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MICROANGIOPATHIC HEMOLYTIC ANEMIA –A RARE CASE REPORT

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ABSTRACT

Thrombotic microangiopathy results from thrombotic occlusion of the microvasculature leading to fragmentation of red blood cells, profound thrombocytopenia, and a microangiopathic hemolytic anemia with elevation of lactate dehydrogenase and negative direct Coomb's test.

MICROANGIOPATHIC HEMOLYTIC ANEMIA –A RARE CASE REPORT

23 year old, G3P2L2, previous two Caesarean sections, with history of 4 months amenorrhoea, admitted for complaints of bleeding per vaginum for the past two days and expulsion of foetus following intake of mifepristone and misoprostol.

She had Irregular cycles, normal flow lasting for 5 days.
Obstetric History of 1st full term caesarean section, antenatal and postnatal period was uneventful.

2nd pregnancy was a full term caesarean section. History of 2 units of blood transfusion for postnatal anaemia.

On examination, anaemic. Per abdomen, no guarding, uterus 16 weeks. Per speculum cervical os open, products of conception seen.

On bladder catheterisation, 200ml blood stained urine drained. Culdocentesis negative. Hemoglobin level dropped to 6.4gm%

Bladder rent was suspected in view of hematuria. Hence proceeded with laparotomy along with urologist. Bladder was found to be intact. Tubal sterilisation done. Check curettage done.

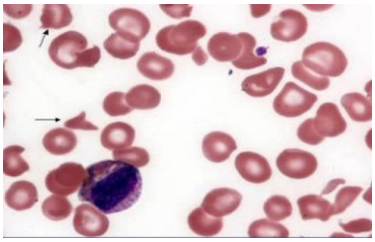
On day 2, patient had persistent hematuria, was anaemic with purpuric rashes and abnormal renal parameters. Treated with 10 units Fresh Frozen Plasma, 3 units Whole Blood, 1 unit Packed Cells and intravenous antibiotics. On day 4, patient deteriorated. Respiratory failure set in. Patient intubated.

TABLE 1: INVESTIGATIONS OF PATIENT ON SUBSEQUENT DAYS:

Hb	**6.4g**	**6.7g**	**7.9g**	**6.6**	**5.7**	**4.9**	**3.9**	**9.5**	**10.9**
Platelet	D1	1.95	0.77	1 lakh	0.3	0.54	0.43	0.66	1.06
urea	32	82	101	73	40	30	32	34	32
creatinine	1.02	1.65	1.34	1.02	1.2	1.1	1.1	1.04	1.02
BT	3min	4min	3min	2min	3min	3min	3min	3min	3min
CT	5min	5min	4min	4min	5min	5min	4min	4min	4min
S.Biirubin		1.6mg	3.41		1.92				
	PT	**T-16.5S C-12.6S**			**T-15S C-15S**	**T-10S C-10.6S**		**T-14.1S C-12.6S**	
	apTT	T-36 S C-30 S			T-30S C-32S	T-19.7S C-26S		T-76 S C-30S	
	INR	1.35							
	LDH				5044	3171		2250	1650
	fibrinogen		226.3						
	D-dimer		47.00						

TABLE 2: COAGULATION PROFILE OF THE PATIENT VARIOUS DAYS

PICTURE SHOWING SPHEROCYTES



Hematologist opinion obtained. Diagnosed as MICROANGIOPATHIC HEMOLYTIC ANEMIA

On day 6, patient had 1 episode of seizure. PLASMAPHERESIS started. Patient regained consciousness. Extubated after 48 hours. Her haemoglobin dropped to 3.9 g/dl and improved to 10.9g/dl after plasmapheresis.

USG of kidneys showed Cortico-medullary density altered; Increased cortical echoes ; bilateral medical renal disease grade 1 / 2 disease.

Peripheral smear showed microcytic hypochromic RBCS; WBCS – leucocytosis and toxic granules; Mild thrombocytopenia; Macrocytes present; Spherocyte 2+ Fever profile was normal.

CT CHEST showed Patchy airspace opacity in apical and posterior segment of right upper lobe; consolidation of right lower lobe. CT BRAIN was normal. Patient discharged on day 21.

Discussion

Thrombotic microangiopathy (TMA) results from red cell fragmentation and platelet trapping with subsequent microangiopathic hemolytic anemia and thrombocytopenia and represents a final common pathway of a multitude of clinical syndromes.

"Microangiopathic" is defined as the presence of a physical blockage (usually fibrin thromboses).Red blood cells passing through small capillaries break apart as they pass through this obstruction. The pathognomonic finding is the presence of schistocytes on the peripheral blood smear.

Pregnancy-associated thrombotic microangiopathy is a rare but serious disorder that is associated with significant maternal and perinatal morbidity and mortality, due to the deposition of fibrin and platelet thrombi in the microcirculation of the placenta. It has been reported to occur in 1: 25,000–1: 100,000 pregnancies (Belford,2004),(Nishida, 2004). Pregnancy can precipitate the disease for the first time or can exacerbate the recurrence of an existent condition (Davies,2009),(George,2006). Pregnancy-associated microangiopathy typically occur during late pregnancy (Bouw,2009); In reviewing the Oklahoma TTP-HUS registry in 335 patients, Terrell et al. (Terrell,2010) did not find any gender or race predilection that was associated with pregnancy-associated microangiopathy, Classic Symptoms of TTP-HUS Microangiopathic hemolytic anemia (MAHA), Thrombocytopenia, Acute renal insufficiency (more common in HUS)(Remuzzi,1998), Neurologic abnormalities (more common in TTP), Fever. Only thrombocytopenia and MAHA without another apparent etiology are required to initiate plasma exchange for presumed TTP-HUS.

Etiology : Idiopathic (37%), Drug associated, autoimmune, infection and postpartum.

Differential Diagnosis:
Vasculitis
Malignant Hypertension
DIC
Antiphosphospholipid Syndrome

ADAMTS13 : ADisintegrin-like And Metalloprotease with ThromboSpondin type 1 repeats. Protease that cleaves ULVWf (Unusually Large Von Willebrand factor) in the circulation. Decreased activity or inhibitor present in TTP, but not HUS .

Treatment:

Plasma Exchange is the main stay of treatment for acquired TTP (Peyvandi,2008), (Michael,2009);Initially performed daily until platelet count normalizes and hemolysis improved. Average of 7-16 daily exchanges needed.

Steroids- prednisolone. Reserved for patients refractory to plasma exchange.

Chemotherapy and antiplatelet agents are used in the treatment (Hauer,2010),(LÓpez ,2009).

Antiplatelet agents are Aspirin (325mg) and dipyrimadole(400mg). Ticlopidine maintenance for 1 year.

Avoid prophylactic platelet transfusion.Unless life-threatening bleeding is present.Provide additional substrate for thrombus formation. MI and strokes have reportedly occurred after transfusion.

Spleenectomy ; chemotherapy, high dose iv igG also aid in treatment

Response To Treatment : Thrombocytopenia require several days. Hemolysis improves, anemia worsens, recovery from renal failure is slow.

Prognosis : Relapses usually occur within the first year. Morbidity/ mortality of relapses less than with initial episodes Mortality up to 90% (without plasma exchange). With plasma exchange the overall mortality has been reduced to 20-30% [F. Peyvandi, 2008]

Remission at 6 months, is approximately 80%, with plasma exchange
However, prognosis is worse for patients with disease resistant to plasma exchange.

CONCLUSION : MAHA is a rare disorder that has the hallmark of fragmented red blood cells and thrombocytopenia. MAHA is a spectrum of disorders that usually present as an HUS/TTP picture. TTP/HUS is caused by different agents (drugs, toxins, infections, pregnancy, and autoimmunity) that damage the endothelium. Because of the rarity of these disorders and the nonspecific clinical and laboratory features, this diagnosis (and its underlying causes) can be easily overlooked or missed leading to the high morbidity and mortality. Therefore, when a patient presents with unexplained thrombocytopenia and a Coombs-test-negative hemolytic anemia, a presumptive diagnosis of MAHA should be considered. No specific therapy can be claimed to cure this group of disorders, however, few interventions are life saving such as the use of plasma infusion and plasma exchange in the management of TTP.

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