Subarachnoid Haemorrhage Complicating Resistant Idiopathic Thrombocytopenic Purpura: A Case Report

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Abstract:

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disease where low platelet counts predisposeto various bleeding tendencies; intracranial haemorrhageis one of them. It is a rare and devastating complication of ITP, mostly presenting as intracerebral (ICH) or subarachnoid haemorrhage (SAH). Here, we report a 32-year-old splenectomized chronic ITP patient on corticosteroid and azathioprine, in whom spontaneous SAH developed. In this case, conservative management resulted in clinico-radiological improvement and showed eventual favourable out-come.

Key words: Idiopathic thrombocytopenic purpura, subarachnoid haemorrhage.

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Introduction:

Idiopathic thrombocytopenic purpura (ITP) causes a characteristic purpuric rash and an increased tendency to bleed.[1] Two distinct clinical syndromes manifest; an acute condition in children and a chronic condition in adults. Serious and possibly fatal complications due to extremely low platelet counts (<5,000/cmm) include subarachnoid or intracerebral hemorrhage, lower gastrointestinal bleeding or other internal bleeding. The mortality rate due to chronic ITP varies but tends to be higher relative to the general population for any age range. Although no data in our country, in a study in Great Britain, it was noted that ITP causes an approximately 60 percent higher rate of mortality compared to gender- and age-matched subjects without ITP.Treament varies according to presentation ranging from observation to steroid, anti-D, steroid sparing agents, platelet transfusion, immunoglobulin, splenectomy and novel agents like rituximab.

Case Report

A 32-year-old female was admitted with a 5-days history of petechial rashes on both lower limbs. She was a splenectomizedchronic ITP patient for last 3 years and was on maintainance steroid and azathioprine along with bisphosphonate, calcium and vitaminD. Since her diagnosis she needed 60 mg of prednisolone regularly to control her symptom with history of relapse upon steroid dose reduction. So, she underwent splenectomy and azathioprine was also required for last two years. This time we increased her prednisolone to 80 mg daily and azathioprine to 100 mg daily as steroid sparing agent.Six days after admission she suddenly developed severe headache; which wascontinuous and throbbing in nature, gradually increasing in intensity. On examination she was pale, normotensive with tachycardia and she gradually became semiconscious without any other focal neurological dysfunction. Few purpuric spots were also noted on her upper limbs. Ocular fundi examination showed subhyloidhaemorrhage.

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At the time of admission, haematological investigations revealed haemoglobin of 8.0 gm/dl with normal total and differential leukocyte counts. Platelet count was 5,000/cmm. Liver and renal function tests were normal. Autoantibody screen was negative. CT scan of the brain revealed SAH (Figure 1). She was given four units of platelet transfusions and IV methylprednisolone, nimodipineand antiemetic. Intravenous immunoglobulin could not be given as it was too costly. The platelet count rose to 26,000/cmm over a period of 5 days. She showed steady improvement in her symptoms over a period of 15 days. In follow-up her platelet counts were serially monitored that remained within 20 to 24,000/ cmm.

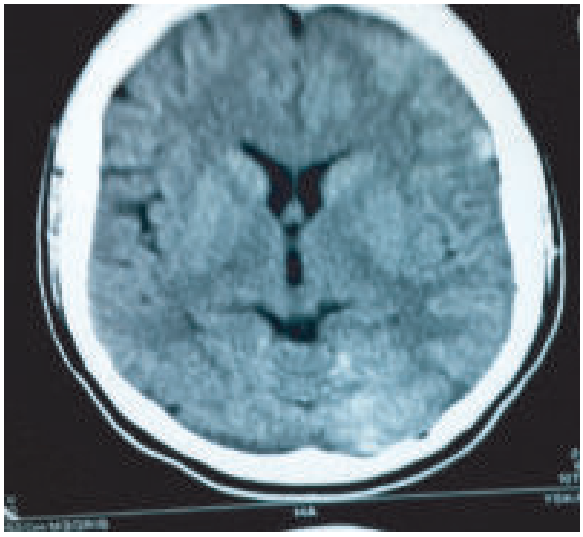

Fig.-1: *CT scan of brain showing subarachnoid haemorrhage*

Discussion:

Platelets play a very important role in haemostasis by forming thrombic plugs which helps in occluding small vessels particularly capillaries. According to Psailaand Bussel[2] antibodies bound to platelet antigens opsonize platelets for clearance by FcãR-bearing cells, mainly in the spleen. Thus Platelet disorder leads to leaking capillaries and in central nervous system thismay cause life threatening intracerebral or SAH. SAH is rare in ITP and a few numbers of cases have been found.[3]

In a metaanalysis, Lee and Kim[3] examined 31 patients with ITP complicated by ICH, in 24 patients there was SAH and a subdural hemorrhage was present in seven. Mean age of the patients with ICH was significantly lower than that in those with subdural hematoma. The mortality rate associated with ICH in ITP those was similar to that in those with spontaneous ICH. In 1998, 74 cases of CNS bleeding associated with ITP were reported[4]. The risk of ICH in ITP is 0.1–1% and occurs predominantly in patients with platelet counts below 5–20,000 cu mm. During the first few days episodes of ICH are extremely rare and the riskof bleeding is 0.1–0.2%.[5]

The onset of ITP in our patient was not associated with any clinically signifcant bleeding despite extremely low platelet counts (10,000cumm). ICH occurred 3 years later when the platelet count was 5,000cumm.

Any condition that results in thrombocytopenia theoretically predisposes a patient to bleeding disorders, including ICH. These conditions may be 1) decreased platelet production, as seen in certain congenital disorders and cases of bone marrow involvement due to radiation, drugs, vitamin B12 or folic acid deficiency, leukemia or myelodysplastic syndrome 2) increased platelet destruction, as in ITP, and other diseases including thrombotic thrombocytopenic purpura, post-transfusion purpura, and DIC 3) abnormal sequestration, usually in the spleen, as in cirrhosis. Cases of thrombocytopenia-induced ICH have been linked to use of certain medications, as well as to uremia, alcohol use, and liver transplants or medication.

Our patient was a known case of ITP without any features of other causes of thrombocytopenia and relevant investigations including blood counts, liver and renal function tests and autoantibody screen were normal.

Koide et al. studied 96 patients who had hemorrhagic cerebrovascular disease. Among them, only 16 (16.7%) had thrombocytopenia, half of them presented with SAH and the remaining showed intraparenchymal hemorrhage.[6] In another study- seven adults, aged 16 to 61 years, with idiopathic thrombocytopenic purpura, having a life-threatening episode underwent emergency splenectomy. Six patients had progressive intracranial bleeding and one had postsurgical intra-abdominal bleeding. All patients were saved by surgery, except one for whom operation was delayed. There was no postoperative bleeding or surgical complication.Here immediate splenectomy was the treatment of choice in any patient with idiopathic thrombocytopenic purpura

complicated by life-threatening hemorrhage. But Verloy P, Lamers BJ, de Haan GJ et al managed successfully a patient with bilateral subdural haematomas with platelet rich plasma and immunosuppressive therapy with steroids.[7]

Our patient was already splenectomized and responded to platelet rich plasma and immunosuppressive therapy with steroids.

Half of ITP patients have additional risk factors for ICH including malformation of cerebral arteries or veins, CNS injury, menstruation, infection (e.g. viral), autoimmune disease (lupus erythematosus. Spontaneous ICH during ITP is seen in the remaining 50% of cases.[8]

In our patient, brain injury, autoimmune disease and medication were excluded. Angio-CTcould not be done, thus we have no data regarding the presence of vascular malformations. Neurologic symptoms in a patient with ITP should be quickly evaluated by CT scan.It is mainly due to haemorrhage into the intracranial compartment and is dependent on the severity of thrombocytopenia. Most experts suggest careful observation for most cases of ITP. However, when neurologic symptoms progresses, more aggressive treatment- emergency splenectomy and craniotomy options must be used. In the earlier studies, the incidence of intracranial haemorrhage ranged from 0.65 to 26 per cent. However, more recent surveys showed an incidence of about 2 percent .The decrease in the incidence of this complication is mainly due to early diagnosis and better management.[9]Splenic artery embolization and recombinant activated factor VII was also used successfully in two different cases having CNS bleeding complicating ITP.[10,11]

In our case, the patient was complaining of severe headache, vomiting, semiconsciousness requiring emergency treatment. Surprisingly patient's symptoms completely resolved over a period of 15 days after raising the platelet count. This may have been possible due to inhibition of repeated capillary micro-haemorrhages by improved platelet function.It should also be noted that a spontaneous, gradual increase in platelet count was observed after discharge.Our case showed that trial of conservative management with elevation of platelet count can be suggested in a case of SAH associated with ITP.

Conclusion:

The aspect of ICH during recurrence of ITP is very interesting, and warrant further investigations to work out prophylactic therapy before incidence of its recurrence with all possible complications. Prompt recognition and early intervention are the keys to improving outcomes when ICH complicates ITP. The mortality is higher in ITP patients poorly responding to steroid therapy and/or intravenous infusion of immunoglobulins.[9]Our patient did respond to high doses of platelet preparations and steroid during the ICH episode.

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