Lupus Nephritis Presenting as Idiopathic Thrombocytopenic Purpura (ITP)

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In Systemic Lupus Erythematosus (SLE) mild thrombocytopenia with platelet counts between 1,00,000 to 1,50,000/ cumm have been noted in 25 to 50 percent of patients; Counts less than 50,000/cumm can occur only in 10 percent.

Report of three cases

Introduction

ITP may be the first sign of SLE, followed by other symptoms as long as many years later. Three to fifteen percent of patients with apparently isolated ITP go on to develop SLE1. While mild thrombocytopenia [platelet counts between 1,00,000 to 1,50,000/cumm] have been noted in 25 to 50 percent of patients of SLE; counts less than 50,000/cumm occur in only 10 percent².

Case 1

S.J. 38-year-old female was seen at Mumbai for haematuria and puffiness of face since June 1997.

In 1988, she was investigated for menorrhagia, bleeding from ears, nose, gums and haematemesis. She gave a history of arthralgia involving both small and large joints and erythematous rash. Laboratory investigations then confirmed that she had idiopathic thrombocytopenic purpura. [Antiplatelet antibodies were detected]. ANA and anti DS DNA were negative. Patient received several immunosuppressive drugs including Azathioprine and Danazol with only temporary response. She underwent splenectomy in February 1990. In January 1997, she developed asymptomatic urinary abnormalities and in June, 1997 she was referred to nephrologist for frank haematuria with puffiness of face.

On examination the positive findings were: cervical lymphnodes were palpable, she was pale. She had erythematous malar rash on both the cheeks. There were nodules on the skin just above the eyebrows; neck and behind the ears. She was normotensive.

Her liver was just palpable. Investigations at this stage in December, 1997 revealed urine protein ++, pus cell 8 to 10/ HPF and R.B.C’s 10 to 20/HPF. Haemoglobin was 9.0 gm with HCT of 22.9; white cell count [WBC] was 7200/cumm with platelet count [PC] of 1,80,000/cumm. Her prothrombin time was 15/seconds with control of 15 seconds.

APTT was 33 seconds (Control: 32 sec.)

Serology revealed the following:

- ANA + ve (> 1:160)
- Anti DS DNA negative
- Anti SS DNA (1:64)
- CIC 139 PEG units
- PAlgG 34.8mg/10⁶ platelet
- Lupus anticoagulants negative

Direct and indirect antiglobulin test on patients red cell-negative.

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Biochemical investigations revealed BUN = 10.0 mg; Serum creatinine 1.0 mg, serum Na+ 137.0 mEq/L, K+ 4.3 mEq/L, Creatinine clearance = 101 ml/min.

Her ultrasonography of kidney and urinary tract revealed

Right kidney 9.8 cm/3.4 cm
Left kidney 10.2 cm/4.1 cm; with normal echo-genicity and P.C. System; with impairment of cortico-medullary ratio.

As the patient was reluctant for renal biopsy she has been observed closely. Her follow up shows that her urinary abnormalities have reduced with a trace of proteinuria; three to five pus cells/HPF, with R.B.C.'s 8-10/HPF, spot protein/creatinine ratio 0.32.

A diagnosis of systemic lupus erythematosus with lupus nephritis presenting nine years earlier as ITP has been made.

Case 2

D.T.F. 43 years, mother of two children, with no pregnancy related complications. Last delivery was in 1980.

In December, 1992 at the age of 37 years, patient consulted a physician for menorrhagia. On examination her B.P. was 130/80 mmHg. Apart from pallor there were no positive findings clinically. Investigations showed: Hb 4.4 gm%; TC 7100/cumm, PC 40,000/cumm, BT 15 min. and CT two min, 40 sec. USG of pelvic organs was normal. Patient was diagnosed to have idiopathic thrombocytopenia and treated with fresh blood transfusion and steroids. She responded and PC increased to 2,10,000/cumm and BT three min. 15 seconds in two weeks.

From May 1993 to July 1997, she had repeated episodes of purpuric rashes and menorrhagia for which she had been given steroids. Anti DS DNA was positive: 190 IU/ml. In September 1997, she was referred to nephrologist for investigation for oedema of feet and ascites. On examination she was normotensive. She had oedema of feet and ascites.

There were no purpuric spots or hepatosplenomegaly. On investigation urine showed +4 protein, 15-20 RBC/HPF and hyaline casts, 24 hours U.Alb: 1.39 gm, PC 1.93,000/cumm, S.creatinine 0.6 mg/dl. Remission was achieved with steroids and was maintained for one year.

In August 1998, she had relapse of proteinuria; Hb 12.8 gm percent, TC 15,200/cumm, PC 3,51,000/cumm, BU 32.0 mg/dl, serum creatinine 1.0 mg/dl, U.Alb. +2, over 24 hours. RBC 0-2/HPF, WBC 2-5/HPF and ANA +ve. Kidney biopsy was done which was s/o membranous nephropathy. [Fig 1 and 2] IF: IgG, C3 along capillary wall. A diagnosis of WHO class V Lupus nephritis was made.

Case 3

Nineteen-year-old female, JP, presented to her local physician four years ago with complaints of purpuric skin rash and right leg oedema. Laboratory evaluation showed Hb 10.2 gm percent; total WBC 6800/cumm with and platelet count 13000/cumm with prothrombin time 15/13 seconds. A presumptive diagnosis of idiopathic thrombocytopenic purpura was made and treated with steroids. Her purpuric rash responded, however, oedema of right leg persisted. It was thought to be due to deep venous thrombosis and treated with oral anticoagulants. She took this treatment for a few months and switched to ayurvedic medication. One year ago she was seen at another hospital for erythematous facial skin rash and fever. Lab investigation showed an active urine sediment, serum creatinine 2.0 mg percent and ANA which was positive. Renal biopsy tissue was inadequate. She was referred here for further evaluation. On examination her B.P. was 160/100 mmHg. She was pale, had a malar skin rash and was oedematous. Investigations showed Hb 6.2 gm percent; total WBC 11,900/cumm; Platelet count 282 x 10^5/cumm. Urine examination showed Alb 2+, RBC 5 to 10 per 24 hours urine protein was 600 mg. Serum creatinine was 2.0 mg percent. Tests for ANA and DsDNA were positive. Renal biopsy showed diffuse proliferative lupus nephritis with full house immunofluorescence. She was treated with steroids, pulse...
cyclophosphamide and antihypertensives. A fortnight later, she returned with generalised tonic-clonic convulsions. Her renal function deteriorated, CT scan of the brain showed multiple hypodense lesions suggestive of infarcts. APTT was prolonged and tests for antiphospholipid antibody were positive. Blood pressure was aggressively controlled, anticonvulsants were added and dose of steroids were stepped up. She improved gradually. Her last evaluation a month ago showed S. Cr. of 0.8 mg percent, urine sediment was inactive and APTT had normalised.

Discussion

ITP is an autoimmune bleeding disorder characterized by development of autoantibodies to one’s own platelets. Although ITP is a self-limited disease in children, it tends to run a chronic course in adults. ITP may be primary or secondary to systemic disease; most commonly systemic lupus erythematosus.

Here, we report three cases of ITP that developed SLE with renal involvement subsequently; during their further course of illness.

In 1960, Rabinowitz and Dameshek emphasized the close relationship between ITP and SLE and suggested that ITP is often a prodrome of SLE[1]. Both ITP and SLE are autoimmune disease, which are pathogenically linked and may share common antiplatelet antibodies[2]. These antibodies are found to be directed against functional glycoprotein components of platelet membrane, including the Gp Iib/IIa and Gp Ib/ix complexes. Diagnosis of ITP is usually one of exclusion of underlying systemic disorders like SLE. Approximately 20 percent of patients with SLE develop ITP at some stage during their course. Whether this is due to specific antiplatelet antibodies against common antigens also found on platelets or to immune complexes is unclear.

Occasionally, ITP occurs in patients who have serological evidence of SLE but who do not meet all of the criteria for the diagnosis of SLE. High-titer ANA and antibodies to SSA/RO or nRNP antigens are often found in patients with ITP but existence of antibodies to SSA/RO or nRNP antigens by itself is not enough to identify those patients with ITP who are at risk of developing SLE[3].

However, patients with a positive ANA are more likely to be older girls with chronic ITP, who are at risk for the development of generalised autoimmune disease. So, patients with ITP and a positive ANA should receive careful follow up for the development or manifestation of other autoimmune diseases and common pathogenic mechanisms between these two entities should be further evaluated[4].

Though, splenectomy is not a treatment of choice in thrombocytopenia due to SLE; several cases in literature have undergone such therapy especially where thrombocytopenia has preceded with manifestations of severe bleeding like menorrhagia as seen in our first case reported here. The diagnosis of SLE was made almost 9-10 years after the first manifestation of severe thrombocytopenia where serology was negative. This case resembles a case published by Yalcin S et al., who reported lupus nephritis in a patient with ITP diagnosed 11 years earlier[5]. Such association though uncommon must be kept in mind in clinical situations associated with thrombocytopenia which has a chronic course. Our Case 1, which manifested with thrombocytopenia had anti S-s antibody 11 years later when she was diagnosed SLE as reported by Adachi et al.[6] Meticulous. Follow up is the only way to arrive at the diagnosis in such cases. Our Case 2 exemplifies typical course with definitive histological diagnosis on kidney biopsy correlated with serology much later during the course of illness.

References