Chest pain in a young patient: an unusual complication of Epstein-Barr virus

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Accepted 9 March 2014

SUMMARY

A 29-year-old man presented with sudden left-sided pleuritic chest pain on a background of sore throat during the preceding week. On examination he had tender cervical lymphadenopathy, he was tachycardic and had a 24 mm Hg blood pressure difference between the left and right arms. Bloods revealed deranged liver function tests and a lymphocytosis. His D-dimer was raised, hence he was treated for presumed pulmonary embolism before imaging was available. Monospot test was positive. He subsequently had both a CT pulmonary angiogram and a CT angiogram of the aorta to exclude pulmonary embolism and aortic dissection. The CT revealed splenomegaly with a large subdiaphragmatic haematoma secondary to splenic rupture. This had likely caused referred pain through diaphragmatic irritation. He was taken to theatre for urgent splenectomy. The unifying diagnosis was infectious mononucleosis complicated by spontaneous splenic rupture secondary to Epstein-Barr virus infection.

BACKGROUND

This is an unusual presentation of splenic rupture caused by a common viral infection (Epstein-Barr virus, EBV). It highlights the serious complications of EBV infection and the importance of a thorough history, differential diagnosis and appropriate investigation of patients presenting with atypical chest pain. This is illustrated through an interaction between general medicine, radiology, general surgery and infectious disease.

CASE PRESENTATION

A 29-year-old man presented with a 5 h history of sudden onset of severe sharp pain in his left upper chest. It was worsened by inspiration and movement and associated with sweating, shortness of breath and an episode of vomiting. He described a flu-like illness in the preceding week when he suffered from fever and a sore throat which were resolving. He denied a productive cough and did not have any calf swelling or haemoptysis. He had a medical history of pericarditis 5 years previously but no risk factors for ischaemic heart disease. His father had an abdominal aortic aneurysm but there was no other notable family history. He had a 6 pack-year smoking history but no illicit drug use. On examination he was sweaty and pale and in severe pain. He had tender cervical lymphadenopathy. He was tachycardic with a heart rate of 111 bpm and his blood pressure was 135/73 mm Hg. His oxygen saturations were 96% on room air. Cardiovascular and respiratory examinations were unremarkable. His chest pain was localised to the upper left chest, made worse by movement and inspiration but not

chest wall palpation. Clinically there was no deep vein thrombosis and Well's score for pulmonary embolism (PE) was 4.5 indicating intermediate risk. His abdomen was soft with minimal epigastric discomfort and no palpable organomegaly. He was found to have a 24 mm Hg blood pressure difference between the left and right arms.

INVESTIGATIONS

Initial ECG demonstrated sinus tachycardia with no ischaemic features but subsequent ECG showed new T-wave inversion in leads III, aVF and V₆.

Arterial blood gas showed normal pH, base excess and bicarbonate with partial pressure of oxygen 10 kPa but a high lactate of 3.4 mmol/L. Alveolar-arterial gradient was 28 (expected 11) suggesting a V/Q mismatch.

Haematological investigation revealed a high white cell count of $27 \times 10^9/L$ with lymphocytosis ($16.3 \times 10^9/L$) and mild neutrophilia ($8.9 \times 10^9/L$) and a D-dimer of 1135 ng/mL (250 ng/mL is the cut-off for PE). Biochemical investigation revealed deranged liver function tests with bilirubin 33 mmol/L, alkaline phosphatase 283 IU/L and alanine aminotransferase 583 IU/L. Troponin I was negative. Monospot test was positive confirming EBV infection and accounting for the liver function and haematological abnormalities.

Anteroposterior (AP) chest radiograph showed clear lung fields with no mediastinal widening.

CT pulmonary angiogram was negative for PE.

CT angiogram of the aorta (thorax and abdomen) excluded an aortic dissection but revealed a large grade III subcapsular haematoma of the spleen of 3.8 cm depth affecting more than 50% of its surface with underlying splenomegaly of 16 cm (figure 1).

DIFFERENTIAL DIAGNOSIS

There is a wide differential diagnosis for this patient's symptoms.

PE was a reasonable suggestion based on a history of pleuritic chest pain in a young patient alongside sinus tachycardia on the ECG and a high A-a gradient on the arterial blood gas (suggesting a ventilation/perfusion mismatch) and the raised D-dimer. The patient did not, however, have any risk factors for PE and maintained oxygen saturations of over 96% on air.

The nature of the chest pain would also have been consistent with an aortic dissection, especially its severity and sudden onset. Additionally, the blood pressure difference between the two arms would have supported this diagnosis (although this actually turned out to be a red herring). The D-dimer is usually raised in acute aortic dissection and values of less than 500 mg/mL have been

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To cite: Raman L, Rathod KS, Banka R. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-201606

Figure 1 Demonstrating the haematoma around the spleen due to splenic rupture (red arrow).

shown to be a useful screening tool to identify patients who do not have an acute aortic dissection.¹ The pain was not the typical central chest pain radiating to the back which is often described in association with aortic dissection and the chest radiograph did not show any mediastinal widening which is sometimes a radiological feature, although the diagnostic accuracy is higher for PA radiographs (sensitivity 90%) than AP radiographs (sensitivity 72%).² This patient also had a family history of aortic aneurysm which may represent a risk factor for dissection especially if in association with connective tissue disease, although there was no suggestion of this.

This patient was partially treated for acute coronary syndrome (ACS) with aspirin based on dynamic ECG changes. ACS is a possibility, but the nature of the chest pain was atypical and the patient's only risk factor was smoking making it an unlikely diagnosis especially at such a young age. The ECG changes were likely to be rate related.

Pericarditis presents with pleuritic chest pain in association with systemic features related to the underlying pathogen. This patient's preceding flu-like illness would be in keeping with development of a viral pericarditis. The ECG, however, did not reflect the changes usually seen in pericarditis; widespread saddle-shaped ST elevation.

Splenic rupture usually presents with left flank or left upper quadrant abdominal pain, sometimes with radiation to the left shoulder (referred pain via diaphragmatic irritation). This patient had only mild epigastric discomfort which was unusual, and he did not have referred shoulder tip pain; rather upper chest pain. His pale, sweaty appearance and tachycardia, however, were early clues that the patient may be developing hypovolaemic shock, although the blood pressure was maintained. The preceding flu-like illness is the crucial clue about an underlying diagnosis of infectious mononucleosis.

Infectious mononucleosis is characterised by fever, malaise, lymphadenopathy and a sore throat, sometimes associated with abdominal pain and hepatosplenomegaly in the context of deranged liver function tests, haematological abnormalities (most commonly lymphocytosis) and positive EBV serology. Differentials include acute viral hepatitis infection, infection with other herpes viruses including herpes simplex, cytomegalovirus

or human herpes virus 6, *Toxoplasma gondii* infection and streptococcal tonsillitis. This patient had most of the clinical findings indicative of acute infectious mononucleosis in the preceding week, despite which diagnosis was difficult due to the atypical presentation of splenic rupture.

TREATMENT

The patient was initially treated in the emergency department with treatment dose enoxaparin for presumed PE based on the history, tachycardia and D-dimer, as well as 300 mg aspirin for possible myocardial infarction in light of the dynamic ECG changes before the troponin I result was available.

Following confirmation of spontaneous splenic rupture the patient was taken to theatre for urgent laparotomy and splenectomy under intravenous antibiotic cover. The spleen was found to be enlarged and actively bleeding from the upper pole. The spleen was brought down with packs, the bleeding controlled with diathermy and the gastrosplenic ligament and splenic artery ligated. A drain was left in situ.

The patient was transfused 4 units of blood postoperatively and carefully monitored on the high dependency unit.

OUTCOME AND FOLLOW-UP

Following his surgery the patient made an uncomplicated recovery and was discharged 1 week later with a diagnosis of splenic rupture complicating acute EBV infection.

He returned for drain removal at 11 days postprocedure and has remained well since then.

He was referred for pneumococcal (23 valent vaccine), *Haemophilus influenzae*, meningitis C and influenza vaccination.

DISCUSSION

EBV is a common enveloped DNA virus (human herpes virus 4) which infects over 95% of the world's population, usually affecting children and young adults.³ Transmission is via the salivary route following which the virus infects epithelial cells and B-lymphocytes and undergoes replication and cell lysis associated with release of virions. Incubation period is between 4 and 12 weeks.⁴ After the initial acute lytic infection, EBV latently infects B cells and epithelial cells as episomes in the cell nucleus. During latency the virus is not actively replicating but can spontaneously reactivate to switch to lytic replication.⁵

The clinical sequelae vary and infection can be asymptomatic especially in children. The most common clinical manifestation is infectious mononucleosis commonly known as glandular fever which is characterised by fever, malaise and a sore throat often with pharyngitis or tonsillitis and sometimes palatal petechiae on examination.³ Lymphadenopathy is common especially of the posterior cervical lymph nodes. Abdominal pain and hepatosplenomegaly (due to lymphocytic infiltration) can occur usually in the context of deranged liver function tests (in over 80%). Patients sometimes present with a rash. Haematological abnormalities occur including lymphocytosis (with >10% abnormal T lymphocytes on peripheral smear) and sometimes thrombocytopenia. Serological testing for EBV and heterophile antibody tests (eg, monospot) are positive.⁶

The acute infection usually runs an uncomplicated course with a self-limiting illness which does not require specific treatment. Spontaneous splenic rupture is a rare but potentially fatal complication which occurs in 0.1–0.5% of all patients with infectious mononucleosis.^{7 8} It is the commonest infectious cause of splenic rupture⁹ and it occurs three times more often in men than women.¹⁰ The pathophysiology is not clear but it may

involve congestion of the parenchyma of the spleen due to lymphoid infiltration.

Diagnosis of spontaneous splenic rupture is often missed due to the absence of a history of trauma. The classic signs of left upper quadrant pain, haemodynamic instability and peritoneal irritation are not always present especially early on which can make diagnosis challenging as demonstrated in this case. Kehr's sign (shoulder tip pain due to diaphragmatic irritation from intraperitoneal blood) is present in only 50% of cases.⁸ It may present with symptoms mimicking PE, ACS, aortic dissection, pneumonia, peptic ulcer disease or even ruptured diverticulitis.^{11 12}

The imaging modality of choice for diagnosis of splenic rupture is abdominal CT with contrast. It is graded using the American association for the surgery of trauma guidelines as I–V based on CT findings.¹³ This patient had a grade III haematoma which was subcapsular involving >50% of the surface of the spleen and actively expanding.

Cases similar to ours have been described in the literature. Shah *et al*¹⁴ described a man who developed sudden onset of severe pleuritic chest pain following a flu-like illness who was found to have a spontaneous splenic rupture secondary to splenomegaly due to infectious mononucleosis. Benz *et al*¹⁵ described a 19-year-old woman who also presented with symptoms of PE in the context of infectious mononucleosis, who was found to have splenic infarcts which were treated supportively as the spleen had not actually ruptured. Their patient had also been found to have ECG changes like the patient we have described here. These cases highlight how variable the presentation of splenic rupture can be and thus the importance of a detailed history, since the symptoms of infectious mononucleosis may be the only consistent clue to aid diagnosis. Fortunately, as our patient had a CT of the upper abdomen to exclude an aortic dissection, the ruptured spleen was seen and he was promptly taken to theatre. Outpatient follow-up of splenomegaly associated with infectious mononucleosis has been suggested as a means of early detection should splenic rupture occur.¹⁶

Learning points

- ▶ Chest pain in young people should always be taken seriously and a thorough history should be elicited before administering anticoagulation or antiplatelet therapy as the bleeding risk is significant and can be serious if the presumed diagnosis is incorrect.
- ▶ Epstein-Barr virus (EBV) is a very common viral infection affecting over 90% of the population, usually resulting in a self-limiting illness requiring supportive treatment only.
- ▶ Splenic rupture is a rare but potentially fatal complication of EBV infection often requiring surgical intervention for which early diagnosis is crucial.
- ▶ Splenic rupture may present in a variety of ways with symptoms which may mimic other more common conditions which makes diagnosis challenging.
- ▶ Splenectomy has implications for the future with susceptibility to infection with encapsulated organisms.

Splenectomy is usually the treatment of choice for patients with splenic rupture. In selected patients who are haemodynamically stable, a conservative approach is sometimes adopted to avoid the serious complication of sepsis postsplenectomy and has been shown to be a successful approach.¹⁷ Patients who undergo splenectomy are at a risk of infection especially with encapsulated bacteria, so should be vaccinated against *Streptococcus pneumoniae*, *H influenzae* and *Neisseria meningitidis* and should receive annual influenza vaccine. Lifelong penicillin prophylaxis is recommended in patients at high risk of pneumococcal infection (children and the elderly, immunosuppressed patients or those who have had a poor response to pneumococcal vaccination). In patients not considered high risk, chemoprophylaxis is considered on an individual basis.¹⁸

Contributors LR and KSRKR wrote the manuscript and RB improved the manuscript for the final draft and approved before submission.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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