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Isolated Type Immunoglobulin G4 Sclerosing Cholangitis: The Misdiagnosed Cholangiocarcinoma

Safi Khuri^{1,2*}

¹General Surgery, Department, Rambam Health Care Campus, Haifa, Israel

²HPB and Surgical Oncology Unit, Rambam Health Care Campus, Haifa, Israel

*Corresponding Author: Safi Khuri, General Surgery Department, Rambam Health Care Campus, Haifa, Israel; Tel: +9725025989342; Email: s_khuri@rambam.health.gov.il

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Editorial

Dear Readers,

Over the last two decades, Immunoglobulin G4 (IgG4) related disease (IgG4-RD), also known as IgG4 related sclerosing disease or IgG4 associated disease has become a well-known medical problem, with increasing incidence. IgG4-RD is defined as a systemic disease characterized by inflammation and fibrosis of the affected tissues [1,2]. Inflammation usually occurs during the early phase of the disease, whereas fibrosis develops later when diagnosis is delayed. Although it is well known as an immune mediated disease, and there is a growing evidence that the disease is an autoimmune in nature, the precise pathogenesis is yet to be known. It usually results in pseudo tumorous swelling of the affected organs, along with high levels of serum IgG 4 plasma cells [3,4]. The affected tissues usually share similar pathological features, with dense lymphoplasmacytic infiltrate rich in IgG4-positive plasma cells being the hallmark findings [2].

IgG4-Sclerosing Cholangitis (IgG4-SC), also known as IgG4 associated cholangitis, is the biliary system manifestation of the IgG4-RD. IgG4-SC is known as a recent type of sclerosing cholangitis that differs from primary sclerosing cholangitis [5]. Previously, cholangitis was classified into two types: primary, which is usually idiopathic, and secondary, which could be due to bile duct stones, cholangiocarcinoma, congenital biliary disorders or postoperative bile duct injury [6]. Nowadays, three types are identified with the emergent of the IgG4-SC type, the most common type, as the third one. IgG4 SC is usually associated with type 1 autoimmune

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pancreatitis (AIP-1) (the proto type of IgG4 RD) in more than 90% of cases. Due to this close association, they are sometimes collectively called sclerosing pancreatocholangitis. IgG4 SC may present in different manners; either as tumorous mass due to segmental bile duct involvement, which should be differentiated from extra-hepatic cholangiocarcinoma, or as a diffuse sclerosing process mimicking primary sclerosing cholangitis [7,8].

Diagnosis of isolated type IgG4 SC is very challenging, and usually misdiagnosed as cholangiocarcinoma, especially IgG4-SC types 1, 3 and 4. Due to differences in biological behaviors, treatment options and survival, it is of immense important to differentiate between these diseases.

Recently, Roos and colleagues had published a project about clinical and translational research in cholangiocarcinoma in a Tertiary Care Experience in The American Journal of Gastroenterology [9]. In her study over 30 years, 323 patients underwent surgery for presumed diagnosis of cholangiocarcinoma, of which about 15% of patients had benign disease on final histopathological report, with IgG4-SC being the most common benign disease. As IgG4-SC is usually associated with pancreatitis or other organ involvement, its diagnosis is usually not challenging, as is the case with the isolated types. several studies over the past decade have been published regarding the non-isolated type, yet, reviewing the relevant papers of the English literature (mainly retrospective studies and case reports), revealed small number (less than 200) of patients reported with isolated type IgG4 SC, and few studies that compare between IgG4-SC and extrahepatic cholangiocarcinoma.

Efforts are ongoing to advance our understanding of the pathogenesis of these underestimated entities, with the aim of impacting how diagnosis and treatment strategies are designed in the future to optimize outcomes for this specific disease.

The scope of this Issue, is to highlight perspectives of clinical presentation, serological tests, novel diagnostic tests and pre-operative histopathological findings to reduce misdiagnosis, unnecessary surgery, and life-threatening complications.

Abbreviations

IgG4-RD: Immunoglobulin G4 related disease

IgG4-SC: Immunoglobulin G4 Sclerosing Cholangitis

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