Autoimmune Pancreatitis with IgG4-Related Cholangiopathy Presenting with Budd-Chiari: A Case Report

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Abstract

IgG4-related disorders (IgG4-RD) encompass multiple fibro-inflammatory conditions that all share a common histopathology which include a lymphoplasmacytic infiltrate consisting, resulting in multiple lesions and fibrosis in a distinctive “storiform” pattern. Positive IgG4 cells on histology and serum IgG4 concentrations do not always have to be elevated. A 38-year-old African American male with a past medical history significant for IgG4-associated Autoimmune Cholangiopathy and Autoimmune chronic pancreatitis presented with a three-day history of epigastric pain. He was found to have both portal and hepatic vein thrombi and imaging suggestive of Budd-Chiari. As his hypercoagulable workup came back negative, we conclude that the chronic inflammatory state secondary to IgG4-RD was sufficient enough to render the patient pro-thrombotic. Patient was started on anticoagulation and Rituximab. The presence of Budd-Chiari is a potentially novel finding. Furthermore, as the hypercoagulability work-up was negative, we presume that the plasmocytic activity was sufficient to cause enough inflammation to result in diffuse clotting.

Keywords: IgG4-related diseases; Autoimmune cholangiopathy; Budd-Chiari syndrome; Hypercoagulability; Autoimmune diseases

Introduction

IgG4-related disorders encompass multiple diseases that all share a common histo-pathology, namely dense lymphoplasmacytic infiltrate, a storiform pattern of fibrosis, and oblitative phlebitis. Specific IgG4 positivity on biopsy or elevated serum IgG4 levels are not required [1]. IgG4-related Sclerosing Cholangitis is a common extra-pancreatic manifestation of type-I Autoimmune Pancreatitis which usually presents with abdominal pain, transaminitis and cholestasis. Budd-Chiari Syndrome is due to hepatic venous outflow tract obstruction either from an underlying hypercoagulable state, malignancy or myeloproliferative disorder among other causes. There has been no clear correlation so far, specifically between IgG4-related diseases and Budd-Chiari Disease.

Case Report

A 38-year-old African-American male with a past medical history significant for chronic autoimmune pancreatitis, complicated by IgG4-associated Cholangiopathy diagnosed by biopsy two years prior, and a cholecystectomy, presented with a three-day history of epigastric pain and nausea. The patient was being maintained on Azathioprine 150 mg, Ursodiol and a tapering dose of Prednisone by his rheumatologist. On admission, labs were significant for an elevated Alkaline Phosphatase of 150 IU (Normal 45.8-113) with normal transaminases. Computed Tomography (CT) of his abdomen and pelvis with contrast showed abdominal lymphadenopathy and a heterogeneous liver. A follow-up MRI confirmed Budd-Chiari with thrombi in the portal, middle and left hepatic veins (Figure 1). The common bile duct measured 7mm. The patient was immediately started on therapeutic low molecular weight heparin for his clot burden in addition to pulse steroids for 3 days. His prednisone taper was restarted at 20 mg daily, and he was discharged to follow up.

Given multiple thrombi, a hypercoagulable work-up was begun. The patient denied any family history of bleeding or clotting disorders, shortness of breath, rash, ulcers or dark urine. A serological work-up was negative for Factor 5 Leiden mutation, anti-cardiolipin antibodies, and Paroxysmal nocturnal hemoglobinuria. The patient remained cholestatic, but transaminases never increased during admission. Antimitochondrial and anti-smooth muscle antibodies were negative, making primary biliary cirrhosis and autoimmune hepatitis less likely. A viral hepatitis panel was also negative. However, serum electrophoresis showed IgG levels elevated at 2261 mg/dL. Follow-up labs confirmed uncontrolled IgG4-RD with IgG4 concentrations of 38.4 mg/dL. Due to the risk for portal hypertension, an upper endoscopy was performed and fortunately was negative for esophageal varices. The patient’s abdominal pain improved with anticoagulation and he was transitioned to Dabigatran 150 mg two times a day. His prednisone taper was restarted at 20 mg daily, and he was discharged to follow up.

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Discussion

Pathophysiology

IgG4 related disease (IgG4-RD) refers to the fibro-inflammatory infiltration of any organ, by plasma cells, yielding a characteristic storiform histological appearance [2]. The histologic appearance is sufficient for diagnosis, as IgG4 positivity or elevated IgG4 serum levels are not sufficiently sensitive [1]. While IgG4-RD has been documented in multiple organs including abdominal lymph nodes, lungs, prostate, thyroid, salivary and lacrimal glands; it is most often found in the pancreaticobiliary system [3] and associated with autoimmune pancreatitis [4]. Indeed, 70% of autoimmune pancreatitis patients also have IgG4-RD [5]. Symptoms usually arise from the local inflammation or mass effect caused by infiltration [5].

Epidemiology and presentation

One study found IgG4-RD is most prevalent among males in their 50’s [6], however there is epidemiological disagreement in the literature. Given that over 50% of IgG-4RD can present with multiple organ involvement, the presentation, while usually pancreaticobiliary, can be varied [6]. There are a few clinical findings that are highly suggestive of IgG4-RD. Retroperitoneal fibrosis is the most common finding in IgG4-RD [7]. It should be noted that such fibrosis can cause multiple life-threatening complications, including sclerosis of the renal arteries, ureters, and aorta [8]. Lymphadenopathy is presents in 80% of cases [9]. IgG4 sclerosing cholangitis, an entity distinct from primary sclerosing cholangitis is present 70% of the time [10]. As mentioned, salivary and lacrimal gland enlargement is also indicative [11], and 50% of cases are associated with diabetes [12].

Most patients will present with obstructive jaundice, and pancreaticobiliary infiltration resembling masses, masquerading as pancreatic neoplasms [13]. Accordingly, differentiation from pancreatic cancer is vital.

Diagnosis

Diagnosis hinges on appropriate clinical suspicion after the more common etiologies for pancreatitis and hepatobiliary disease have been ruled out. Biopsies are often required to reveal plasma infiltrates, storiform fibrosis and obliterative phlebitis (regardless of IgG4 positivity) [14] and while lymph nodes are often prominent, they are rarely sufficient specimens. Tissue diagnosis remains the most convincing standard. Biopsy should reveal dense lymphoplasmacytic infiltrate with characteristic storiform fibrosis and obliterative phlebitis [15]. Serum IgG4 levels are non-sensitive [16], however over 80% of patients do have IgG4 serologies greater than 135 mg/dL [17]. A cut-off of >300 mg/dL is thus recommended for greater specificity [2]. Idiopathic pancreatitis, retroperitoneal fibrosis, sclerosing cholangitis and bilateral salivary or lacrimal gland enlargement should all warrant consideration of IgG4-RD [15].

Treatment

The treatment for IgG4-RD is still being explored. Most of the cases have found success with immunosuppression. Steroids are first line [2]. However, up to 40% of patients experience a relapse. Alternatively, Rituximab has been shown to be effective for both induction therapy and relapse treatment in IgG4-RD [18]. Indeed, maintenance therapy with Rituximab infusions is associated with longer relapse-free survival [18]. New evidence points to Rituximab being effective even without background corticosteroid therapy [17].

The presence of IgG4-RD dramatically increases the risk for malignancy. One study found that IgG4-RD was an independent risk factor increasing the likelihood of cancer by five-fold [19]. This risk was not limited to the hepatobiliary system. Accordingly, IgG4-RD patients should be watched carefully as they can develop complications including cirrhosis, retroperitoneal fibrosis, and portal hypertension. Relapses are common after discontinuation of medical therapy so close follow up is imperative [20].

Conclusion

A radiological review of cases found that 80% of IgG4-RD patients had narrowing or thrombosis of portal, splenic or mesenteric veins. Our patient not only had a portal thrombus, but hepatic venous thrombi indicative of Budd-Chiari. As the more common causes of hypercoagulability were ruled out, we propose that Budd-Chiari resulted from chronic inflammation secondary to IgG4-RD. Notably, this inflammation occurred despite immunosuppressive therapy. This is a potentially novel finding.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding this publication.

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