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CASE REPORT

Splenic rupture masquerading as pulmonary embolus in the context of acute Epstein–Barr virus infection and secukinumab therapy

Ceit V Cunningham[1]

Amit KJ Mandal[1]

Tagrid Hoque[1]

Rahul Chauhan[1]

Constantinos G Missouris[1,2]

Author details can be found at the end of this article

Correspondence to:
Constantinos G Missouris;
dinos.missouris@nhs.net

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Introduction

Atraumatic splenic rupture is a rare complication of Epstein–Barr virus infection, resulting from splenic infiltration by inflammatory cells. A woman with ankylosing spondylitis, for which she was taking the monoclonal antibody secukinumab, presented with pleuritic chest pain after a short history of fever and sore throat. She was treated for pulmonary embolus with low molecular weight heparin and developed splenic rupture. The patient was subsequently diagnosed with acute Epstein–Barr virus infection. The authors suspect that secukinumab amplified the inflammatory response and, alongside administration of low molecular weight heparin, heightened the risk of splenic rupture.

Case report

Before the COVID-19 pandemic, a 22-year-old woman presented with pleuritic chest pain after a prodromal illness of fever and sore throat. Past medical history was significant for ankylosing spondylosis, for which she was receiving monthly secukinumab (150 mg) subcutaneous injections.

Physical examination was unremarkable. Initial laboratory investigations were notable for a D-dimer level of 800 umol/litre (normal range <500 umol/litre), lymphocyte count of 9.98×10^9/litre (normal range $1–4 \times 10^9$/litre), alanine aminotransferase level of 350 IU/litre (normal range 35 IU/litre), alkaline phosphatase level of 218 IU/litre (normal range 35–129 IU/litre) bilirubin level of 43 umol/litre (normal range <21 umol/litre) and lactate dehydrogenase level of 437 U/litre (normal range <250 U/litre).

A single treatment dose of subcutaneous low molecular weight heparin (dalteparin 12 000 IU) was administered to cover pulmonary embolus. Over the next 12 hours, the pleuritic chest pain intensified and radiated to the left shoulder tip, and the patient developed diffuse abdominal pain and went into hypovolaemic shock. Urgent computed tomography of the abdomen confirmed intra-abdominal bleeding collecting in the splenic capsule, indicating spontaneous splenic rupture (Figure 1). In light of this, computed tomography pulmonary angiography was not pursued. The patient was ventilated before prophylactic splenic artery embolisation. She developed abdominal distension and four quadrant peritonism 24 hours after the procedure, with haemoglobin level dropping from 146 g/litre on admission to 72 g/litre (115–165). Her C-reactive protein level rose from 11 mg/litre to 126 mg/litre (<4) and the white cell count jumped to 19.74×10^9/litre (4–11), with lymphocytes and monocytes predominating. Repeat computed tomography showed extensive fluid in the abdominal cavity and disfigured spleen (Figure 2). Uncomplicated splenectomy was performed.

The spleen weighed 150 g and measured 120 × 75×35 mm. Macroscopic examination revealed an incomplete capsule and surface haematoma. Histological examination of multiple sections revealed focal disruption of the capsule with haematoma formation within the parenchyma and focal infarction with acute inflammatory infiltrates.

Admission blood film was analysed, which showed reactive and atypical lymphocytes. Serological tests found IgM positivity consistent with acute Epstein–Barr virus infection and Epstein–Barr encoding region in situ hybridisation detected Epstein–Barr virus in splenic tissue sections. A diagnosis of Epstein–Barr virus-associated infectious mononucleosis with secondary atraumatic splenic injury was made, potentially exacerbated by secukinumab therapy and the administration of low molecular weight heparin. At 1-year follow up, the patient is well and has not been re-prescribed secukinumab.

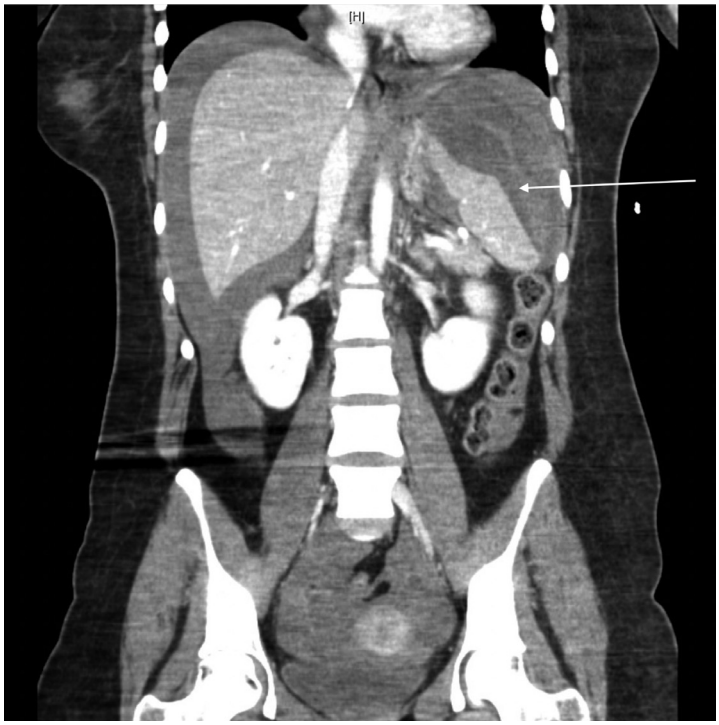

Figure 1. Computed tomography of the abdomen in coronal view, demonstrating a large intraperitoneal peri-splenic haematoma (arrow).

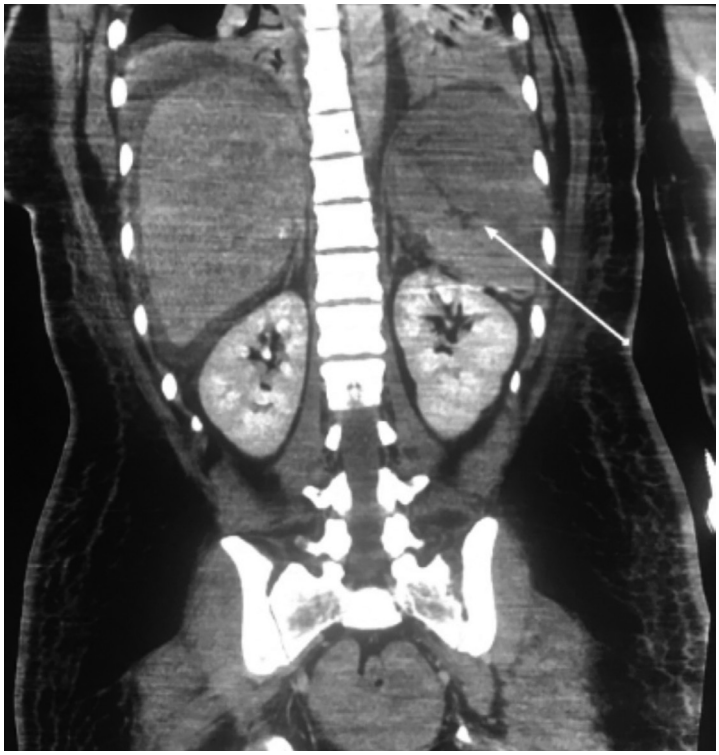

Figure 2. Computed tomography of the abdomen in coronal view demonstrating irregular border of the splenic parenchyma, indicating a ruptured spleen (arrow) and an extensive amount of fluid within the abdominal cavity.

Discussion

Splenic rupture is an unusual complication of Epstein–Barr virus infection, being reported in <0.5% of patients (Barlett et al, 2016). The underlying pathogenetic mechanism is thought to be related to splenic infiltration by lymphocytes, activated T and B cells and macrophages,

Learning points

- Spontaneous splenic rupture is a rare complication of Epstein–Barr virus infection resulting from a heightened immune response with splenic infiltration by lymphocytes, activated T and B cells and macrophages.
- Pleuritic chest pain may be an atypical presentation of peri-splenic haematoma. Shoulder tip pain in dermatomes C3 and C4 should alert clinicians to consider splenomegaly causing diaphragmic irritation as a differential diagnosis.
- Therapeutic monoclonal antibodies, such as secukinumab, may amplify the risk of splenic rupture in patients with chronic inflammatory conditions and concomitant Epstein–Barr virus infection through cytokine release syndrome.

which enlarge the spleen beyond the protective rib cage, rendering it vulnerable to rupture either spontaneously or traumatically.

Secukinumab is a monoclonal antibody that inhibits interleukin-17a. It is licenced to treat ankylosing spondylitis and psoriasis. Interleukin-17a is a key cytokine that mediates host defence mechanisms in various bacterial and viral infections. Inhibition of the production of interleukin-17a by type 17 helper T cells can modify the body's response to viral infections, including Epstein–Barr virus. Both therapeutic monoclonal antibodies such as rituximab and Epstein–Barr virus infection have been implicated in spontaneous splenic rupture, which typically presents with abdominal pain.

Thus far, there are two published case reports documenting treatment with rituximab and a speculative association with spontaneous splenic rupture, with both patients having underlying lymphoproliferative disorders (Nair et al, 2016; Williams and Chiruka, 2019). Cytokine release syndrome or 'storm' is postulated to be the underlying mechanism. Administration of monoclonal antibodies may initiate an inflammatory cascade, resulting in high levels of cytokine release and leading to spontaneous splenic rupture, particularly during states of lymphocytosis. Furthermore, in patients with haematological malignancies, the risk of splenic rupture following monoclonal antibody therapy is amplified by the degree of disease burden, which is reflected in high numbers of circulating lymphocytes – a parallel drawn in this case.

Patients with chronic inflammatory conditions, including ankylosing spondylosis, can exhibit dysregulated cytokine storm following antigen infections. Epstein–Barr virus specifically stimulates the type 17 helper T cells to produce interleukin-17a, and patients with autoimmune disease are more sensitive to this mechanism, which results in higher production of interleukin-17a. The underlying ankylosing spondylosis in this patient may have further upregulated the response to Epstein–Barr virus, and previous treatment with an interleukin-17a antibody may have augmented the response through positive feedback mechanisms or immunosuppression, leading to fulminant Epstein–Barr virus infection. This is arguably reflected in this patient's laboratory investigations, which demonstrated elevated levels of liver enzymes, lactate dehydrogenase and D-dimer, all of which are markers of cytokine release.

Conclusions

The authors suspect that acute Epstein–Barr virus infection resulted in splenomegaly as a result of lymphocytic infiltration and treatment with secukinumab further amplifying the inflammatory response and heightening the risk of splenic rupture. Administration of low molecular weight heparin was likely the cumulative precipitant for splenic rupture in this setting. The mortality rate with delayed diagnosis of splenic rupture approaches 15% and, although rare, it should be considered as a differential for pleuritic chest pain, especially in young patients who would otherwise be considered low risk for pulmonary embolus.

Author details

[1]Department of Medicine, Wexham Park Hospital, Frimley Health NHS Foundation Trust, Slough, Berkshire, UK

[2]Department of Clinical Cardiology, University of Nicosia Medical School, Nicosia, Cyprus

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