Case Report

Idiopathic thrombocytopenic purpura (ITP) – a rare cause of PPH

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Abstract

A patient named Mrs R.B aged 22 yrs Para 2 was admitted with bleeding per vagina for last 2 months since her delivery and purple spots over the extremities over last 10- 15 days. She attended several hospitals and received treatment along with 14 bottles of blood transfusions. Still she continued bleeding per vagina and her Hb% in next day of admission was 2.7 gm%. Her platelet count was less than 10,000. After a lot of deliberation, the case was diagnosed as P2L1 with secondary PPH due to chronic Idiopathic Thrombocytopenic Purpura. She was treated accordingly. She received PRBC 7 units, platelet 6 units, whole blood 1unit. She was discharged after her secondary PPH was cured with Hb% 11.6 gm% and platelet count 140000/cumm. The ITP is a diagnosis of exclusion. The case is presented to highlight that in the management of PPH, if the treatment does not respond, one should think of rare cause like ITP. It is the awareness of the doctors that can help the patients.

Keywords: Idiopathic thrombocytopenic purpura, awareness.

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HISTORY OF PRESENT ILLNESS

The patient complains of bleeding per vagina for last 2 months following birth of a child on 18th July'12.The bleeding was bright red in color without passage of clots and was not foul smelling. The patient had delivered a term 2 kg female baby at Kamal Singh Primary Health Centre on 18th July'12, spontaneous vaginally and there was history of primary PPH. Subsequently she was discharged, but at home she had again developed excessive bleeding per vagina, for which she was admitted into Kokrajhar Civil Hospital Where she received one unit of BT, antibiotics and oxytocics and was referred to Bongaigaon civil Hospital with a diagnosis of "P2 with primary PPH with severe anaemia with puerperal sepsis." But patient went home and as she was not relieved, was again admitted into a private nursing home "Subham Hospital Kochbihar", West Bengal. In that Hospital, D and E ws done on 27th August'12 and she received 8 units of blood transfusion with antibiotics and other conservative measures. She was discharged after D7 of hospital staying. At home she again developed the same problem and attended Gauhati Medical College Hospital (GMCH) - Emergency on 21st September'12. During the admission period she received 6 units of blood transfusion, antibiotics and again D and E was done and was discharged on 24th September 12. At home, again she had heavy vaginal bleeding, with purple spots on the extremities (10-15 days) with severe general weakness, giddiness and fall down twice. So, she has attended GMCH Emergency on 28th September'12.

History of current Pregnancy

1st Trimaster- She had usual 1st trimaster symptoms. There was no history of any other Drugs and X-ray exposure. 2nd Trimester - No h/o pain abdomen, bleeding or discharge per vagina. She had three antenatal check up in 2nd trimester. She had received Tab Iron, Folic acid and Calcium regularly and no abnormal finding was detected in all the three ANCs. In second trimester, no H/O bleeding or discharge P/V, 3rd Trimester. She complains of increase frequency of micturition again without burning sensation. She had three ANC during 3rd trimester and nothing abnormality was detected. There

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was no history of bleeding or any discharge P/V during that period. She was taking IFA and Calcium tab regularly.

History of labour

The onset of pain was on 18-07-12 in the morning, when she was at home and she was brought to the Kamal Singh PHC on the same day. The pain was gradually increasing, intermittent in nature and spasmodic in character. She delivered a healthy female baby of 2 kg spontaneous vaginally on same day without episiotomy. There was primary PPH after delivery of the baby.

Baby Tone

Female	2 kg
18/07/2012	Time-??

The baby cried immediately after birth. The baby was given breast feeding within 30 minutes of delivery. The baby feeds well and sleeps well. No prelactal feed was given initially. The baby passed meconium 8 hours after delivery and micturated 6 hours of delivery. But after one week, due to ill health of the mother artificial feeding was given. The baby vomited frequently after artificial feeding and died after two months of age due to unknown reason. Menstrual History- Cycle: 28-30 days, Regular. Duration of Bleeding phase 8 - 10 days. Flow: Amount-average not associated with passage of Clots, 6 - 7 pad/day. Contraceptive History: Patient has taken Oral contraceptive pills for few cycles before this pregnancy, but she could not remember the period when she has taken it.

Other History

NO past history of Jaundice, Rheumatic Fever, Heart Disease, Hypertension, DM, TB, Asthma, Kidney Disease, Venereal Diseases, thyroid disorder, malaria, blood dyscrasias. History *blood transfusion* present for PPH of the current pregnancy. *Past surgical history*: She had not undergone any major gynaecological and general surgical intervention. **Family History:** No. H/o similar disease in Family members. No h/o Hypertension, DM, TB, Asthma, Multiple pregnancies, Hereditary Diseases, Jaundice, Liver Disease, blood dyscrasias, congenital malformation in the family. **History of allergy:** Nothing suggestive.

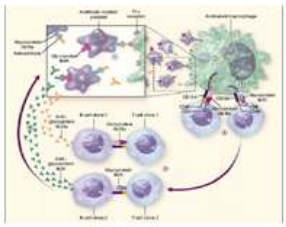
EXAMINATION (28/09/12 at 06:30 AM) Appearance-Ill looking. Mental state and Intelligence- Alert, conscious of average intelligence. Nutrition status-average Pallor- Severe pallor present. Icterus- Absent. small purpural spots are seen in upper limbs. Per abdominal examination: Few *Small purpural rash seen.* No local raise of temperature. Soft and tenderness present over lower abdomen. No palpable lump present. Spleen and liver not palpable. Perineum examination : A. Inspection: Vulval pad and surrounding clothes were soaked with fresh blood. No swelling, tear, laceration was noted in the perineum and in the paraurethral area. Sphincter reflexes appeared normal. B.Palpation :- No local raise of temperature. Perineum was soft and no swelling was found. Labia majora Labia minora, urethral orifice appeared normal. Per speculum examination: Vagina was full of clots. Os – Parous (after removal of clots). Cervix – Healthy. Fresh blood was coming out through os. Vaginal wall healthy, no growth or tear, laceration. Per vaginal and bimanual examination: Cervix normal and parous. Os open, permits one finger, soft. No other mass palpable, uterus bulky, adnexae free. Per rectal examination: Rectal mucosa free. No pararectal haematoma present. Tone of the anal sphincter normal. Systemic Examination- Normal. *Gastrointestinal system.* No organomegaly detected.

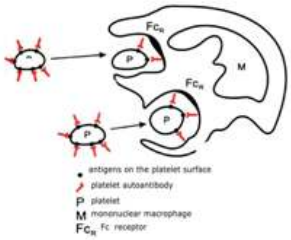
Basic information of ITP

In ITP autoantibodies or immune complex bind to platelets and causes their premature peripheral destruction. Chronic ITP is an *indolent* disorder of *insidious onset* with multiple remissions and relapses, occurs predominantly in *adult* women(3F:1M),and is not preceded by infection or associated with any underlying disease. *Spleen is not palpable in chronic ITP* and in presence of splenomegaly, alternative diagnosis should be considered. Incidence in pregnancy is 1-2/1000 live births; accounts for about 3% of cases of of thrombocytopenia at delivery. Autoantibodies IgG > IgM are directed against specific platelet glycoproteins GpIIb/IIIa or GpIb/ix in majority of patients. GpIIb /IIIa are sites for fibrinogen binding during platelet aggregation. Thus, in addition to causing destruction of PLT, these autoantibodies also induce PLT dysfunction by blocking GpIIb/IIIa receptors. Antibody coated PLTs are recognized by Fc receptors on macrophages and rapidly destroyed mainly in spleen. Won Y W *et al* (Re.7) reported 31 pregnancy with chronic ITP diagnosed before or during pregnancy, the treatment protocol include platelet transfusion (48.4%), corticosteroid (22.6%), IV IgG (16.1%). The delivery by C.S was 51.7%, vaginal delivery was 48.3%. The bleeding was not excessive during delivery. There was no case of infant suffering from clinical sign of hemorrhage. Hence, they conclude that safe delivery is possible with healthy baby. In our case, the immense suffering was due to not getting the proper diagnosis. Health Unlocked (Ref. 8) reported a case of five and half months of pregnancy with platelet 22,000/cu mm- a case of chronic ITP. She was getting prednisolone and IV IgG. Her platelet count has improved, which was similar to our case. The American College of Haematology (Re.9) in their guideline in 2011 said that a pregnant patient with ITP should get

corticosteroid and IV IgG. The mode of delivery should be as per obstetric indication.

The foetus may get affected by autoantibody crossing placenta. The newborn (10%) may be affected from ITP mother with platelet less than 50,000/ cu mm (Re. 10, 11). In 1- 2% cases, there may be intracranial hemorrhage (Neonatal autoimmune thrombocytopenia-NAIT). In our case the baby may have suffered from similar problem but the baby died before the case came to us. As per severity, platelet transfusion may be necessary in newborn. It is recommended that serial platelet count should be done in 1st few days of life in such newborn.





Provisional diagnosis

The patient Mrs R B, P2L1, 22 years Hindu from Kokrajhar district presented at 71 days of normal vaginal delivery with past H/O menorrhagia, no family H/O bleeding disorder now presented with *PPH, severe pallor, purpuric rash, not responding to DandE, antibiotics, haemostatics and repeated blood transfusions has provisionally diagnosed as a case of "P2L1 with secondary* PPH due to ITP."

Differential diagnosis

ITP, DIC, Massive BT, Post transfusion purpura, Infection, SLE, HIV, Cirrhosis, Hepatitis C, Leukemia, Aplastic anaemia, Mylodysplasia Medications(Quinine, Heparin, Cephalosporin, Vancomycin, Lithium, Digoxin, Isoniazid, cytotoxic drugs, penicillin), Radiation Congenital heart disease, Osteopetrosis, Evans syndrome, Megaloblastic anaemia.(Folate, B12, anorexia). Hypersplenism, Hypothermia, Metastatic carcinoma, Pre-eclampsia, HELLP

Evaluation of thrombocytopenia

Low platelet count - CBC and PBS to be done - If no abnormality of other blood cells. Causes may be: ITP, TTP, Drugs, Autoimmune disorder, HIV infection. If abnormality of blood cells present:- Causes may be :- ITP, TTP(Thrombotic thrombocytopenic purpura), HUS, DIC, aplastic anaemia, hypersplenism, pseudothrombocytopenia,megaloblastic anaemia, leukemia, mylodysplasia. *(Haematology by Dr S M Kawthalka)*

INVESTIGATION

Date	INV	Result
	Blood gp	O+ve
28/9	Hb%	2.7 gm/dl
	RBS	60 mg/dl
	S. Creat	0.6 mg/dl
	Tc	7880/cumm
	DCL	N55, L38, M7, Eo
	PT	13.6 sec
	APTT	32.4 sec
	LFT	Total biliburin= 2.1mg/dl other=WNL
	S. Beta HCG	<2 mIU/ml
	PLT	Next Slide

Date	INV	Result
	DTC	Negative
	ICT	Negative
	CRP	5 mg/l
	Urine for Hb	Not detected
	HBsAg	NR
	HIV	NR
	Anti HCV	NR
	VDRL	NR
	S. TSH	1.56
	Free T4	11.9
	BT	2 min, 30 Sec
	CT	3 min 45 Sec

Investigation (PLT)

Date and Place	PLT Count/Cumm
26/08/13 Kochbihar	PLT count=1.2 lac
28/09/12 GMCH	PLT count=1.9 lac
01/10/12 GMCH Haematology Lab	PLT count= below 10,000
03/10/2012 GMCH	PLT count= 47,000
08/10/2012 GMCH	PLT count= 9,500
31/10/2012 GMC	PLT count=1.4 lac

Investigation

Date	Test	Result
01/01/2012	RBC	0.78 millions
	HCT	7.7%
	MCV	98.7
	MCH	29.5pg
	MCHC	29.9 g/dl
	DLC	N 68, L22, M6, E3, B1
	Other Investigation	
	ANA	Negative
	USG	No arganomegaly present
		Uterus bulky (9.8 x 6x 4.3) Cm3. Minimal endometrial collection
	PBS	Normal
	CBC	Normal

Bone Marrow aspiration report after Rx (31/10/2012)

Test	Result
HB	11.6 gm %
TC	5,300 /Cumm
PLT	140, 000/Cmm
DLC	
N	82%
L	15%
E	3%
M	0%
B	0%
Megakaryocytes	2%
Myelogram	1%
blast	
Prom yelocytes	2%
Myelocytes	9%
Metam yelcytes	10%
Band neutron	18%
Segmented	23%
Neuto	
Lymphocytes	15%
Erythroblast	20%

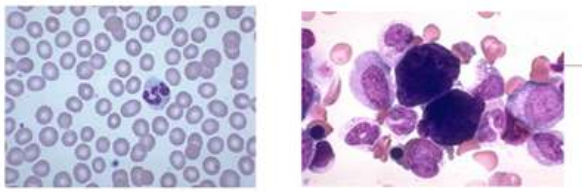


Figure 1: Two bare megakaryocyte nuclear masses ITP marrow

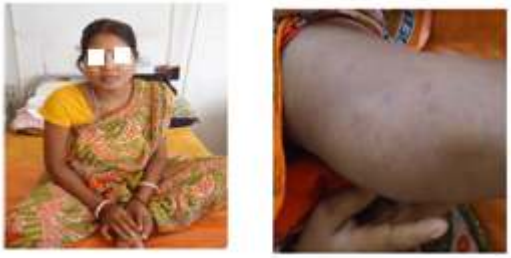


Figure 2: Coming to the final diagnosis by exclusion of other causes

(Exclusion of other causes)- The diagnosis of ITP is a process of exclusion. First we should determine that there are no blood abnormalities other than low platelet count, and no physical sign except for signs of bleeding. To exclude other causes DIC: Coagulation screen - BT, CT, PT, APTT was normal), Massive BT: Both Coagulation factor (FV and FVIII) and PLT decrease. Infection- (No fever, Tc, DLC, CRP normal, no splenomegaly, PBS MP absent), SLE (ANA negative), HIV (HIV I and II NR), Cirrhosis (No related C/F,USG,LFT not suggestive), Hepatitis C (HCV – NR), Leukemia (No abnormal leucocytes in PBS, Bone marrow), Aplastic anaemia. (No pancytopenia, BM), Mylodysplasia (No abnormal leucocytes, BM), Post- transfusion purpura: Rare, bleeding occurs 1W-10D following BT in multiparous, donor PLT contains HPA-1a Ag which is lacking in Pt's PLT, but sensitised with previous fetus. Radiation: (No history), Medications(Quinine, Heparin, Cephalosporin, Vancomycin, Lithium, Digoxin, Isoniazid): (NO H/O using such drug), Congenital heart disease- (No history, no suggestive C/F), Osteopetrosis (BM), Evans syndrome : (DCT and ICT Negative), Megaloblastic anaemia- (Folate,B12, anorexia) (No macrocytosis), Hypersplenism-(No splenomegaly, pancytopaenia) Hypothermia-(No history), Antiphospholipid syndrome, Metastatic carcinoma (No C/F and BM), Pseudothrombocytopenia (No PLT clumping)

DIAGNOSIS OF ITP

Diagnosis of ITP is based on combination of the following features :-Mucocutaneous type of bleeding insidious onset in chronic ITP,No other abnormality on physical examination, presence of isolated thrombocytopenia in CBC. (iron deficiency anaemia may be present due to excessive blood loss.), Bone marrow examination is normal, Exclusion of other causes of thrombocytopenia. (From Essentials of Haematology 2008.1st Edn.)

Final diagnosis

The patient Mrs R B, P2L1 presented at 71 days of normal vaginal delivery with past H/O menorrhagia, no family H/O bleeding disorder, now presented with secondary PPH(off and on bleeding after delivery) *with severe pallor, purpuric rash, no organomegaly with thrombocytopenia*, *normal PBS* and *BM study not responding to D* and *E, antibiotics, haemostatics and repeated blood transfusions has finally diagnosed as a cases of* ***P2L1 with Secondary PPH due to chronic ITP***

Treatment

Aim with drugs that reduces reticuloendothelial uptake of antibody bound PLT, Decreases antibody production,Increases PLT production. Commonly used drugs are :- Steroids (Prednisolone 1mg/kg), Rh(D) immunoglobulin in Rh- positive patient, Intravenous gamaglobulin (IV IgG), dose 2 g/kg total in divided doses over 2-5 days. (Fc receptor blocker), Refractory cases – Additional immunosuppressive. Azathioprine, Thrombopoietin receptor agonist :- Romiplostim (Sc route), Eltromobopag(oral), Splenectomy.(Rarely done now),PLT transfusion :- Only in emergency situations, H. pylori eradication, Experimental :- Dapsone, Rituximab a monoclonal antibody against B cell.

Management

A.Resuscitation B. Blood and blood product-SHE RECIEVED PRBC 7 U, PLT 6 U AND WHOLE BLOOD 1 U, C. *Antibiotics and other conservative treatment,* Inj Ceftriaxone 1 gm IV 12 hourly ANST, Tab. Regestrone 5 mg TDS, Tab. Folvite 5 mg TDS. Viminta

Powder 2 tsf with milk 12 hourly, Inj Iron sucrose 200 mg in 100ml of NS a/d, Tab Trapic 500 mg TDS,*D. Definitive treatment for ITP*- Inj Methylprednisolone 1gm in 300 ml of NS IV slowly daily into 3 days given. Tab. Prednisolone 80 mg once daily x 14 days given. Next Tab. Prednisolone 40 mg once daily continued until and after discharge. Intravenous immunoglobulin (IV Ig) 1 gm/kg/day for 2 days given.

Discharge

Patient condition was gradually stabilized; she was discharged from hospital on 06/11/12. At the time of discharge she was asymptomatic, Hb%= 11.6gm%, Tc= 5300/Cumm, DLC= N82+ L15+ E3+ M0+B0 PLT= 140,000/Cumm, Tab. Prednisolone 40 mg OD to continue till further visit. After about one month, she came for check up and she has taken prednisolne tab for about 1month. She was in good health. Usualy tab prednisolone tab is tapered of in about one month. She is doing well till last contacted over phone.

CONCLUSION

When usual line of management of PPH does not respond, one should think of other rare causes like ITP. History and Clinical examination are more important than the laboratory investigations for diagnosis. Sometime the laboratory report may be misleading. If one has serious doubt, the test to be repeated in good laboratory. ITP is a diagnosis of exclusion. It is the awareness of the Doctors that can help patients. It is the multidisciplinary approach of Haematologist, Pathologist and Gynaecologist for the diagnosis and management of ITP.

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