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IMMUNOGLOBILIN G4 –RELATED AUTOIMMUNE PANCREATITIS SIMULATING PANCREATIC CANCER –REGRESSED COMPLETELY FOLLOWING CORTICOSTEROID THERAPY-A CASE REPORT WITH BRIEF REVIEW OF LITERATURE''

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ABSTRACT

Autoimmune Pancreatitis has been highlighted a lot in view of marked responsiveness to corticosteroid therapy on its clinical path. Insight specifically, on type1 Autoimmune Pancreatitis or IgG4-related Autoimmune Pancreatitis has escalated significantly over the last decades as well as inspite of separate pathophysiology along with results in type1 as well as type2 Autoimmune Pancreatitis are still believed to be separate kinds of same type1 Autoimmune Pancreatitis or IgG4-related disease Here we present a case report of a type 1 Autoimmune Pancreatitis or IgG4-related disease who recovered completely following steroid therapy and despite so much advancements in knowledge still whipples was considered in such with a pancreatic cancer stamp just in view of age in such cases without attempting to discriminate if it could get treated without surgery.

KEYWORDS: IgG4-related Autoimmune Pancreatitis; steroid therapy; pancreatic cancer differential diagnosis.

INTRODUCTION

Autoimmune Pancreatititis(AIP) believed to be a subkind of chronic Pancreatititis(CP) as well as represents about5% of all CP patients.[1] Mostly its presentation is as a focal mass simulating pancreatic cancer. Following the description of initial few cases.[2,3] variations in demographics pathology along with clinical presentation demonstrated the presence of 2 unique subkinds of AIPnamely type 1 AIP(AIP1)or lymphoplasmacytic sclerosing Pancreatititis (LPSP) as well as Type 2 AIP (AIP2)or idiopathic duct centric chronic Pancreatititis (IDCP).[4] In view of both problems displaying a significant response to steroids, both (AIP1 along with AIP2 were believed to be 2 separate poles or presentations of AIP.

Subsequently, a lot of variations in histology, demographics, clinical presentation as well as results became clear, that pointed that every AIP subkind might be its own totally separate as well as independent disease, having the commonality of response to a particular treatment (like steroids), a phenomenon that is obvious in other disease(like rheumatic disorders, oncology). This has resulted in certain authors to think that they are different, even utilizing a different nomenclature which considers their particular pathophysiology, histology as well as clinical features.: Autoimmune Pancreatititis that is referring to AIP1 as well as IDCP when referring to AIP2.[5]

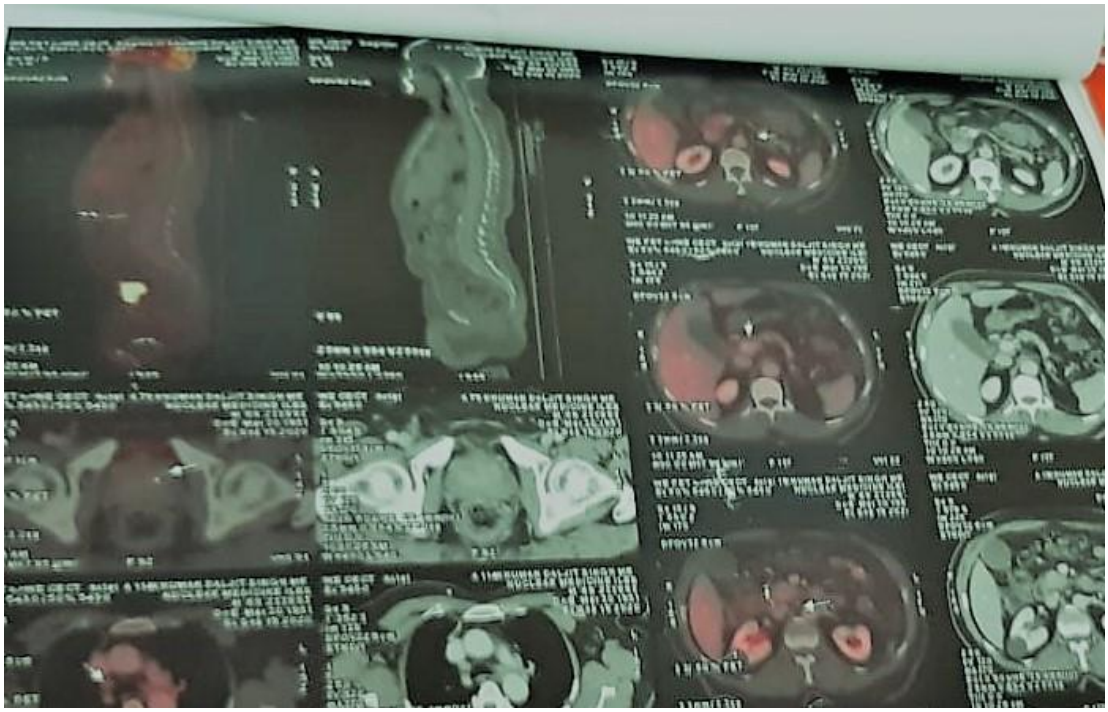
CASE REPORT

A69 year old male was noticed as developing asymptomatic jaundice. For this liver function tests (LFT) were advised.

It was noticed that serum biririubib(SB) along with transaminases were increased. On palpation of abdomen, a mass was felt in the abdomen. LFT-SB-5.5mg/dl(0.1-1.2) (Shiny medical clinical centre), Indirect- 5.0mg/dl (0.1-.25, SGOT153IU/L (5-50), SGPT247IU/L (5-50), GGT 220(53-`120),TP 7.2gms/dl (6.6-8.8), Alb

3.9gms/dl (2.8-4.5),Glob 3.3(1.5-3.0),GGT300IU/L(5-40)18/9/ 2020 -CA19.9-10.2 U/Ml(0-37)

For this an **MR Cholangopancreaticograph(16/9/2020)** was planned It revealed evidence of dilatation of common bile duct (CBD) in suprapancreatic portion merging 10mm in porta IHBR mildly dilated Cystic duct has low insertion and is dilated Gall bladder(GB) is overdistended wall is normal in thickness, no pericholagic cystic fluid collection /inflammation is seen. An altered area of signal intensity is seen in uncinate process and head of pancreas. Both CBD and main pancreatic duct(MPD) show at cut off at the margin of this lesion This lesion measures approximately 2.6x2.7cm in size The CBD distal to the lesion appears normal in caliber. A portion of intrapancreatic portion of CBD is not visualized. MPD is dilated in tail, body and neck region with caliber of approximately 3.5mm. Distal MPD in the region of head is not visualized. On contrast scan differential poor enhancement is seen in the area of altered signal intensity in the head and uncinate process region. No evidence of MRCP reveals hypoenhancing lesion in uncinate process and head of pancreas causing enhancement (figure1) 19/9/2020-**PET Scan** showed (figure2)-Protocol 1omCi of 18F FDG injected iv after uptake period e.g 50-70'CT Acquisition auto mAs 120 &Vp was obtained followed by PET Acquisition in 3D mode in 128slices TOF PET CT System with LYSO Crystals. The study was acquired from level of vertex to mid thigh. CT Data was used for attenuation correction, anatomic localization. Reconstruction fused. PET CT images were projected in in 3 axis for analysis Contrast used (Visipaque iv contrast oral mannitol. Additional Delayed imaging upper abdomen with oral positive contrast was performed .Blood sugar prior to FDG injection -112 mg% Findings –Overall quality of the study –good –SUV Max mentioned in report is in g/ml. Standardized to lean body mass Head and neck –age related cortical atrophic changes are noted in bilateral brain parenchyma. Dental related artefacts are noted particularly obstructing the locoregional anatomy. Mild FDG uptake is noted in palatine tonsils. SUV Maxon rt 2.0 with lt side tonsilloliths with mild FDG avid subcentric bilateral level II III, IV & V cervical lymph nodes noted Normal physiologic distribution is seen in brain and rest of head and neck region. Non FDG and fibrotic changes seen in B/L upper lobes no evidence of any metastasis.



Impression

Physiologic FDG distribution in the entire axial and appendicular skeleton. No focal FDG avid lymphosclerotic lesions noted in the skeleton. Mildly metabolically active hetogenously enhancing isodense in the head and uncinate process of pancreas with abrupt cut of dilated CBD and MBD at this levels resulting in upstream dilatation of proximal CBD, CHD, primary biliary confluence and mild bilobar abdominal lymph nodes as described suspicious for neoplastic etiology – suggested biopsy correlation 2) no definite scan evidence of abnormal metabolically active disease in rest of the body in the study.

Fibroscan in Liver diseases done did not show any significant changes for Chronic HBV Infection,- Chronic HCV Infection or for non acute fatty liver disease (NAFLD.).

HIV, HBsAg HCV were negative

CBC-Hb-13.6gm(13-17.0), TLC-8200(4000-11,000 cells/cumm, DLC-P61(40-75), L28(20-45)E06(01-

06)M05 (02-08) B0(00-02), ESR 60 mm/1st hr (0-09), Platelets 1.91 lakhs. cumm(1.5-4.5), pcv-41.2%(upto 47), MCV -92.8(76-96), MCH30.6(27-32)Pg

Echocardiography–showed he was fit to undergo prolonged surgery.

Thus with a provisional diagnosis of cancer of pancreas it was decided to proceed straight with open surgery in view of no evidence of metastases on PET Scan and large lesion thus an endoscopically directed biopsy was by passed.

On opening the abdomen on 10/10/2020it was found that the lesion was very large and the surgeon thought it was not fit for whipples surgery, thus after discussion with physician it was decided to only take 4 areas of biopsy from lesion, biopsy from lymph node, ligate the huge feeding vessel to the tumour, GB removal and drain the distended CBD and proceed only further after HPE report. Following 6 days of surgery HPE revealed Pancreatic head replaced by cones showing distorted architecture areas of fibrosis with atrophy of pancreatic acini, moderate lymphocyte plasmocytic infiltration is seen. At places residual islet cells are seen. No evidence of malignancy seen. The hepatic lymph node displayed reactive hyperplasia but no malignancy. On Immunohistochemistry(IHC)-IgG4 Positive 20-22 plasma cells/HPF were seen.

Gall Bladder (GB)-lined by simple columnar epithelium. Thus IgG4 Positive lesion suggestive /of autoimmune pancreatitis type 1 in a limited area. Advice- compare with serum IgG4 levels and repeat biopsy from different areas of cut off CBD, and pancreatic duct with double duct not likely suggestive /of pancreatic head neoplasm.

Serum IgG4 showed 3,53g/L(ref range 0.3-2.0).
Post op serum bilirubin decreased to total -0.9(0.2-1,3)
Indirect -0.3mg/dl(0-1.1ng/dl)
Direct 1.06mg/dl(0-0,3)
SGOT(AST)-108iu/l(17-57
SGPT(ALT)-158(21-72)
Gamma GGT 302(18-73)
AP-318IU/L(30-120)

He was started 40mg prednisolone daily till he developed marked haemoconcentration with Hb 15g/dl, platelets 5.25lac TLC-16,200 although afebrile from 19th October, which was decreased to 20mg on 3rd November Following that after 11/2 mths of 20mg prednisolone he had a repeat MRCP. CT Findings on 28//11/20 revealed post operative status with residual lesions in uncinate process of pancreas without any differential enhancement No evidence of locoregional lymphadenopathy or any liver parenchymal lesion was seen. Thus present scan reveals MPD measuring 1.5mm caliber CBD is also prominent -5mm in diameter Pancreas show slightly irregular outline, however no differential enhancement seen in the dynamic phase as com to pancreas. This area measures about 1.5x1.4cm in size and appears separate from superior mesenteric artery and veins. Pancreatic body and tail area as such are mildly atrophic. Liver is normal. GB –Surgicall resected with clips/'sutures in porta hepatic and peripancreatic region s/o post operative sulcus. After this the prednisolone dose was reduced to 10 mg from 2nd December and 5mg from 9th December, gradual tapering it.

3. DISCUSSION

3.1Autoimmune Pancreatitis (Iimmunoglobilin G4-Related Disease Pancreatitis Or lymphoplasmacytic sclerosing Pancreatitis)

This disorders possesses clinical, histologic as well as serum properties as well as probably depicts the early documentations by Sarles etal.[2] &Yoshida etal.[3] The existence of a dense lymphoplasmacytic infiltrate gives it a 2nd name ''LPSP''.

Presently, it is thought to be the most common presentation of immunoglobilin G4 -Related Disease(IgG4-RD), that is a systemic fibrotic problem which manifests with fibrotic along with tumor like lesions in various organs as well as is correlated with escalated amounts of IgG4 subclass.[6] About 41% of IgG4-RD patients present with Pancreatic involvement. Significantly in practically 50% of cases ,the pancreas is the only site for the presentation of this disease ,with almost 51%of IgG4-RD Pancreatitis subjects form other organ involvement(OOI)in the course.[5]

3.1bDemographics

AIP or IgG4-RD Pancreatitis has >presence in Asia,with it implicating men basically in the 7th decade with a male:female ratio 3:1.[7] Japanese surveys conducted in various time periods evaluated a total prevalence of 4.6-10.1 cases /10000 inhabitants along with an incidence of 1.4-3.1 new cases/10000 inhabitants,pointing that the awareness of physicians in addition to diagnostic tools have become better with time.[8] As per the International surveys conducted,[6] it appears that IgG4-RD Pancreatititis is more common in Asia, as compared to Europe along with North America ,although no particular knowledge regarding its global incidence as well as prevalence is given.

3.2 Pathophysiology

Despite various modes as well as immunologic pathways have been evaluated IgG4-RD Pancreatititis pathogenesis continues to be not understood. The part of IgG4-subclass has been under examination since it got acknowledged that the patients with AIP, at that time known as sclerosing Pancreatititis with escalated plasma amounts.[9]

3.2a IgG4 subclasses

The IgG family are made up of 4 classes that get divided as per the sequence of the heavy chain(HC) constant domains. IgG exists in 4 lower levels along with

possesses weaker ability of binding the Fc Y receptors as well as C1q of complement but via a Fab-arm exchange (the switch of HC as well as attached light chain [LC]). It possesses the capacity to develop'' half antibodies''. These half antibodies'' are asymmetric as well as aid IgG to recognize 2 separate antigens. This property is accompanied with the incapacity to cross link antigens along with generate immune complexes ,causing a total anti inflammatory function.[10] This anti inflammatory property is perplexing ,in view of escalated inflammatory infiltrate, in addition to fibrotric event seen in Pancreatic specimens from cases influenced by IgG4-RD Pancreatitis.

The anti inflammatory property of IgG4, in addition to T as well as B cell mediated both acquired along with innate immunity stimulates the query if it is escalated serum amounts of IgG4 plasma cells in implicated organs act either as stimulating factor or might depict an over expressed phenotype .T cell as well as B cell possess a central part in by IgG4-RD Pancreatititis(AIP1 /LPSP).

3.2b T cells

The escalated inflammatory infiltrate seen in IgG4-RD implicated organs constitutes a remarkable amounts of regulatory Tcells(Treg) cells having the property of an escalated amount of Th2 cells as well as regulatory cytokines(interleukin 4(IL4),IL-5,IL-10) as well as transforming growth factor β(TGFβ). This combination with separate Treg) cells subpopulation counts (escalated Treg CD24+CD25 along with memory Treg cells) causes a greater generation of IgG4, pointing that an escalated IgG4, amount are secondary growth factors not the disease initiators.[21,23]

It appears that IgG4 generation gets stimulated by escalated peripheral Treg cells as well as escalated amounts of inducible costimulator (ICOS)-positive Treg through IL-10, wheraeas ICOS negative Treg cells stimulate fibrosis through TGFβ.This points that IgG4 is not the triggering factor or working like an anti inflammatory factor.[11]

3.2c B Cells

Akin to Tcells, a disturbance in various Breg cells sub populations as well as plasmablasts appear to have a critical part in IgG4-RD. This implies that acquired as well as innate immunity, both have a key part in the etiopathogenesis of this disease. Pancreases from patients possessing AIP1 have a positive toll like receptor 2(TLR-2) as well as a TLR4 basophil infiltrate.[12] Basophil activation might stimulate the existence of M2 macrophages which in turn could have certain implication on the earlier detailed Th2 environment ,influencing the generation of IgG4 through TLR4 .These findings validate that the escalation of IgG4 occurs secondarily ,thus not the triggering factor.

Certain documentations point that neutrophils extracellular traps along with peripheral eosinophils might also be implicated in the generation of AIP1. Nevertheless, it appears that a switch towards Th2 response is the cause for the escalated eosinophils along with IgE amounts. Significantly, peripheral eosinophilia has been documented to occur in 12-29% of IgG4-RD Pancreatititis. Despite no association among peripheral as well as tissue eosinophils has been documented, certain authors have posited that escalated peripheral eosinophils or tissue infiltration might also add to the diagnostic value of serum IgG 4 amounts.[13]

3.2d Autoimmunity

Simulating different immune mediated conditions the existence of various auto antibodies (like lactoferrin and carbonic anhydrase II) as well as the expansion of oligoclonal plasmablasts of the IgG4 subkind propose an autoimmune mode.

Nevertheless, the basic knowledge that IgG4-RD(AIP1) mainly implicates elderly men that the observed auto antibodies do not have a significant part in the generation of pathogenesis, that till now no IgG4 auto antibodies have got isolated as well as that escalated amounts of particular Treg population have been seen (i.e what you do not anticipate in autoimmune conditions where Treg amounts are anticipated to be less) are the discussions against autoimmunity.[13]

3.2eMore Factors

All these above mentioned immune properties appear to take place in genetically prone subjects. Particular haplotypes or Polymorphisms in the HLA (DRB1*0405-DBQ1*0401) CTLA2 and FRCL3 genes have been detailed but the factors which trigger are still query.[14]

It has been pointed that Helicobacter pylori infection might be a risk or factors which triggers. Certain patients possess antibodies against the plasminogen binding protein of the bacteria which could crossreact with a markedly expressed protein in acinar Pancreatic cells. Other probable factors which trigger are exposure to external antigens, paraneoplastic reactions as well as allergies.[15]

Despite most of influenced cases are nonatopic or atopy prevalence is no >general population, certain authors have pointed IgG4-RD presents features akin to allergic reactions.[16] Even despite the existence of vasculitis – like lesions, IgG4-RD has got incorporated into the 2012 Revised Chapel Hill Consensus Conference as an aetiology of large vessel vasculitis.[17]

These complicated inflammatory, anti inflammatory as well as immune response crosstalks point that IgG4-RD might be secondary to a B cell mediated condition, or a Th2 /Treg- mediated condition or from a pro inflammatory as well as pro fibrotic phenotype.

As per Uchida,[18] Kamisawa etal.[19] posited that IgG4-RD Pancreatititis might be believed to be a complicated condition, probably occurring from intricate immune along with inflammatory crosstalk occurring at the same time .What is the precise trigger for these crosstalks as well as if they besides their sequences are limited to some particular genetically susceptible persons who get exposed to a particular environmental factors still needs clarification.

3.3Diagnosis along with Clinical Manifestation

IgG4-RD Pancreatitis (AIP1 /LPSP) manifests with typical histologic, imaging clinical as well as serum properties. Classically, patients with a diffusely or focally increased pancreas simulating cancer. Usually it is an incidental observation or secondary to the diagnostic evaluation of jaundice ,a sign present in upto 60% of cases Other symptoms are abdominal (30%) or back pain (15%), acute pancreatitis(5-10%),weight loss (15%); with certain series detailing pancreatic vascular complications.[6,8]

AIP1 might present acutely (like obstructive jaundice as well as /or diffuse or focal, Pancreatic swelling) or late presentation (suggestive of painless chronic Pancreatitis). Those manifesting as acute Pancreatitis usually are mild with less chances of local or systemic complications.

In view of imaging aberrations tend to be the initial Clinical presentation, diagnosis can be thought of when some particular or ‘’classical’’ image properties like these are observed i)absence of lobularity as well as diffuse Pancreatic enlargement i.e an escalated size of the gland without density variation or a sole mass larger than 2/3 rd of the total pancreas(65-70%),long main pancreatic duct (MPD)stenosis in the corresponding region without considerable dilation of the upstream duct, post contrast enhancement in the enlarged pancreas at the arterial phase that is usually recovered at the delayed phase on the dynamic CT (i.e delayed enhancement; separate from Pancreatic cancer ,where poor enhancement continues in the delayed phase), peripheral capsule like rim(49%) as well as hyperintense.

In case these typical properties are lacking or are only partially existent(atypical presentation),then extra cues need to be observed .Collateral proof considers enhanced IgG4 serum amounts (a diagnostic precision of upto95%) with amounts2xabove the upper limit of normal) along with other organ involvement (OOI) (Lile biliary structures which are observed in upto50% of cases. Enlarged salivary glands pulmonary nodules retroperitoneal fibrosis, interstitial nephritis usually correlated with a dense plasma cell IgG4+infiltrate) that can present prior to, synchronously or following Pancreatic involvement.[20]

Palez-Luna etal.[21] documented15cases of histology proven AIP1 (LPSP), the commonest presentation was weight loss(87%), followed by abdominal pain(60%), as well as bile duct stenosis(53%) as compared to the classical’ presentation, only 2 cases presented a 2 fold escalation of serum IgG4. In to patients mean age of Manifestation was 47.5 yrs, with slight enhanced male gender.[22]

Escalated serum IgG4 (>135mg/Dl)have got documented in upto70-85% of cases. A cutoff point of >2 times escalation above the upper limit of normal in serum IgG4 has got recommended besides in view of its diagnostic precision ,but also in view of <escalation of serum IgG4 has been observed in upto10% of Pancreatic cancer as well as other nonspecific inflammatory Pancreatico-biliary conditions[REV IN 21].

Mostly this extra knowledge given adequate proof to validate the diagnosis of IgG4-RD Pancreatitis, making histological evaluation (pancreas biopsy rarely required.

The recent IgG4-RD diagnostic consensus has pointed that 2 HPE items which occur in uptill 90% of AIP1 as well as only in 5% of Pancreatic cancer cases need to be present in tissue specimens for consideration of diagnosis:40%of IgG4 positive plasma cells as well as >10 IgG4 positive plasma cells/HPF]rev in 21].

The ultimate diagnostic test on ruling out malignancy is evaluation of the response to steroids [rev in 21]

Various diagnostic criteria given in Asia/Europe and North America .Till now sensitivity, specificity as well as accuracy for all AIP1 cases are89-95%,100%and 94% respectively Till now endoscopic ultrasound-guided biopsy appears to be the method of choice for acquiring pancreatic tissue Various reports on advantage, disadvantage as well as utilizing of various methods(like fine needle aspiration or fine needle biopsy have been advocated as well as , deciding that the method as well as technique has to be individualized along with depend on every endosonographer and center expertise]rev in 21].

In certain cases the IgG4+ to IgG4+ plasma cell ratio in regular endoscopic biopsies from ampulla of vater have aided in validating the diagnosis of IgG4-RD Pancreatitis along with believed to be a surrogate when ultrasound-guided biopsies or serum IgG4 are not conclusive or unavailable.

Mostly lot of collateral proof (serum, imaging, OOI) to arrive at a diagnosis ,hence histology is mostly not mandatory. It might be needed if the subset of cases believed to be indeterminate AIP ornot otherwise specified (AIP-NOS) where clinical, serum, along with imaging presentations are not conclusive. Certain of these cases might represent IDCP,but rest might be actually atypical cases of of IgG4-RD Pancreatitis[rev in 21].

3.4 Treatment

Steroids continue to be the cornerstone for treatment of AIP(IgG4-RD Pancreatitis), as compared to patient who did not receive any treatment , corticosteroids achieve remission in upto 90-99% of cases.[23] Until contraindicated, Steroids need to be delivered to all naïve patients as well as to any patient attempting to induce remission. Other immunosuppressants like azathioprine as well as methotrexate are inefficacious in inducing remission in addition to their use has been limited to maintainance therapy as steroids sparing agents. Rituximab presents an adequate method for remission induction in case Steroids are contraindicated.

As per an International consensus indications for treatment in symptomatic patients are Pancreatic involvement abdominal as well as back pain and OOI like obstructive jaundice secondary to bile duct stricture. Further asymptomatic cases with persistent Pancreatic masses on imaging are persistent LFT abnormalities need therapy.

In patients presenting with biliary stricture in case jaundice is mild, with no signs of cholangitis are existent drainage might not be required If indicated, it presents an opportunity to obtain tissue to rule out malignancy in atypical cases.

Though 10-20%of cases might improve spontaneously without any treatment, significant along with irreversible complications like Pancreatic insufficiency as well as refractory biliary structures of others have been reported in patients left untreated or when treatment got delayed.

Various steroid regimens have got utilized. The International consensus,[25] recommends an initial dose of prednisone of either 0.6-1.0mg/kg for a minimum of 20mg /d. This needs to be delivered for2-4wks as well as then tapered down at a rate of 5mg /week until stopped. The usage of higher doses(30-40mg)for 4 weeks, which is the preferred approach of these authors,[21] is correlated with faster results .Regimens shorter than 4 wk as well as doses <20mg /d or equivalents are not advocated. Steroid response needs to be analysed within 2-4wks after its starting and ideally by same method that was originally utilized. About 86-100%will show a decrease or disappearance of (like shrinkage of enlarged pancreas, disappearance of hepatic or lung nodules, receding retroperitoneal fibrosis etc) Such a response confirms the diagnosis as well as is an indication to complete treatment. Mostly 3-6 mths after steroid treatment, the thickness of the enlarged pancreas reduces by 60-70%.[24]

Although the response to steroids is part of the diagnostic criteria, particularly in atypical or IgG4-negative cases. It should never be considered prior to extensive workup to rule out malignancy has been conducted (that includes endoscopic ultrasound-guided fine needle aspiration biopsy). Further when steroid response is not present alternative diagnosis needs to be considered, as well as the patient will need to undergo diagnostic re evaluation.[24]

Relapse takes place in 24-65% of AIP(IgG4-RD Pancreatitis) patients.[25] This rate escalated following omitting of steroids as compared to that seen during tapering or maintenance treatment (67%vs15%vs18% respectively).

Nationwide studies from Japan-72,76,77] prefer maintenance treatment over the12wk regimen These studies demonstrated a significant less Relapse(26%)in cases on 5m/d on of prednisone as compared to no maintenance treatment group (45% Relapse).These amounts attained a plateau at 7yr as well as continued to be unaltered at the10yr follow up.

Inspite of the documented advantages long term steroid treatment correlated complications need to be considered. Against maintenance treatment, discussions are absence of any gain seen following7yrs of treatment as well as the initiation of dose along with time based steroid treatment correlated complications like osteoporosis, myopathy along with infections .About 50% of patients getting steroid maintenance treatment presented a minimum of 1 steroid –associated complications, once accumulative loss of 10,000mg was reached or exceeded or when treatment continued for >5yrs. AIP(IgG4-RD Pancreatitis)usually influences elderly people; this group has more chances of manifesting steroid treatment correlated complications as compared to their younger counterparts. The International consensus as well as all authors advocate individualize maintenance treatment, on the basis of disease activity along with existence of high risk factors for relapse serum IgG4, IgGE, eosinophil as well as IL-2 soluble Receptor have been ,documented as biomarkers of disease activity as well as subsequently, potential predictors of therapy response as well as relapse. A high Relapse risk has been associated with high IgG4 pretreatment serum IgG4(>x4 upper limit of normal) persistent high to minor reduction following steroid initiation, proximal biliary involvement as well as multiorgan involvement (>2organs).[24]

Knowing the significant side effects correlated with longterm steroid treatment once remission has been obtained, persons with a high risk of relapse or with 1st relapse episode need to be put on maintenance treatment as well as relapse avoidance therapy. The recommendation is to introduce steroid sparing agents (like azathioprine or 6 mercaptopurine). Doses as well as care are same as those seen in disorders where they are prescribed (like autoimmune hepatitis). Long time use of thiopurines has been correlated with a 5.3 fold risk of generating lymphoproliferative disorders (especially in males over 65 yrs) among neoplastic as well as haematologic complications.

In resistant patients of AIP (IgG4-RD Pancreatitis) or in those having contraindications or side effect associated with the steroid treatment along with immune modulators rituximab offers a great alternative.

Rituximab is a chimeric monoclonal antibody which targets CD29B lymphocytes. Various protocols of delivery have got utilized with slight Variation in primary results. The rheumatoid arthritis protocol,[25] delivers 2 perfusions of rituximab 1000mg 15d apart, as well as the Mayo Clinic protocol utilizes 375mg/ml intravenous rituximab infusions wkly x4wks as well as then every 2-3mth x20mths for an average of 10 perfusions. The reported efficiency of rate prefers the Mayo Clinic protocol(67% vs 83%respectively),but the recurrence rate within 3yrs of stopping rituximab is similar (40%vs 45%) via maintenance treatment with rituximab reduces recurrence, it is correlated with an escalated risk of infection. Follow up details over 3yrs are not available.

CONCLUSIONS

Our patient is a male patient in his 7th decade as seen in most IgG4-related Autoimmune Pancreatitis along with showed increased peripheral eosinophilia although borderline along with peripheral escalation of IgG4- that was 2 times the normal besides the histopathological IHC showing IgG4 positive plasmacytes and lymphocytes infiltration whose only presentation was incidental jaundice with weight loss as presentation and besides bile involvement no other organ involvement was seen and responded very well to steroid doses of 1i/2 mths and right now needs only a maintainance dose of 5mg prednisone and follow up twice yearly ,otherwise he has completely recovered. Although our patient underwent a laporotomy just seeing increased eosinophils with enhanced IgG4 levels even biopsy can be by passed and just on basis of escalated IgG4 suspecting IgG4-related Autoimmune Pancreatitis only steroid therapy can be tried and laporotomy only in case of failure of response to steroids.

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