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A Rare Case Report on IgG4 Related Diseases

Dr Deepika Wadhera[1], Dr Ramesh Kumar Kundal[2], Dr Mohanvir Kaur[3], Dr Najinder Preet Kaur[4], Dr Arshiya Bansal[5]

[1](Junior resident),
[2](Professor & Head),
[3](Assistant Professor),
[4](Junior resident),
[5](Junior resident),
Department of Pathology, Government Medical College, Patiala
Corresponding Author: Dr Deepika Wadhera

Abstract: *IgG4-related disease (IgG4-RD) is a newly recognized disorder, characterized by massive IgG4+ lymphocyte and plasma cell infiltration, storiform fibrosis, causing enlargement, nodules or thickening of the various organs, simultaneously or metachronously [1–4].The present case report describes the clinical case of a 62 year male with complaint of fever, jaundice, abdominal pain & loss of weight since 1 month. CECT Whole Abdomen shows hepatospleenomegaly,subdiaphragmatic and abdominal lymphadenopathy .Exploratory laparotomy done & abdominal lymph nodes sent for histopathology shows features of Florid follicular lymphoid hyperplasia with infilteration by plasma cells in interfollicular area. Causes of increased plasma cells in lymph node were to be ruled out therefore IHC of abdominal lymph node was done which depicted reactive lymphoid hyperplasia with increased IgG4 positive plasma cells(>50/hpf) along with increase plasma cell in interfollicular area that are polytypic for kappa/ lambda leading to diagnosis of IgG4 RD and treatment of corticosteroid was started.The diagnosis of IgG4-RD was based on a combination of features that include clinical parameters, imaging and histopathology, immunohistochemistry .*

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I. Introduction

IgG4-related disease (IgG4-RD) is a relatively recently recognized chronic multi-organ autoimmune disease of unknown origin with a tendency to develop lesions at multiple sites throughout the body [5] .Previously, this disorder was known as IgG4 multi-organ lymphoproliferative syndrome (IgG4 MOSLP), IgG4 sclerosing disease, or IgG4-related systemic plasmocytic syndrome (SIPS). Recently, it is simply recognized as IgG4-RD, the main features of which are tumor-like swelling of involved organs (mainly lacrimal glands, salivary glands and the pancreas), in association with lymphoplasmacytic infiltrate enriched in IgG4-positive plasma cells and variable degrees of fibrosis with a characteristic ‘‘storiform pattern’’ [6] .The involvement of various organs, including the central nervous system, thyroid gland, lungs, biliary duct, liver, gastrointestinal tract, kidneys, prostate gland, and lymph nodes has also been reported (7) .Lymphadenopathy is observed in up to 80% of patients, and is sometimes the presenting manifestation of the disease [8,9] .The diagnosis of IgG4-RD rests on a combination of clinical and histopathological features, including serum IgG4 levels elevated above the upper limit of normal.(10) The first therapeutic choice for management of IgG4- RD is the steroid treatment [11, 12] . Early diagnosis, although diffcult, is important because most patients respond well to corticosteroids in 2-4weeks. (13)

II. Case Report

A 62 year old male presented to Department of Surgery ,Rajindra Hospital , Patiala with complaint of on & off fever, jaundice and abdominal pain associated with loss of weight & loss of appetite since 1 month .On Per abdomen examination liver and spleen were palpable. Left middle cervical lymphnode palpable.
HB : 9 gm/dl
S.Bilirubin : 7.8 mg/dl
Direct bilirubin : 2.8 mg/dl
Indirect bilirubin : 5 mg/dl,
SGOT : 120 Unit/ml,
SGPT : 79 Unit/ml ,
Alkaline Phosphatase : 486 IU/L,

Bence jones protein : Negative
CECT whole abdomen done which revealed hepatospleenomegaly , subdiaphragmatic and abdominal lymphadenopathy .Also calcified atheromatous plaque seen in major abdominal vessels.
FNAC of cervical lymph node shows features of reactive lymphadenitis.
Bone marrow aspiration was markedly hypercellular marrow with plasmacytosis.
Midline exploratory laparotomy done & abdominal lymph node specimen was sent for histopathology to Department of Pathology ,Rajindra Hospital, Government Medical College ,Patiala.

Microscopic features
Multiple sections from lymphoid tissue show extensive follicular lymphoid hyperplasia with infilteration by plasma cells in interfollicular area. Histopathological feature were those of Florid follicular lymphoid hyperplasia. Differentials diagnosis of increased plasma cells in lymphnode:
Autoimmune disorder
SLE
IgG4 RD
Castleman disease
Small B Cell lymphoms
Extramedullary plasmacytoma,
IHC was adviced to rule out causes of increased plasma cells in lymph node.

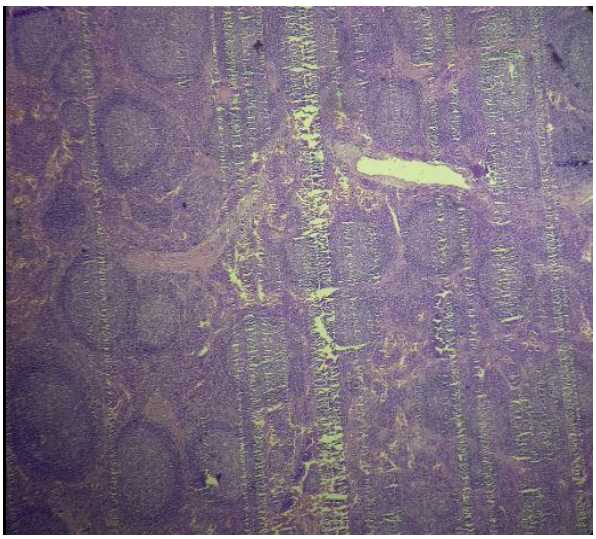

Figure1. At 4X

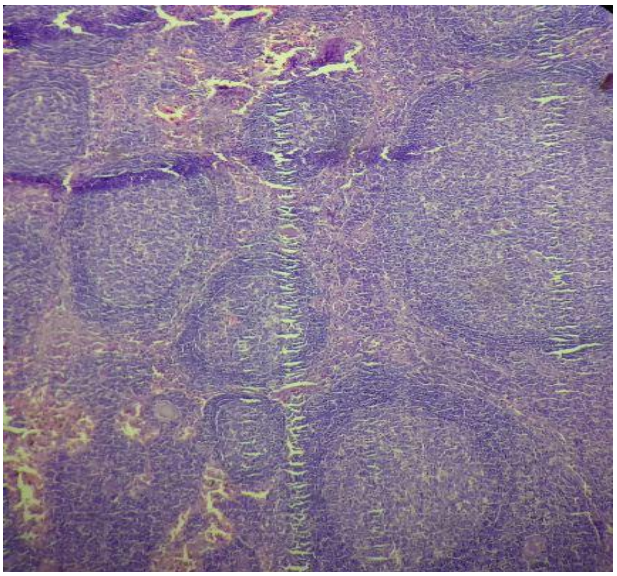

Figure 2. At 10X
Figure 1 &2. Lymph nodes show extensive follicular lymphoid hyperplasia

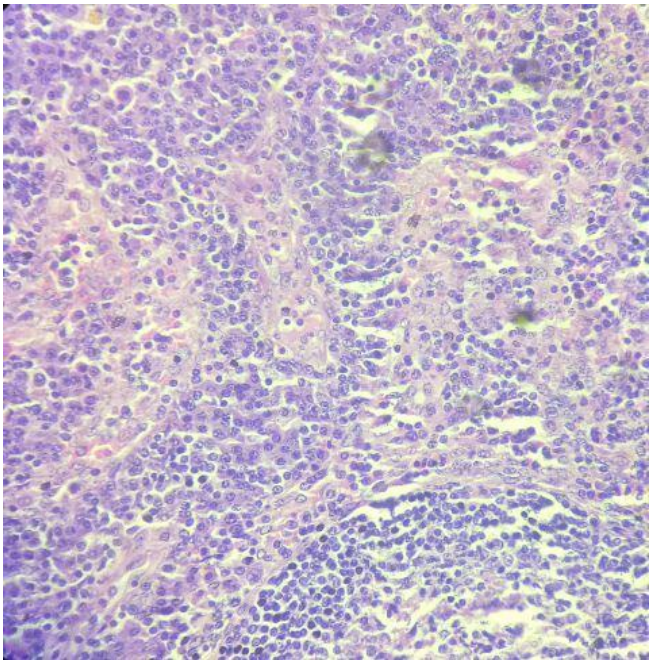

Figure 3. At 40X Plasma cells in the interfollicular area

III. Discussion

At present IgG4-RD is believed to be a systemic disease and diagnostic criteria for IgG4-RD [14, 15] include: (1) single or multiple organs with diffuse or localized swelling, masses, nodules and/or hypertrophic lesions; (2) elevated serum IgG4 levels (≥135 mg/dL); and (3) histopathologic features that include marked lymphocytic and plasma cell infiltration and fibrosis, with IgG4-positive plasma cell infiltration (IgG4/IgG positive cell ratio of 40% and IgG4-positive plasma cells exceeding 10/HPF). Diagnosis of IgG4-related is confirmed when all of the following are fulfilled: (1), (2) and (3). Diagnosis is likely if criteria (1) + (3) are fulfilled, possible if (1) + (2) are fulfilled and unlikely if only (1) presents**.**In this case, these criterias were fulfilled . According to an international consensus from 2015, 2 out of the 3 major findings need to be present: (1) dense lymphoplasmacytic infiltrate; (2) storiform fibrosis; and (3) obliterative phlebitis in veins and arteries. (16,17)

Five histologic patterns of lymph node involvement have been described in IgG4 related disease; namely, multicentric Castleman's disease-like (Type I), follicular hyperplasia (Type II), Interfollicular expansion (Type III), progressive transformation of germinal center-like (Type IV), nodal inflammatory pseudotumor-like (Type V).[18] In the present case, the histopathology findings was florid follicular lymphoid hyperplasia with infilteration by plasma cells in interfollicular area.

Our patient had fever,jaundice ,abdominal pain , cervical lymphadenopathy & hepatospleenomegaly with CECT whole abdomen findings of hepatospleenomegaly,subdiaphragmatic and abdominal lymphadenopathy . On histopathology of abdominal lymphnodes, features were those of Florid follicular lymphoid hyperplasia with infilteration by plasma cell in interfollicular area .Further ,IHC of abdominal lymph node was done which depicted reactive lymphoid hyperplasia with increased IgG4 positive plasma cells(>50/hpf) with increased plasma cell in interfollicular area that are polytypic for kappa/lambda.

IHC Markers :CD3+,CD20+,CD10+,BCL2+,CD5+,CD23-Highlights dendritic cell meshwork in follicles ,CD138 +,Kappa, Lambda+, IgG+, IgG4 +
Cyclin D1- non immunoreactive.
The patient was diagnosed with IgG4 RD and started on treatment with corticosteroids.
The case is reported to bring emphasis on IHC in disorders with increased plasma cells in lymph nodes ,so that early diagnosis of IgG4 RD is made and treatment with corticosteroid can be started .

IV. Conclusion

IgG4-related disease (IgG4-RD) is a systemic condition that often affects multiple systems, resulting in a wide variety of clinical manifestations.The morphologic changes and IHC are important but not suffcient for diagnosis since other non-IgG4-related conditions may fulfill these criteria and have to be excluded, including autoimmune diseases, infections, neoplastic processes, and non-specifc reactive changes. The awareness of this rare entity can help in making a timely diagnosis and prevention of the sequelae

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