Review Article

International Journal of Clinical Rheumatology

Review of the Literature and Tasks Learned by the Rheumatology Residents about the Primary Immunodeficiency Association with Systemic Lupus Erythematosus

Abstract

Primary immunodeficiency diseases (PID) represent a miscellaneous group of conditions performing from inherited blights in the development, development and normal function of vulnerable cells; therefore, turning individualities susceptible to intermittent infections, mislike, autoimmunity, and malice. In this retrospective study, autoimmune conditions (AIDs), in special systemic lupus erythematosus(SLE) which arose associated to the course of PID, are described. Classically, the literature describes three groups of PID associated with SLE(1) insufficiency of Complement pathway factors,(2) blights in immunoglobulin conflation, and(3) habitual granulomatous complaint(CGD). presently, other PID have been described with clinical incarnation of SLE, similar as Wiskott – Aldrich pattern(WAS), autoimmune polyendocrinopathy candidiasis ectodermal dystrophy(APECED), autoimmune lymphoproliferative pattern(mounts) and idiopathic CD4 lymphocytopenia. Also we present findings from an adult cohort from the inpatient clinic of the Rheumatology Division of Universidade Federal de São Paulo. The PID instantiations set up by our study group were considered mild in terms of inflexibility of infections and mortality in early life. Therefore, it's possible that some immunodeficiency countries are compatible with survival regarding contagious vulnerability; still these countries might represent a strong prepping factor for the development of vulnerable diseases like those observed in SLE.

Keywords: Autoimmune complaint • Primary immunodeficiency• Systemic lupus erythematosus • Antibodies insufficiency

Robin Christensen*

Department of Pediatrics and School of Rehabilitation Sciences, University of Ottawa, Canada

***Author for Correspondence:**

Christensen@rb.com

Received: 02-May-2023, Manuscript No. fmijcr-23-101177; **Editor assigned:** 04-May-2023, Pre-QC No. fmijcr-23-101177 (PQ); **Reviewed:** 18-May-2023, QC No. fmijcr-23-101177; **Revised:** 23-May-2023, Manuscript No. fmijcr-23-101177 (R); **Published:** 29-May-2023, **DOI:** 10.37532/1758-4272.2023.18 (5).107-111

Introduction

Primary immunodeficiency diseases (PID) represent a miscellaneous group of conditions performing from inherited blights in the development, development and normal function of vulnerable cells. PID frequently have an important inheritable base leading to different vulnerable diseases associated with infections, autoimmune conditions and other malice in cases. Since these are natural conditions, generally with well- defined inheritable blights and mendelian heritage, children are the most predominant cases. On the other hand, autoimmune conditions (AIDs) have a complex multifactorial polygenic etiology in which environmental triggers play an important part in their pathogenesis and represent a group of further than 70 known conditions. Remarkably, AIDs represent one of the most common clinical phenotypes of numerous forms of PID, only overcome by the frequence of infections. Systemic lupus erythematosus (SLE) is amulti-organ autoimmune complaint characterized by a range of clinical instantiations that generally affects women in reproductive age. In SLE, polyclonal hypergammaglobulinemia and multiple autoantibodies are produced generally against nuclear antigens. These autoantibodies deposit on several organs, including feathers,

skin and joints, causing severe inflammation. Although SLE cases have hypergammaglobulinemia, they frequently present severe infections, especially while entering immunosuppressive treatment [1].

Infections by opportunistic pathogens are generally seen in cases with PID. These infections, either clinical or subclinical, may represent the primary detector for the development of autoimmunity. In genetically fitted individualities, habitual exposure to environmental factors can promote the development of autoantibodies numerous times before the complaint onset. Cases with SLE present an increased vulnerability to infection inpre-clinical phase of complaint. Classically, the literature describes three groups of PID associated with SLE insufficiency of Complement pathway factors picky and partial blights in immunoglobulin conflation(particularly insulated IgA and IgM scarcities) and habitual granulomatous complaint(CGD). still, among clinical compliances, several other PID may also sometimes be associated with SLE or SLE- suchlike pattern instantiations. These include Wiskott – Aldrich pattern(WAS) autoimmune polyendocrinopathy candidiasis ectodermal dystrophy(APECED) autoimmune lymphoproliferative pattern(mounts) idiopathic CD4 lymphocytopenia(ICL) partial T cell immunodeficiency and hyperactive-vulnerable dysregulation(including autoimmunity, seditious conditions and elevated IgE product) [2].

Materials and Methods

Complement scarcities

The Complement system is composed by a group of tube and faces cell- proteins with important part in ingrain and acquired humoral vulnerable system, responsible for the destruction of microbial agents and concurrence of circulating vulnerable complexes. In SLE, the deposit of vulnerable complexes containing multiple autoantibodies and activation of the Complement system intervene towel damage. Paradoxically, scarcities in factors of early rudiments of the classical pathway are explosively associated with the development of SLE. In addition, insufficiency in factors of the late common pathway (C5, C6, C7, C8a and C8b) as well as some rudiments of the indispensable pathway (C3 and Factor I) are only sometimes associated with SLE. Inheritable scarcities of these factors might contribute towards SLE pathogenesis by dwindling vulnerable complex concurrence capacity. The literature is controversial in respect to mannose-binding lectin (MBL) and antibodies against MBL in the pathogenesis of SLE. Some authors and this includes our group, have described the presence of increased MBL insufficiency in SLE cases (unpublished data). Still, farther studies should be conducted for a better explication of this association with SLE [3, 4].

Picky IgA insufficiency

Picky IgA insufficiency (SIgMD) is the most common PID (ranging from 1400 to 13000).9 since the maturity of cases are asymptomatic, this complaint may be unnoticed during nonage or indeed on adult phase. These cases present intermittent sino- pulmonary infections, mislike, gastrointestinal complaint, endocrinopathy, malice and autoimmunity (Table 2). Ultimately, cases with SIgAD evolve to CVID. SIgAD is constantly set up in cases preliminarily diagnosed with autoimmune complaint similar as Graves ' complaint(GD), type 1 diabetes(T1D), celiac complaint(CD), myasthenia gravis(MG), SLE, and rheumatoid arthritis(RA).28 A high frequence of SIgAD was described in juvenile SLE(5.2) and in adult onset SLE(2.6).8 It's hypothecated that the absence of mucosa IgA may reduce concurrence and neutralization of antigen and pathogen, which serve as triggers for breaking vulnerable forbearance. Still, the association between SIgAD and SLE isn't fully understood yet [5].

Hyperactive- IgM pattern

Hyper- IgM pattern (HIGM) is an on-classical PID characterized by antibody insufficiency with the absence of IgG and IgA but normal or increased IgM situations. Different inheritable mutations can beget this PID; including mutation of CD40 ligand gene(CD40LG gene-linked HIGM), CD40 gene, Activation- convinced DNA- cytidine deaminase gene(AICDA gene, also known as AID) and uracil DNA glycosylase gene(UNG). Cases with HIGM generally present during nonage opportunistic infections and autoimmune conditions (autoimmune cytopenia, nephritis, seditious bowel complaint, autoimmune hepatitis, arthritis, hypothyroidism and SLE). Autoimmune incarnation are more frequent in cases that present HIGM due to mutations in AID, still, autoimmune instantiations have also been reported in other types ofHIGM.29, 30 There are veritably many cases reported on the concurrence of SLE and AID or UNG associated Hyper- IgM [6].

Insulated IgG class insufficiency

IgG class insufficiency is defined as a serum IgG class position that's further than two standard diversions below the normal mean for age. IgG class insufficiency can be associated with intermittent infections of the upper and lower respiratory tracts. Pathogens are generally limited to bacteria and respiratory contagions. Because

IgG2 is important in the response to polysaccharide antigens, IgG2 class-deficient cases generally have infections with Haemophilus influenza or Streptococcus pneumoniae.33 In grown-ups, insufficiency of IgG3 class is the most common, whereas in children IgG2 is the most current IgG class insufficiency. IgG class insufficiency may be seen in confluence with other primary vulnerable insufficiency diseases, similar as ataxia- telangiectasia and IgA insufficiency.34 An IgG class insufficiency might do as an isolated single IgG class insufficiency or as a insufficiency of two or further IgG sorts. The literature describes sporadic cases of autoimmune incarnation in cases with IgG class insufficiency, like IgG 1,39 IgG440 and combined IgG2 and IgG4 class insufficiency.41 The frequence might be advanced, still those cases might go unnoticed, since IgG sorts serum position determination isn't included in routine evaluation of SLE cases. Jesus etal.(2011) also showed the concurrence of IgG2 insufficiency in5.5 of the juvenile SLE cases studied, representing 21 of all PID cases in their series [7, 8].

Autoimmune lymphoproliferative pattern

Autoimmune lymphoproliferative pattern (mounts) is an autosomal dominant complaint caused by abnormalities in Fas- intermediated lymphocyte apoptosis, with clinical features of splenomegaly and lymphadenopathy, and colourful autoimmune instantiations. Mounts caused by heterozygous mutations in the Fas gene (TNFRSF6; mounts Type Ia) make up the maturity of linked cases. Mounts caused by mutations in other factors involved in the Fas apoptosis pathway have been linked, including FasL(TNFSF6; mounts Type Ib), Caspase 8(NRAS) and Caspase 10 (CASP10) (the ultimate two, mounts Type II). There's also a group of cases with ALPS phenotype, abnormal Fas- intermediated apoptosis, but no linked mutation in the Fas pathway(mounts Type III).62, 63 Immunological abnormalities characteristic of mounts include the presence of increased number of circulating CD4 – CD8 lymphocytes(double negative), as well as T- and B- cell lymphocytosis and polyclonal hypergammaglobulinemia. Autoimmune haemolytic anemia and vulnerable thrombocytopenia are the most common autoimmune features seen in ALPS. Autoimmune neutropenia and the presence of anticardiolipin antibodies are also frequently present, whereas autoimmune hepatitis, uveitis, and glomerulonephritis are much less common instantiations in these cases.63 The literature describes a case of SLE- suchlike pattern in a 59- time-old woman with arthritis, low fever, intermittent hypotension, confusion, macular skin rash with telangiectasia and perivascular lymphocyte infiltration, cytopenia without abnormal cells, hepatosplenomegaly, pericardial and pleural effusion, cervical lymph knot shots and verbose large B cell carcinoma. This case was described with autoimmune lymphoproliferative pattern- suchlike pattern [9, 10].

Conclusion

PID are a group of monogenic conditions in which mutations of certain genes can lead to increased vulnerability to infections but may also affect in loss of central and/ or supplemental forbearance. Thus, AIDs are common among cases with a different array of PID. Immunoglobulin insufficiency forms a peculiar group of PID, in which the heritage appears to be polygenic and there's a wide inflexibility diapason, with mild forms that generally remain unnoticed. Our findings in adult cases with SLE suggest that AIDs can present a advanced frequence of less severe forms of PID without severe infections. The presence of some forms of PID was associated with certain phenotypic tricks in SLE cases. The literature and our findings show that PID and AIDs constantly attend and cases with autoimmune conditions should be precisely covered for the presence of PID and vice versa.

Discussion

Between 2009 and 2011, our group followed 315 successive adult SLE cases at the Rheumatology Division inpatient clinic of the University Hospital of Universidad Federal de São Paulo. The purpose of the study was to totally track a comprehensive array of PID in a large cohort. Once the complaint exertion could impact the results, all cases were followed until achieving complaint quiescence. Fifteen cases remained with active complaint throughout the follow- up and were, thus, barred from the analysis. Cases followed were generally ladies(16 males and 284 ladies), with39.58 ±12.54 mean times-old(age ranging from 18 to 61 times), mean complaint duration of10.74 ±8.15 times(complaint duration from 1 to 53 times) and mean age at SLE onset of28.79 ±10.89 times-old(SLE onset from 3 to 69 times). Total frequence of infections in SLE cases was 28(9.33). Those cases were classified using the warning signals for primary immunodeficiency lately revised.70 unfortunately thecross-sectional design of our study couldn't allow the maths of mortality rate. Nine cases had intermittent airway infections, whereas 15 presented intermittent urinary tract infections and three, skin furunculosis. Two cases presented intermittent oral/ genital Herpes simplex and two others had Herpes zoster infection. Also, two cases manifested mycobacterial

infection one had pulmonary tuberculosis and the other hanseniasis. In the present series, other autoimmune conditions were observed in 47 individualities (15.66) (including rheumatic autoimmune conditions (n = 32) andnon-rheumatic autoimmune conditions (n = 20)), some of which presenting further than one autoimmune condition. Eighty- four cases(28) were linked with impunity blights compatible with classical PID(Table 3), and in four cases(1.3) further than one associated PID were linked(SIgAD IgG2; SIgAD IgG4; IgMD IgG2 in 2 cases). Else from our results, the literature describes one case of SIgMD accompanied with IgG4 insufficiency (Ideura etal. 46). Interestingly, one case presented a respiratory burst profile bloodied enough to be classified as a CGD gene carrier but no case presented the profile compatible with full-bloated complaint. Our clinical and laboratory findings have demonstrated that the PID observed in SLE cases are considered mild in terms of inflexibility of infections and mortality. We presume that those PID are compatible with supposedly normal life, but that the consequent long-standing antigenic burden may be a threat factor for the development of AIDs, represented in this cohort by SLE. Generally, severe forms of PID are diagnosed at early stage of life, while on-severe or mild forms of PID instantiations are substantially asymptomatic.20 We set up that 28 of our cohort of adult SLE cases was constituted by mild PID which allowed a longer survival rate, passing unnoticed during nonage. This could conceivably explain the absence of ails similar as CVID, CGD and HIGM. Unexpectedly, in our cohort the presence of IgM, anon-classical form of PID, was veritably frequent. We also observed in our cohort a large number of SLE cases with IgG class insufficiency, while literature reports only some cases of insulated insufficiency of IgG2 and IgG4.18, 41, 71, 72 In our study, all cases with IgG4 insufficiency and 75 of those with IgG3 insufficiency had lupus nephropathy, which is above the ~ 50 frequence in the whole cohort. In addition, cases with IgM presented lower frequence of oral ulcers. Piecemeal from IgG4 and IgG3 deficient cases, the remaining cases didn't present a important severe phenotype regarding the presence of infections and lupus instantiations.

Our findings regarding the association of immunoglobulin insufficiency and the development of autoimmune complaint could be incompletely explained grounded on the ‘ waste disposal ’ thesis, which presuppositions that blights on the concurrence of dying cells increases the threat of developing autoimmunity since these cells give the source of bus antigens responsible for driving autoantibody product inSLE.7 also, because SLE is associated with a humoral aggravated response, the presence of a primary dysfunction of B lymphocytes may be considered as a prepping factor for unstable IgG sorts conflation, which may be considered as a factor for the development of SLE. These results suggest that mild immunologic blights might be compatible with patient survival, but at the expenditure of some habitual load and unborn consequences to the vulnerable system, which could lead to the development of vulnerable diseases characteristic of SLE in the majority. The study findings give ground to farther examinations that could deeply explore the participation of PID in the pathogenesis of SLE and other autoimmune rheumatic and non-rheumatic complaint.

Conflict of Interest

None

Acknowledgment

None

References

1. Jerosch J. Effects of Glucosamine and Chondroitin Sulfate on Cartilage Metabolism in OA, Outlook on Other Nutrient Partners Especially Omega-3 Fatty Acids. *Int J Rheumatol.* 969012 (2011).
2. Taniguchi S, Ryu J, Seki M *et al*. Long-term oral administration of glucosamine or chondroitin sulfate reduces destruction of cartilage and up-regulation of MMP-3 mRNA in a model of spontaneous osteoarthritis in Hartley guinea pigs. *J Orthop Res*. 30, 673-678 (2012).
3. Imagawa K, de Andrés MC, Hashimoto K *et al*. The epigenetic effect of glucosamine and a nuclear factor-kappa B (NF-kB) inhibitor on primary human chondrocytes-implications for osteoarthritis. *Biochem Biophys Res Commun.* 405, 362-367 (2011).
4. Uitterlinden EJ, Jahr H, Koevoet JL *et al*. Glucosamine reduces anabolic as well as catabolic processes in bovine chondrocytes cultured in alginate. *Osteoarthritis Cartilage.* 15, 1267-1274 (2007).
5. Jones IA, Togashi R, Wilson ML *et al*. Intra-articular treatment options for knee osteoarthritis. *Nat Rev Rheumatol*. 15, 77-90 (2019).
6. Reginster J-Y, Bruyere O, Neuprez A *et al*. Current role of glucosamine in the treatment of osteoarthritis. *Rheumatology.* 46, 731-735 (2007).
7. Leffler CT, Philippi AF, Leffler SG *et al*. Glucosamine, chondroitin, and manganese ascorbate for degenerative joint disease of the knee or low back, a randomized, double-blind, placebo-controlled pilot study. *Mil Med.* 164, 85-91 (1999).
8. Reginster JY, Neuprez A, Lecart MP *et al*. Role of glucosamine in the treatment for osteoarthritis. *Rheumatol Int.* 32, 2959-2967 (2012).
9. Houpt JB, McMillan R, Wein C *et al*. Effect of glucosamine hydrochloride in the treatment of pain of osteoarthritis of the knee. *J Rheumatol*. 26, 2423-2430 (1999).
10. Scholtissen S, Bruyère O, Neuprez A *et al*. Glucosamine sulphate in the treatment of knee osteoarthritis, cost-effectiveness comparison with paracetamol. *Int J Clin Pract.* 64, 756-762 (2010).