Case report

Spontaneous splenic rupture in a patient with infectious mononucleosis

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SUMMARY

We present a case of spontaneous, atraumatic splenic rupture secondary to Epstein-Barr virus (EBV) infection, in a young, female patient. Splenic rupture is a rare complication of EBV infection, but is associated with the highest mortality. Additionally, this case illustrates the diagnostic challenge in a patient presenting in atypical manner, with only left-sided pleuritic chest pain, and lacking any of the classical tonsillitis symptoms associated with EBV infection.

BACKGROUND

Epstein-Barr virus (EBV) is a common pathogen which causes glandular fever. This is a clinical syndrome, otherwise known as infectious mononucleosis, which usually presents with a sore throat and flu-like symptoms, including fever and fatigue. It is most commonly a self-limiting illness with few complications. This case is interesting due to the lack of any classical glandular fever symptoms and the presenting feature being a rare, potentially fatal, complication of the infection.

This case outlines the difficulty in diagnosing splenic rupture in the absence of any previous symptoms, and how it is easy to mistake this complication for many other unrelated pathologies. It highlights the importance of attention to detail in interpreting blood results and acting on clinical suspicion when pain is out of proportion to the working diagnosis.

CASE PRESENTATION

A 22-year-old woman initially presents to the emergency department with a 1-day history of left-sided pleuritic chest pain. She has no cough or shortness of breath, no palpitations or dizziness, no coryzal symptoms, no nausea, vomiting or abdominal pain.

The patient has previously been fit and well with no significant medical history. She has not had travelled anywhere recently or had any recent illnesses. Physical examination is unremarkable and observations show she is haemodynamically stable, but do reveal a fever of 38.1°C. A chest X-ray, performed to rule out any consolidation, confirms clear lung fields and blood tests reveal a C reactive protein (CRP) of 18 mg/L with a normal white cell count of $4.48 \times 10^9/L$. She is diagnosed with a presumed mild viral respiratory tract infection.

For the next 10 days, she continues to suffer from the left-sided chest pain but is well enough to go to work. However, 11 days after her initial

presentation, she becomes more unwell with a fever, nausea and vomiting, and increasing left-sided chest pain.

Fourteen days after the first presentation, the patient represents to the emergency department with the above symptoms. The left-sided chest pain is still pleuritic in nature, but is now more severe and radiating to the left shoulder and left side of her neck. Additionally, she has now developed left upper quadrant abdominal pain, which is exacerbated by lying down flat or lying on her left side.

Physical examination finds mild cervical lymphadenopathy but normal tonsils and a normal cardio-respiratory examination, other than limited deep inspiration due to pain. Only limited examination of the abdomen is possible due to the severity of the pain and the patient's inability to lie flat. However, soft palpation even on the right side of the abdomen exacerbates the left upper quadrant pain, and there is guarding around the left upper quadrant.

INVESTIGATIONS

Observations reveal a fever of 38.0°C, tachycardia of 111 beats per minute, hypotension of 95/63 mm Hg and normal saturations and respiratory rate.

Blood results show a CRP of 49 mg/L, and a mildly raised white cell count of $11.3 \times 10^9/L$. The white cell differential reveals lymphocytosis of $7.29 \times 10^9/L$, whereas the neutrophil count is normal. Also of note is a significant drop in haemoglobin to 110 g/L, from a baseline of 136 g/L 2 weeks previously, a thrombocytopenia of $101 \times 10^9/L$ from a baseline of $165 \times 10^9/L$, and deranged liver function tests (alanine aminotransferase 233 unit/L, aspartate transaminase 343 unit/L, alkaline phosphatase 253 unit/L, bilirubin normal). A negative pregnancy test confirms the patient is not pregnant.

An erect chest X-ray again shows clear lung fields, and no free air under the diaphragm.

DIFFERENTIAL DIAGNOSIS

Until this point, the working differential diagnoses had been an atypical pneumonia and/or lung abscess, pulmonary embolism, ectopic pregnancy, and—on first glance of the blood results—potentially an atypical presentation of cholecystitis. However, the blood results were not in keeping with any of these differentials and were more suggestive of a viral hepatitis.

A call from the haematology laboratory clinched the diagnosis of EBV. The laboratory had performed a blood film identifying atypical lymphocytes

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Figure 1 Bedside FAST scan showing free fluid behind the spleen.

suggestive of EBV, which was then confirmed by a subsequent monospot test.

Relating this result back to the patient's symptoms, it seemed possible that she was experiencing tender splenomegaly secondary to EBV. However, clinically her pain was still out of proportion, and the hypotension, tachycardia and drop in haemoglobin and platelet counts were suggestive of a potential splenic rupture. A bedside focused assessment with sonography for trauma (FAST) scan ([figure 1](#)) and subsequent triple phase CT scan ([figure 2](#))

Figure 2 CT scan image of splenic haematoma.

confirmed splenomegaly measuring up to 14.7 cm with a 3 cm perisplenic haematoma and haemoperitoneum.

TREATMENT

The patient was treated with fluid resuscitation and analgesia during the diagnostic process; she required intravenous morphine due to the severity of the pain.

OUTCOME AND FOLLOW-UP

The patient was transferred to Resus and then intensive treatment unit (ITU), due to haemodynamic instability suggestive of ongoing bleeding. The surgical team were on stand-by for an emergency splenectomy if needed. However, her case was successfully managed conservatively without the need for a splenectomy and she was admitted for 2 weeks for monitoring and pain control.

DISCUSSION

Infectious mononucleosis, otherwise known as glandular fever, is a very common infectious disease caused by EBV. It is widely accepted within the literature that over 90% of the adult population worldwide has been infected with the virus. It is transmitted via saliva which is where it gets its colloquial name of 'the kissing virus'. Many people infected with the virus will remain asymptomatic, particularly those infected before the age of 10 years.¹ Some may suffer only very mild, viral, upper respiratory tract symptoms. Healthy people will continue to shed EBV for many months,¹ meaning the source of the virus is rarely evident. Those infected in adolescence or young adulthood are more likely to develop the more severe symptoms associated with the clinical syndrome: a triad of fever, pharyngitis and lymphadenopathy, as well as malaise and fatigue. However, infectious mononucleosis is usually a self-limiting illness. Although it is common to suffer from fatigue for many weeks to months after the acute illness, more serious complications are rare. These include meningo-encephalitis, myocarditis, pericarditis, pancreatitis and splenic rupture.² Splenic rupture occurs in just 0.1%–0.5% of cases of infectious mononucleosis,³ but is the most common cause of death from the infection, with a mortality of 9%.⁴ Prompt diagnosis and management are, therefore, critical in such cases.

A comprehensive systematic review⁴ of case reports of splenic rupture in infectious mononucleosis between 1984 and 2014 finds the average age of occurrence to be 22 years. Interestingly, it finds splenic rupture to be more common in males (70%), consistent with other literature,¹ making this case even more unusual. The systematic review also showed that 86% of cases were atraumatic. This highlights the importance of counselling patients diagnosed with infectious mononucleosis as to which symptoms may be suggestive of splenic rupture, and not simply advising them to avoid contact sports. The current National Institute for Health and Care Excellence (NICE) guidance advises 'to avoid contact or collision sports or heavy lifting for the first month of the illness (to reduce the risk of splenic rupture)'. It also advises seeking urgent medical attention if a patient develops abdominal pain, but perhaps this should have more emphasis and be more specific given the high associated mortality of the complication. Additionally, the systematic review found that while the average interval from initial symptoms of infectious mononucleosis to splenic rupture was 14 days, the range was up to 8 weeks and therefore recommends the avoidance of contact sports and vigorous activity for 8 weeks.

However, to be able to counsel a patient on the risks of splenic rupture, a prior diagnosis of infectious mononucleosis is required.

One of the difficulties in identifying the splenic rupture in this case was the lack of the prior diagnosis of infectious mononucleosis, as well as the atypical presentation of pleuritic chest pain. This is reflected in a limited number of similar cases in the literature^{5 6} both with pleuritic-type chest pain, which were initially diagnosed and treated as a pulmonary embolism. These atypical presentations raise the question of how best to make the diagnosis of splenic rupture and/or EBV in more unusual presentations.

The most common symptom to present with in a case of splenic rupture is abdominal pain (88%),⁴ more specifically left upper quadrant pain. Rarer presentations include pleuritic left-sided chest pain^{5 6} and left shoulder pain.⁷ The left shoulder pain is known as Kehr's sign, and is a classic sign of a ruptured spleen, seen in 50% of cases.³ It is caused by diaphragmatic irritation resulting in referred pain to C3 and C4 dermatome, as the phrenic nerve supplying the diaphragm shares the C3 and C4 nerve roots with the supraclavicular nerves. This case should be a reminder to consider splenic rupture as a differential diagnosis in cases of left upper quadrant abdominal pain, and left-sided pleuritic chest pain where no other obvious cause is identified.

With regard to diagnosing atypical presentations of EBV infections, it is first important to review the more common presenting symptoms. One study looking only at those with confirmed EBV infections found 98% to present with a sore throat, fever, cervical lymphadenopathy and enlarged tonsils, 85% to have pharyngeal inflammation and 50% to have petechiae on the soft palate.⁸ A different study looked at a group of 700 patients aged over 16 years, all presenting with a sore throat, and attempted to find a correlation of signs and symptoms in the 15 patients in which EBV was confirmed on serological testing.⁹ Though a somewhat limited study, this suggested the most useful physical examination signs that indicate a diagnosis of infectious mononucleosis are the presence of splenomegaly (sensitivity of 7%, specificity of 99%), and posterior cervical, axillary and inguinal lymphadenopathy. The absence of cervical lymphadenopathy and fatigue are most useful in dismissing the diagnosis.^{9 10} In the case presented here, only cervical lymphadenopathy was picked up on physical examination. Although perhaps if a full abdominal examination had been possible, this may have identified splenomegaly.

In this case, the diagnosis of infectious mononucleosis was largely informed by the laboratory investigations, notably the lymphocytosis and the deranged liver function tests. Hepatitis with deranged liver function tests is seen in 80% of cases of infectious mononucleosis.¹ Of these, the hepatitis is asymptomatic in 90%–95% of cases, with only a few presenting with jaundice or right upper quadrant abdominal pain.¹ While the deranged liver function tests seen in EBV hepatitis cannot differentiate EBV from other causes of viral hepatitis, they can be a useful early diagnostic clue for infectious mononucleosis, when seen in conjunction with consistent clinical signs. The other useful non-specific laboratory investigation is a full blood count showing raised lymphocytes. This is included in one existing diagnostic criteria for the infection: known as the Hoagland criteria. They state 'at least 50% lymphocytes and at least 10% atypical lymphocytes in the presence of fever, pharyngitis and adenopathy, and confirmed by a positive serologic test'.^{8 9} Again, almost all of these criteria were met in this case, except the pharyngitis. This highlights the importance of using the white cell differential to pick up a lymphocytosis, and doing a blood film to help narrow down the diagnosis.

The monospot test is a specific diagnostic test for EBV infection. This is a heterophile antibody test performed by doing

red cell or latex agglutination assays. Sensitivity has been reported as 81%–95%, with a specificity of 98%–100%, meaning that a positive result almost always indicates infection, but a negative test does not always exclude a diagnosis.¹¹ It is worth noting that it can take 2–5 weeks for heterophile antibody titres to peak.¹¹ Therefore, a negative test within the first 2 weeks of symptom onset should be repeated if infectious mononucleosis is still suspected, or serological testing can be performed. The monospot test remains the recommended first-line investigation in the UK by the NICE guidelines.¹² But serological testing for IgG and IgM antibodies to the viral capsid, early antigens and nuclear antigens is also available and reported to have a higher sensitivity when compared with the monospot test. The presence of IgM antibody to the viral capsid indicates acute infection or reactivation. This is detectable from symptoms onset, peaking at 2–3 weeks, and finally becoming undetectable at around 4 months. But the presence of the IgG antibody against the viral capsid cannot be used in isolation to distinguish a current infection from a previous episode: levels take 2–3 months to peak and will subsequently remain detectable for life. Used in combination, these viral serology tests have a reported sensitivity of 95%–100%^{11 13} and are therefore much more sensitive than the heterophile antibody test. However, most likely due to a higher cost and lower availability, viral serology is currently only recommended if a patient suspected of having EBV infectious mononucleosis is found to be heterophile antibody negative or in patients who are immunocompromised or younger than 12 years.¹²

In this case, the combination of physical examination findings, non-specific laboratory investigations and the monospot test led to the diagnosis of EBV infection without the need for viral serology. This aided the clinical diagnosis of splenic rupture, subsequently confirmed on imaging.

Learning points

- ▶ Splenic rupture is a rare, but potentially fatal, complication of Epstein-Barr virus (EBV) infection.
- ▶ In these rare cases of splenic rupture, secondary to EBV, a high proportion are atraumatic. This highlights the importance of counselling patients on the risk of splenic rupture and the symptoms to look out for in confirmed/suspected cases of EBV, not simply advising the patient to avoid contact sport.
- ▶ In young adult patients presenting with left upper quadrant pain, or pleuritic left-sided lower chest pain, include splenic rupture in the differential diagnosis, even in the absence of typical tonsillitis symptoms.
- ▶ The lymphocytosis and deranged liver function tests are important guiding differential diagnosis towards EBV infectious mononucleosis.
- ▶ A negative monospot test does not rule out EBV infection, particularly if performed within 2 weeks of symptom onset.

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