CASE REPORT

Autoimmune hepatitis and eosinophilic granulomatosis with polyangiitis: a rare association

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SUMMARY

We describe a case of 40-year-old woman who presented to our hospital with symptoms of non-radiating epigastric pain for 4–5 days associated with nausea and vomiting. Her history was significant for asthma with recurrent exacerbations, polyneuropathy and recurrent sinus infections. Liver function tests revealed cholestasis. Antinuclear antibody and antismooth muscle cell antibody were positive. Liver biopsy revealed active chronic hepatitis with cholestasis. A diagnosis of autoimmune hepatitis was made. All other causes of cholestatic jaundice were ruled out. Her history of recurrent asthma exacerbations, eosinophilia, recurrent sinus infections and positive myeloperoxidase antibodies was suggestive of eosinophilic granulomatosis with polyangiitis. She was found to have combination of autoimmune hepatitis and eosinophilic granulomatosis with polyangiitis, a rarely reported association in the medical literature. She was started on prednisone for her autoimmune hepatitis. On follow-up with her gastroenterologist, her transaminases were trending down and she was symptomatically better.

BACKGROUND

Autoimmune hepatitis (AIH) is an autoimmune liver disease (ALD) of unknown aetiology characterised by circulating autoantibodies, increased immunoglobulins in blood and presence of inflammation on liver biopsy.¹ It is diagnosed by diagnostic criteria and scoring system developed by Autoimmune Hepatitis Group.² It is classified into two types according to the type of autoantibodies present. Eosinophilic granulomatosis with polyangiitis (EGPA) previously known as Churg-Strauss syndrome is a vasculitis of small-sized arteries characterised by chronic rhinosinusitis, asthma and peripheral blood eosinophilia.³ There is no diagnostic criteria until now to diagnose EGPA; the classifications most commonly used are that of American College of Rheumatology (ACR)³ and the Lanham criteria.⁴ Very few cases have been reported in the literature about the rare association between ALDs (autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis) and small vessel vasculitis (EGPA, granulomatosis with polyangiitis, microscopic polyangiitis).⁵ We report a rare case of association of type 1 autoimmune hepatitis and EGPA in a 44-year-old woman and present a brief review of the literature about this rare association.

CASE PRESENTATION

A 40-year-old woman presented to our hospital with symptoms of progressive epigastric pain for

4–5 days. The pain was sharp, non-radiating and associated with nausea and vomiting. She reported of yellowing of eyes and dark urine. She also reported of loss of appetite and weight loss. She occasionally took non-steroidal anti-inflammatory drugs and tramadol for body ache; however, she denied intake of Tylenol. She migrated to our area from New York 5 years ago. She had no history of recent travel, recent blood transfusion or multiple sexual partners. Her medical history was significant for asthma since childhood and eosinophilia. Review of records suggested that her eosinophil count was elevated (>10%; absolute eosinophil count >550 cells/mL) on routine blood work in the preceding 5 years. She had been admitted multiple times in past for asthma exacerbation and treated with steroids and bronchodilators; her last admission was 2 months back. Her medical history was positive for recurrent sinus infections with multiple sinus surgeries. Her medical history was also suggestive of generalised neuropathic pain in her upper and lower limbs. No prior history of liver problems was present. She denied intake of alcohol or recreational drugs. Her vital signs in the emergency department revealed temperature of 37.1°C, pulse of 74/min, respiratory rate of 16/min and blood pressure of 116/72. Her physical examination was significant for mild icterus and tenderness in the epigastrium and periumbilical region without guarding or rigidity. No tenderness in right upper quadrant was appreciated. Rest of the systemic examination was within normal limits.

INVESTIGATIONS

Liver function tests revealed total bilirubin of 3.9 mg/dL (normal 0.3–1 mg/dL) with direct bilirubin of 2.4 mg/dL (normal 0.0–0.2 mg/dL), aspartate transaminase (AST) 488 IU/L (normal 13–39 IU/L), alanine transaminase (ALT) 526 IU/L (normal 7–52 IU/L) and alkaline phosphatase of 538 IU/L (normal 34–104 IU/L). Her liver function tests were normal 4 months prior. Her international normalised ratio was 1.1 (normal 0.9–1.1) and albumin was 3.2 g/dL (normal 3.5–5.7 g/dL). Urinalysis revealed bilirubinuria. Total white cell count and electrolytes were normal. Urine was positive for bilirubinuria. Her transaminases trended up to 1600 during hospitalisation. Ultrasound scan of the right upper quadrant revealed mild increase in hepatic echogenicity and mild ductal dilation possibly steatosis. The gallbladder was normal with no stones and pericholecystic fluid. HIDA scan revealed non-visualisation of gallbladder, biliary tree and small intestine suggesting

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cholestasis or intrinsic hepatocellular dysfunction. Her hepatitis viral serologies were all negative. Tylenol level, salicylate level and alcohol level in blood were negative. Antinuclear antibody (ANA) was positive in homogeneous pattern with titre of 1:640. Antismooth muscle cell antibody was positive. Antimitochondrial antibody was negative. She underwent liver biopsy revealing active chronic hepatitis with cholestasis.

Review of her previous laboratory tests revealed chronic eosinophilia up to 27% of her white cells (absolute eosinophil count 2370 cells/mL). She was also found to have positive anti-myeloperoxidase antibody (MPO). High resolution contrast tomography of chest was performed which revealed multiple nodules largest of 5 mm and new mediastinal adenopathy. No cavitation or consolidation was seen. She had never undergone electromyography for workup of her neuropathy. CT scan of sinuses revealed extensive pansinus disease with postsurgical changes. No histopathology results of her past sinus surgeries could be obtained on review of her medical records.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses of her abdominal pain and abnormal liver function tests included autoimmune hepatitis, viral hepatitis, toxin ingestion (Tylenol, salicylate), primary biliary cholangitis and primary sclerosing cholangitis.

Differential diagnoses of cholestasis on liver biopsy include choledocholithiasis, neoplastic bile duct stricture, drugs (anabolic steroids, contraceptive pills, erythromycin), autoimmune cholestatic liver diseases like primary biliary cholangitis, primary sclerosing cirrhosis and autoimmune hepatitis.⁶ Cholestasis on liver biopsy is detected only in a small subset of patients with autoimmune hepatitis.⁷

Her clinical picture of abdominal pain, liver function tests, positive antismooth muscle cell antibody and findings on liver biopsy was suggestive of autoimmune hepatitis.²

Her history of recurrent asthma attacks, eosinophilia, sinus infections, polyneuropathy and positive MPO were suggestive of EGPA.³

TREATMENT

She was started on prednisone 20 mg daily. Her symptoms improved and she was discharged home to follow-up in couple of weeks in gastroenterology clinic with liver function tests.

OUTCOME AND FOLLOW-UP

On follow-up visit with her gastroenterologist after a month, she was feeling better and her transaminases had trended down with AST of 152 IU/L and ALT of 159 IU/L.

DISCUSSION

The association of autoimmune hepatitis and EGPA has rarely been reported in the literature. Tovoli *et al*⁵ reported a case of 27-year-old man with history of type 1 hepatitis since age 16 who presented with acalculous cholecystitis and was diagnosed with EGPA. He had hypereosinophilia on presentation with normal levels of total serum IgE. He was negative for antineutrophilic cytoplasmic antibody (ANCA) and ANA was positive at low titre.

So far no studies are available to explain the coexistence of autoimmune hepatitis and EGPA. It is difficult to determine if the association is causal or co-incidental. One reason for it could be small number of reported cases of autoimmune hepatitis and EGPA.

One possible mechanism to explain the association between autoimmune hepatitis and EGPA is the role of regulatory T cells (Treg) in both diseases. Treg suppresses inflammatory responses

and plays a vital role in negative regulation of immune-mediated inflammation.⁸ Treg express high levels of cytotoxic T-lymphocyte antigen 4 and forkhead transcription factor forkhead box P3. Various studies have suggested defective Treg function in autoimmune hepatitis.^{9–12} Maintenance of numbers of Treg in patients with chronic eosinophilic pneumonia and asthma inhibits development of EGPA. This suggests that Treg have a role in establishing which patients with asthma chronic eosinophilia will develop active EGPA.

HLA also has been suggested as a possible link. This is supported by the presence of similar human leukocyte antigen genotypes between various forms of ALD and small vessel vasculitis. Primary sclerosing cholangitis and autoimmune hepatitis are strongly associated with HLA A1-B8-DR3.^{13 14} Similar HLA genotype has been reported to be associated with granulomatosis with polyangiitis as well.¹⁵ HLA DRB1*08 has been associated with primary biliary cholangitis.¹⁶ EGPA is associated with HLA DRB1*04 and *07 and HLADRB4.¹⁷ So far there are no HLA genotypes associated with both autoimmune hepatitis and EGPA.

Other possible explanation has been suggested to be ANCA. However, there are different targets of ANCA in autoimmune hepatitis and EGPA. In autoimmune hepatitis, ANCA is directed against an antigen localised in the nuclear lamina¹⁸ while in EGPA ANCA is directed against myeloperoxidase.¹⁹

Autoimmune hepatitis and EGPA is a rare but possible association. Knowledge of such entity can help us to promptly act if a patient with autoimmune hepatitis presents with extrahepatic manifestations suggesting EGPA. It will help in the diagnosis of EGPA and prevent complications from both diseases.

Learning points

- ▶ Although rare, we should think of autoimmune hepatitis as one of the causes of hepatitis in a patient with a history of eosinophilic granulomatosis with polyangiitis (EGPA) or other small vessel vasculitis.
- ▶ Clinical features of EGPA associated with AIH can mimic extrahepatic manifestations of autoimmune liver diseases.
- ▶ EGPA can be a cause of recurrent asthma exacerbation and sinus infection in a patient with autoimmune hepatitis or other autoimmune liver diseases.

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