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CASE REPORT

Combined immune thrombocytopenic purpura and immunoglobulin A nephropathy: a similar pathophysiologic process?

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Abstract

IgA nephropathy is one of the most common forms of glomerulopathies. It is an immune complex-mediated glomerulonephritis diagnosed by the presence of mesangial IgA deposits that are often associated with mesangial cell proliferation. The IgG, C_3, IgM, or other immunoglobulin light chains may be co-existed with IgA. Its pathogenesis suggested that it is responsible for enhancing the production of proinflammatory cytokines, chemokines, and growth factors. Platelet-derived growth factor (PDGF) has also been implicated as a modulator of disease activity. Immune thrombocytopenic purpura (ITP) is a bleeding disorder caused by thrombocytopenia that is not associated with a systemic disease. Its pathogenesis suggested an autoimmune disease in which IgG is thought to damage megakaryocytes, which are the precursors of platelet cells. Several studies reported that PDGF levels were higher in normal subjects than in patients with ITP. Moreover, ITP is a disease related to the antibody. Thus, our aim is to examine whether a similar pathophysiological relationship exist between ITP and IgAN that may be mediated by PDGF and/or IgG.

Keywords

IgA nephropathy, IgG, immune thrombocytopenic purpura, PDGF, possible pathophysiologic association

History

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Introduction

Immunoglobulin A nephropathy (IgAN) is the commonest form of primary glomerulopathies world-wide.[1,2] The etiology of primary IgA nephropathy is unclear. IgA nephropathy is initially presented by mesangial IgA deposition, which is composed of predominantly polymeric IgA of the IgA1 subclass (polymeric IgA1).[2–4] The factors leading to disease development are poorly understood, but are thought to include the deregulated synthesis and metabolism of IgA, and the mesangial cell reaction to mesangial IgA accumulation. Furthermore, environmental factors including dietary antigens and mucosal infections may deregulate the mucosal immune system and drive the generation of pathogenic IgA immune complexes. It is also a complex polygenic disease that involves both major histocompatibility complex (MHC) and non-MHC susceptibility alleles.[5] Interleukin (IL)-6 may also play a prominent role in pathogenesis, but other factors including IL-1, platelet-derived growth factor (PDGF), tumor necrosis factor, free oxygen radicals, and vascular cell adhesion molecule-1 have also been implicated as modulators of the disease.[6,7]

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Immune thrombocytopenic purpura (ITP) is a clinical syndrome in which a decreased number of circulating platelets (thrombocytopenia) manifests as excessive bleeding, bruising (purpura), or extravasation of blood from the capillaries into the skin and mucous membranes (petechiae).[8,9] In persons with ITP, the platelets are coated with autoantibodies specific for the platelet membrane antigens that results in splenic sequestration and phagocytosis by mononuclear macrophages. The shortened life span of the circulating platelet cells, together with insufficient platelet cell compensation by the bone marrow megakaryocytes, results in a decreased platelet count. In ITP, an abnormal autoantibody that is usually immunoglobulin G (IgG) with specificity for one or more platelet membrane glycoproteins (GPs) binds to circulating platelet membranes.[10–12] In a previous study, it was determined that the PDGF levels are elevated in patients with ITP.[13] In this article, we presented a case that presented both IgAN and ITP, and examine the possible pathophysiological relationship.

Case presentation

A 26-year-old woman was admitted to our clinic for a routine check-up without complaints. Her history included occasional urine color changes to red and/or brown. The physical examination determined the patient was normal. Laboratory analyses included a complete blood count

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(WBC: 13,900/mm^3, RBC: 5.01×10^6/mm^3, Hb: 15.5 g/dL, Plt: 14,000) and urine analysis (protein (+++), glucose (−), nitrite (−), RBC: 26, WBC: 2). The results of a full biochemistry and other signs indicated the patient was normal. Thus, the patient was determined to have both hematuria and thrombocytopenia. Further laboratory examinations were performed to evaluate the hematologic pathology and the patient's history for thrombocytopenia. The peripheral blood smear showed giant platelets in some areas. The abdominal ultrasonography was within a normal range. The bone marrow biopsy demonstrated an occasional increase in megakaryocytes numbers. Thus, the patient was considered to have ITP. Hematuria was determined using microscopic examination of the urine, which showed dysmorphic erythrocytes and rare erythrocyte casts. The proteinuria level was 1 g/day in a 24-h urine collection sample. Consequently, glomerular disease was suspected and further laboratory analyses revealed a IgA level of 4 g/L (0.7–3.1), while ANA, IgG, IgM, C3, C4, anti-HBsAg, HBsAg, and anti-HCV levels were also within the normal range. Recurrent episodes of painless macroscopic hematuria (brown- or tea-colored urine) were present in the patient and these episodes occurred within 1–2 days of an upper respiratory infection (synpharyngitic). Moreover, in the kidney biopsy revealed mild mesangial cell proliferation and in the immunofluorescence microscopy demonstrating moderate mesangial IgA deposits. Hence, the diagnosis for patient was thought to be IgAN.

Discussion

PDGF is a potent mitogen for cells of mesenchymal origin including smooth muscle cells and glial cells.[14,15] Although it is synthesized and released by the platelet cells upon activation, it is produced by a plethora of other cells including smooth muscle cells, activated macrophages, and endothelial cells.[16] During the late maturation stages, its signaling has been implicated in tissue remodeling and cellular differentiation, and in inductive events that involved patterning and morphogenesis. In addition to driving mesangial cell proliferation, PDGF isoforms have been shown to direct the migration, differentiation, and function of a variety of specialized mesangial and migratory cell types during development and into adulthood.[17] PDGF plays a role in embryonic development, cell proliferation, cell migration, and angiogenesis.[18] It has also been linked to several diseases such as atherosclerosis, fibrosis, glomerulosclerosis, and malignant diseases.[19] In addition, PDGF is a required element in cellular division for fibroblasts, a type of connective tissue cell. It has been reported that PDFG levels are elevated in patients with ITP.[13,20,21] It is believed that growth factors such as PDGF have a role in IgAN pathogenesis.[7,22] Considering that PDGF increases cell proliferation, it may explain the mesangial proliferation observed in IgAN. Hence, the relationship between ITP and IgAN may be mediated by PGDF. On the other hand, it has been reported that patients with IgAN showed IgG and IgM disposition in the mesangium. It is known that IgG has a role in ITP pathogenesis. Consequently, both PDGF and IgG may share common pathways in the pathogenesis of these two diseases. Thus, we first hypothesized that ITP may cause IgAN by elevating PDGF levels. Second, IgG may lead to a common pathway in ITP and IgAN pathogenesis.

Declaration of interest

None of the authors has a financial interest in any of the products or methods mentioned in this article.

References

1. D'Amico G. Natural history of idiopathic IgA nephropathy and factors predictive of disease outcome. *Semin Nephrol.* 2004;24:179–196.
2. Tomino Y. Spontaneous animal model, ddY mouse, for studying the pathogenesis and treatment in patients with immunoglobulin A nephropathy. *Nephrology (Carlton).* 2010;15(1):1–6.
3. Emancipator SN. IgA nephropathy: morphologic expression and pathogenesis. *Am J Kidney Dis.* 1994;23:451–462.
4. Galla JH. IgA nephropathy. *Kidney Int.* 1995;47:377–387.
5. Donadio JV, Grande JP. IgA nephropathy. *N Engl J Med.* 2002;347:738–748.
6. Floege J. The pathogenesis of IgA nephropathy: what is new and how does it change therapeutic approaches? *Am J Kidney Dis.* 2011;58(6):992–1004.
7. Boor P, Eitner F, Cohen CD, et al. Patients with IgA nephropathy exhibit high systemic PDGF-DD levels. *Nephrol Dial Transplant.* 2009;24(9):2755–2762.
8. Stasi R. Patho physiology and therapeutic options in primary immune thrombocytopenia. *Blood Transfus.* 2011;9(3):262–273.
9. Yu HM, Liu YF, Hou M. BAFF – an essential survival factor for B cells: links to genesis of ITP and may be of therapeutic target. *Med Hypotheses.* 2008;70(1):40–42.
10. Stasi R, Evangelista ML, Stipa E, et al. Idiopathic thrombocytopenic purpura: current concepts in pathophysiology and management. *Thromb Hemost.* 2008;99(1):4–13.
11. McMillan R. The pathogenesis of chronic immune thrombocytopenic purpura. *Semin Hematol.* 2007;44(4 suppl 5):S3–S11.
12. Chan H, Moore JC, Finch CN, Warkentin TE, Kelton JG. The IgG subclasses of platelet-associated auto antibodies directed against platelet glycoproteins IIb/IIIa in patients with idiopathic thrombocytopenic purpura. *Br J Hematol.* 2003;122(5):818–824.
13. Katoh O, Kimura A, Fujimura K, Kuramoto A. Progression activity for platelet-derived growth factor in plasma of patients with idiopathic thrombocytopenic purpura and aplastic anemia. *Nihon Ketsueki Gakkai Zasshi.* 1989;52(1):113–117.
14. Hannink M, Donoghue DJ. Structure and function of platelet-derived growth factor (PDGF) an drelated proteins. *Biochim Biophys Acta.* 1989;989(1):1–10.
15. Heldin CH. Structural and functional studies on platelet-derived growth factor. *EMBO J.* 1992;11(12):4251–4259.
16. Vinay K. *Robbins and Coltran Pathologic Basis of Disease*. China: Elsevier; 2010:88–89.
17. Hoch RV, Soriano P. Roles of PDGF in animal development. *Development.* 2003;130(20):4769–4784.
18. Bocci G, Loupakis F. The possible role of chemotherapy in antiangiogenic drug resistance. *Med Hypotheses.* 2012;78(5):646–648.
19. Ostendorf T, Eitner F, Floege J. The PDGF family in renal fibrosis. *Pediatr Nephrol.* 2012;27(7):1041–1050.
20. Kuter DJ. Future direction swith platelet growth factors. *Semin Hematol.* 2000;37(2 Suppl 4):41–49.
21. Shiraishi T, Morimoto S, Itoh K, et al. Radio immunoassay of human platelet-derived growth factor using monoclonal antibody toward a synthetic 73-97 fragment of its B-chain. *Clin Chim Acta.* 1989;184(1):65–74.
22. Naito T, Nitta K, Ozu H, et al. Clinical assessment of the significance of platelet-derived growth factor in patients with immunoglobulin A nephropathy. *J Lab Clin Med.* 1997;130(1):63–68.