LDH > 600 U/L
Plasma AST > 100 U/L
During the initial 48 hr of hospitalisation Haematocrit fall > 10 percent
Hypocalcaemia < 2.0 mmol/L
BUN rise by > 1.8 mmol/L
Fluid sequestration > 4 litres
Hypoalbuminaemia < 32 g/L
Hypoxaemia < 60 mmHg (FIO2 0.21)

A multiple factor scoring system (ideally APACHE II with a modification for obesity) should be carried out at the end of the first 24 hours after presentation to allow identification of the 25% of patients with a predicted severe attack. It has high sensitivity and specificity for diagnosis of acute, severe pancreatitis (75% and 92% respectively). This should be repeated at 48 hours to identify a further subgroup who appear to be moving into the severe category.
The APACHE II scoring system parameters.

Physiological	Laboratory
Temperature	Oxygenation ($P_a 0_2$)
Heart rate	Arterial pH
Respiratory rate	Serum:
Mean arterial pressure	sodium
Glasgow coma score	potassium
	Creatinine
	Haematocrit
	White blood cell count

7. Lenny's attending physician would call the Medical Retrieval Unit (MRU) on an 1800 number and discuss the case with an MRU specialist. This person would then co-ordinate the retrieval team as well as the intensive care bed. Once the retrieval team arrive at the rural hospital they would then assess and take over the management of the patient. There would be communication amongst the team, the MRU specialist and the Intensivist of the hospital accepting the patient as to the current situation and the required treatment to stabilise the patient to allow safe transfer.

8. In regard to the pathogenesis of chronic pancreatitis, a possible common pathway for pancreatic damage appears to be the inappropriate activation of enzymes within the pancreas. This has been well demonstrated in the case of hereditary pancreatitis where genetic abnormalities have led to unopposed trypsin activity within the pancreas itself. Chronic alcohol intake is also believed to increase the level of trypsinogen relative to its inhibitor. Human trypsinogen has a propensity to autoactivate, and any relative impairment or deficiency of inhibitor proteins will lead to unopposed enzyme activity and possible pancreatic damage.

It is believed that the intrapancreatic enzyme activity leads to the precipitation of proteins within the duct lumen in the form of plugs. These then form a nidus for calcification but are also the cause of ductal obstruction leading to ductal hypertension and further pancreatic damage. Cytokine activation and oxygen stress are thought to play a role in perpetuating this process.

In summary, the proposed pathologic mechanisms of chronic pancreatitis are as follows:

- intraduct plugging and obstruction (e.g. alcohol abuse, stones, tumours)
- leakage of enzymes from the pancreas into surrounding tissues -protease, lipase, elastase; destruction of adjacent tissues
- direct toxins (e.g. ETOH) and toxic metabolites. These act to release cytokines to produce collagen and establish fibrosis. Cytokines also act to stimulate inflammation.
- oxidative stress (e.g. idiopathic pancreatitis).
- necrosis-fibrosis (recurrent acute pancreatitis that heals with fibrosis).
- ischaemia (from obstruction and fibrosis)
- autoimmune disorders. Chronic pancreatitis has been found in association with other autoimmune diseases such as Sjögren's syndrome, primary biliary cirrhosis and renal tubular acidosis.

To distinguish from acute pancreatitis:

- Serum amylase and lipase levels are rarely significantly elevated in established chronic pancreatitis.
- While low levels of serum trypsin are relatively specific for advanced chronic pancreatitis, they are not sensitive enough to be helpful in most patients with mild-to-moderate disease.
- Steatorrhoea is a manifestation of advanced chronic pancreatitis (> 90% of the pancreas has to have been destroyed).
- Faecal elastase level will be abnormal in the majority of patients with moderate to severe pancreatic disease.

Diagnosis of chronic pancreatitis requires morphologic abnormalities to appear on imaging procedures:-

- abdominal X-ray – pancreatic calcifications, often considered pathognomonic of chronic pancreatitis, are found in approximately 30% of cases, more common with alcoholic pancreatitis, rare in the idiopathic form.
- contrast-enhanced CT scan – in the presence of pancreatic calcification and a dilated pancreatic duct the diagnosis of chronic pancreatitis can be easily established. The sensitivity and specificity of CT scan are 80% and 85% respectively. Pancreatic atrophy is common.

References:

Gardner T, Berk B, Pancreatitis, acute. eMedicine. Gastroenterology

Obideen K, Yakshe P, Pancreatitis, chronic. eMedicine Gastroenterology. Update 16 June 2008