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Original Research Paper

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A RARE CASE OF OSLER-WEBER-RENDU SYNDROME IN PREGNANCY

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ABSTRACT Hereditary Haemorrhagic Telangiectasia is a genetic vascular disorder, having five variants depending on underlying gene mutations and characterised by aneurysms and arterio-venous malformations. Larger AVMs present most commonly in the brain, lung, and liver. The diagnosis is mainly clinical based on the Curacao Criteria. Serious Neurological complications can occur in up to 10% of cases. Pregnancy associated hormonal changes affect the cardiovascular system manifesting in the second and third trimesters. Majority of the pregnancies are uneventful, but severe complications and even death can occur. HHT in pregnancy is considered high risk and needs management by a multi-disciplinary team. Women with HHT planning pregnancy should be counselled regarding the rare but serious risks. Strict antenatal surveillance and prior awareness of the diagnosis of HHT is usually associated with good pregnancy outcomes.

KEYWORDS : Hereditary Haemorrhagic Telangiectasia, aneurysms, arterio-venous malformations

INTRODUCTION

Hereditary Haemorrhagic Telangiectasia (HHT) is a genetic vascular disorder affecting blood vessels throughout the body, inherited as autosomal dominant. Also known as Osler-Weber- Rendu Syndrome after the doctors who published the first series of cases (1). HHT has five variants depending on underlying gene mutations, all of which are related to the transforming growth factor-beta (TGF-β) signalling pathway. Type 1 (mutations in the endoglin (ENG) gene) and Type 2 (mutations in the activin receptor-like kinase-1 (ALK-1) gene) comprise approximately 90% of all the cases (2).

HHT is characterised by an alteration in structure of the vessel walls with resulting formation of aneurysms and arterio-venous malformations (AVM). Small AVMs or telangiectasias, are seen on buccal, nasal, and gastrointestinal mucosa, as well as on face, lips, tongue, and fingers. Larger AVMs present most commonly in the brain, lung, and liver (2). The diagnosis is mainly clinical based on the Curacao Criteria consisting of four components namely family history of a first degree relative with HHT, mucocutaneous telangiectasias at characteristic locations such as fingers and lips, recurrent and spontaneous epistaxis, and visceral AVMs. The diagnosis is definite when three criteria are met, possible if two are fulfilled, and unlikely if less than two are present (1). Management is guided by the specific AVM present. The most serious complications are due to neurological involvement such as cerebral infarction and cerebral arterial embolism that can occur in up to 10% of cases (1).

Pregnancy with HHT is high risk with implications for both mother and baby. Pregnancy associated hormonal changes affect the cardiovascular system resulting in exacerbation of blood shunting through the already abnormal vascular beds. Complications occur most often in second and third trimesters when the changes of peripheral vasodilation and increased cardiac output are at the maximum (3). While most pregnancies are uneventful, severe complications have been reported including heart failure, intracranial haemorrhage, pulmonary haemorrhage, stroke and even death. Awareness of the diagnosis of HHT has been associated with improved outcomes in pregnancy (2).

We report a case of a pregnant women who was undiagnosed till she presented with complaints during the pregnancy and subsequently went through a course of cascading complications.

Case report

Mrs. XYZ, 27 years old, G3A2 with BMI of 24 booked with us at 13 weeks of gestation, had previous spontaneous miscarriages at 15 weeks and 11 weeks of pregnancy. No history of previous medical or surgical illness. She was screened positive for hypothyroidism and high risk for preeclampsia and started on thyroxin and ecosprin. Cervical cerclage done at 19 weeks in view of short cervix. Fetal ultrasound revealed no abnormality.

She had episodes of epistaxis started from 16 weeks. Her haemoglobin was 10 and platelet count 1.87 lakhs. Her maternal grandmother had recurrent epistaxis but no other contributory family history was elicited. Around 20-weeks of pregnancy, blood pressure records were normal, but she developed progressive, pitting, painless, bilateral pedal oedema for which she was reviewed by physician. At 27 weeks, she was diagnosed with gestational diabetes which was controlled on medical-nutrition therapy.

By 30 weeks of pregnancy, there was increasing pedal and abdominal wall oedema, persistent tachycardia, bounding pulses, parasternal heave, grade 4 systolic murmur, and a total weight gain of 25 kg in pregnancy with normal blood pressure records. Chest X ray showed cardiomegaly and 2D echo confirmed evidence of hyper dynamic circulation with dilated atria and IVC, increased velocities, mild TR and PAH but maintained LV/RV systolic function and was assessed by cardiologist. She refused admission. Advised Tab. Furosemide on outpatient basis with emphasis on need for further evaluation and inpatient monitoring.

In view of multiple episodes of epistaxis and positive family history, MRI [Fig. 1 and 2] done at 31 weeks revealed hepatomegaly, liver and spleen telangiectasias, mild cardiomegaly with minimal pericardial effusion, consolidation in anterior basal segment of left lower lung lobe, hyper intensities in bilateral globus pallidies. She was admitted as a probable case of Osler-Weber-Rendu Syndrome with possible high output cardiac failure. Fetal wellbeing monitoring showed normal growth and no distress.

Monitored in ICU due to febrile episodes and dyspnoea and received antibiotics, diuretics and beta-blocker. Fever profile (blood and urine cultures, Malarial test, Viral markers) was negative. After 48 hours of admission, she developed increasing drowsiness, inappropriate response to verbal commands, echolalia and brisk DTR with no other focal neurological deficit. She was transferred to a subspecialty centre under care of neurophysician.

Further on she had persistent hypoglycemic episodes, GCS did not improve, remained in drowsy arousable state, and was found to have high serum ammonia levels (125 μmol/L). Repeat MRI brain confirmed hepatic encephalopathy. An emergency caesarean section was done at 32 weeks in view of fetal distress, 1.2 kg, baby girl, with APGAR of 7,8,9 delivered. The surgery was uneventful. She received packed RBCs and FFP transfusions due to deranged liver function and coagulopathy [Table I]. Autoimmune profile was negative. Post-delivery her condition continued to deteriorate. The acute hepatic failure was followed by renal failure managed by continuous renal replacement therapy. Further complications in the form of hypotension, seizures and fever spikes were dealt with. But despite all the efforts she had cardiac arrest a week post- delivery and succumbed.

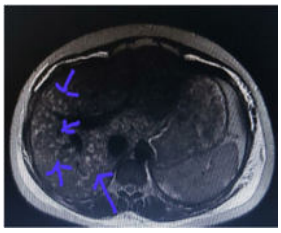

Fig 1 MRI T1weighted image showing multiple hyperintense lesions in right lobe of liver

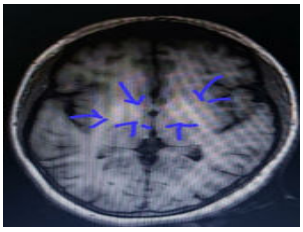

Fig 2 T1 weighted image showing white areas (hyperintense) in Globus pallidus which is a part of basal ganglia

Table 1: Investigation chart

	32wks, D0 (Day of admission)	**D3**	**D5**	D6	D7	D8	D9	D10	D11
Hb(gm/dl)/PCV	12.2/ 36.6		13.1	11.7/38.6	11.1/35.7	10.5/34.3	10.8/34.6	11.6/36.7	11.4/37.2
Platelet count (lakhs/cumm)			3.30	2.84	2.17	2.15	1.98	1.94	0.84
Electrolytes –Na/K/Cl (mmol/L)	132/3.9/107	133/5.1/109	134/4/106	134/3.87/105	136/3.99/108	140/4.15/109	142/4.28/118	147/4.27/116	148/4.7/117
Creatinine(mg/dl)	0.6		0.85	0.86	1.27	1.33	0.88	0.71	1.03
Urea(mg/dl)			36	37	52	80	98	81	68
SPCR	0.1								
Total Bilirubin (mg/dl)	2.5[1.5/1.0]	2.7[1.6/1.1]	4.07[2.9/1.17]		6.30[4.72/1.58}	5.52	7.00	6.51	6.24
SGPT(IU/L)	28	30	39		45	53	59	64	67
SGOT(IU/L)			62		89	139	150	152	239
LDH	290								
Prothrombin time (test/control) (sec)			28.6/14.3	28.9/14.3	30.4/14.3	24.2/14.3	24.7/14.3	26.8/14.3	42.8/14.3
INR			2.07	2.09	2.21	1.74	1.77	1.93	3.16
APTT(test/control)(sec)				41.4/29.2		37.6/29.2	34/29.2	34.1/29.2	43.4/29.2
Fibrinogen (mg/dl)				289					

DISCUSSION

HHT is a rare genetic disorder that can have serious implications especially to the mother during pregnancy. Important to note that maternal morbidity and mortality is more in previously undiagnosed women who were not on medical supervision (4)

Bleeding from the Pulmonary AVMs resulting in haemothorax is the most frequent complication reported in literature. Complications resulting from hepatic, cerebral and spinal AVMs are rarer comparatively but with life threatening consequences (4). Awareness of the diagnosis of HHT and management of the AVMs before pregnancy has been associated with improved outcomes (2). This underlines the need for screening prior to conception.

HHT can affect the fetus in the form of intrauterine growth restriction or even fetal death due to chronic hypoxemia, maternal hypotension, or maternal death. However, complications like miscarriage and preterm delivery were not found to be statistically significant as compared to the general population (4).

If a pregnant woman is first diagnosed in pregnancy as was in this case, the recommendation is to screen for AVMS by MRI. If asymptomatic or mild symptoms like epistaxis, no active intervention should be done besides close monitoring of both mother and baby with low threshold for hospitalisation. Antibiotic prophylaxis is recommended in labour. For those in whom brain AVMs have not been excluded, prolonged labour should be avoided (2).

CONCLUSION

HHT in pregnancy is considered high risk and needs management by a multi-disciplinary team consisting of maternal medicine specialists and subspecialty physicians in a tertiary care centre with ICU facility. Women with HHT planning pregnancy should be counselled regarding the rare but serious risks. They should be reassured that close obstetric care and prior awareness of the diagnosis of HHT is usually associated with good pregnancy outcomes.

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