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Evans syndrome in a young man with rare autoimmune associations and transplanted liver

Matthew Dominic McCarthy, A G Mohamed Fareeth

Acute Medicine, East Lancashire Hospitals NHS Trust, Blackburn, UK

Correspondence to
Dr A G Mohamed Fareeth; mohamed.fareeth@elht.nhs.uk

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SUMMARY

Evans syndrome is classically characterised by two or more cytopenias occurring either concomitantly or sequentially. Most commonly, these are autoimmune haemolytic anaemia and immune thrombocytopenia purpura. It is mostly associated with specific autoimmune conditions such as systemic lupus erythematosus and lymphoproliferative disorders. We present a case report of Evans syndrome in a young man with primary sclerosing cholangitis and Crohn's disease, neither of which are classically associated with the condition. The case also further adds to the number of case reports of Evans syndrome occurring in patients following liver transplantation.

BACKGROUND

Evans syndrome is a rare autoimmune condition that is characterised by the presence of two or more cytopenias, most commonly warm autoimmune haemolytic anaemia (AIHA) and immune thrombocytopenia purpura (ITP), and rarely immune neutropenia. These conditions may occur simultaneously or sequentially.[1 2] The condition is thought to have a prevalence of 1–9 per million people per year, with up to 50% of cases occurring secondary to an underlying disease process such as infection, primary immunodeficiencies, autoimmune conditions such as systemic lupus erythematosus, haematopoietic stem cell transplants and lymphoproliferative disorders.[3–5] Evans syndrome is thought to be more difficult to treat than immune cytopenias in isolation, and a recent multicentre observational and retrospective study has shown it to be highly relapsing and commonly marked by severe complications.[5] In this case, we present a case of Evans syndrome in a young male patient who was the recipient of a liver transplant due to primary sclerosing cholangitis (PSC) with a recent diagnosis of Crohn's disease.

CASE PRESENTATION

A man in his early 20s presented with a 1-day history of painless jaundice, lethargy and shortness of breath. He stated that his urine was dark with no changes noted in his stools. He detailed no symptoms suggestive of infection, although his temperature was recorded at 38.3°. He had a complex medical history composed of a liver transplant indicated for PSC in 2016, previous ITP treated with rituximab also in 2016 and he had recently been diagnosed with Crohn's disease with terminal ileal involvement and patchy inflammation throughout the colon identified through colonoscopy. An earlier CT of the abdomen had shown evidence of ileitis and small bowel disease. His normal immunosuppressive regimen composed of tacrolimus and azathioprine, although the azathioprine had recently been held by his liver transplant team due to his taking of moderate doses of oral steroids for his active Crohn's disease.

On examination, he appeared markedly jaundiced with scleral icterus and pallor with pale conjunctivae. His spleen was palpable 4 cm below the diaphragm. There was no obvious hepatomegaly.

INVESTIGATIONS

Haemoglobin at presentation was 66 g/L, with a drop to 52 g/L 2½ hours later. White blood cell count was 13.7×10^9/L, with neutrophils at 8.4×10^9/L. Mean corpuscular volume was 108 fL, with percentage hypochromic cells at 6%. Percentage reticulocytes were elevated at 27.4% identifying a regenerative anaemia. LDH and haptoglobin were also suggestive of haemolysis with lactate dehydrogenase raised to 881 IU/L and haptoglobin low at <0.08 g/L. Conjugated bilirubin was normal at <1 µmol/L. D-dimer was significantly elevated to 1308 ng/mL. Platelets were at normal levels at 220×10^9/L. Blood film identified the presence of spherocytes, stomatocytes and polychromasia. Direct antiglobulin test was positive for IgG antibodies.

Chest X-ray and ECG were both unremarkable.

Given the history of prior ITP with the clinical picture and blood results strongly suggestive for AIHA, he was treated for Evans syndrome.[6]

TREATMENT

Initial treatment composed of two units of red blood cells, with a subsequent increase in red blood cells to 82 g/L. He was transferred to the care of haematology following discussion with his liver transplant primary team. He was continued on tacrolimus and was treated with steroids. Despite this, he required a further transfusion with one unit of blood. He was discharged home with tapering steroids and underwent four cycles of rituximab.

Outcome and follow-up

The patient had an initial improvement in his haemoglobin as an outpatient which had increased to 115 g/L with platelet count of 189×10^9/L one month following discharge. Three months after discharge, he was readmitted once more with haemolytic anaemia with a haemoglobin of 73 g/L. An ultra sound scan of the abdomen performed had shown a shrunken left liver lobe with a query of

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echogenic material in the portal vein. Thrombus was confirmed in the right posterior portal vein on CT of the abdomen, which also identified progression of splenomegaly from 16 to 20 cm when compared with a scan done one year previously. He was transferred to the care of his primary liver team to assess for graft rejection.

DISCUSSION

Our patient was not diagnosed with conditions most typically associated with the development of Evans syndrome; however, he had an extensive autoimmune history having developed PSC, Crohn's disease and ITP independently at various points in his life. These conditions are not commonly associated with Evans syndrome.

Little is known about Evans syndrome in adult patients with solid-organ transplants. However, a review of the literature has identified multiple case reports of Evans syndrome in paediatric patients following liver transplant.[7–11] It is therefore possible that Evans syndrome as a complication of solid-organ transplant, and in particular liver transplant, is potentially overlooked in adults.

Furthermore, there is also not a strong association between Evans syndrome and inflammatory bowel disease (IBD) with only a single case study identifying an association between ulcerative colitis and the condition and none found regarding Crohn's disease.[12] Our case may be the first published case of Evans syndrome in an adult with Crohn's disease. Additionally, PSC and concurrent Crohn's disease represent approximately 7%–10% of PSC-IBD patients.[13–15]

The combination of PSC and Crohn's disease may increase the risk of further autoimmune disease, with 50% of cases in one review having been complicated by autoimmune phenomenon, including AIHA.[16]

It should be stated that isolated AIHA without ITP is frequently associated with IBD. It is more common with ulcerative colitis than Crohn's disease, and it is associated with greater disease severity and the presence of concurrent extraintestinal manifestations.[17–20] In the two case reports found regarding AIHA and Crohn's disease; both patient's had ileal disease like the patient presented here.[15 16]

Evans syndrome is considered harder to treat than isolated warm AIHA, with a study of 68 patients finding only 32% in remission at a mean follow-up of 4.8 years.[1] Although a single reported case of a 40-month complete remission of postliver transplant Evans syndrome in a paediatric patient has been reported. In this instance, the patient underwent a splenectomy and cessation of tacrolimus, with tacrolimus thought to underpin the disease presentation.[8]

Learning points

- This is a classic case of Evans syndrome with sequential occurrence of cytopenias in a young patient. However, it is notable as he has multiple autoimmune conditions that may have predisposed to it but are not commonly associated with it.
- This case report adds to the increasing number of reports centred around Evans syndrome occurring in patients following solid-organ transplant.
- Autoimmune haemolytic anaemia (AIHA) in inflammatory bowel disease is associated most with ulcerative colitis; however, we present evidence that suggests it can be associated with Crohn's disease and PSC and that the combination of both may confer increased risk for AIHA.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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