Klippel-Trenaunay Syndrome and Gestational Trophoblastic Neoplasm

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Background: Klippel-Trenaunay syndrome is a non-heritable venous malformation with bone and soft tissue hypertrophy and cutaneous nevi. **Case characteristics:** Neonate with Klippel Trenaunay syndrome born to a mother with past history of Gestational trophoblastic neoplasm. **Observation:** Antenatally, a fetal vascular malformation was identified ultrasonologically at 29 weeks gestation. Acute myeloid leukemia was diagnosed in mother at 33 weeks gestation. **Message:** A rare association of Klippel Trenaunay syndrome and gestational trophoblastic neoplasm with the possible role of either hyperglycosylated Human Chorionic Gonadotropin or chemotherapy as a link is highlighted.

Keywords: *Teratogens, Human Chorionic Gonadotropin, Vascular malformations.*

A neonate with Klippel-Trenaunay syndrome was born to a mother who had Gestational trophoblastic neoplasm 4 years ago. Possible role of either hyperglycosylated human chorionic gonadotrophin (HCG-H) elaborated by the neoplasm or long term teratogenicity of chemotherapeutic agents used for the neoplasm, in the etiology of the syndrome is discussed.

CASE REPORT

A 36-week-old male neonate born of vaginal delivery had large irregular compressible bluish purple swellings of varying consistency with superficial venous blebs and varicosities in the whole of right gluteal region and lower limb (***Fig.*1**) and the whole of left thigh and lower limb laterally. Lower limbs were large compared to rest of the body with associated soft tissue hypertrophy. Blood investigations were normal. MRI showed multiple communicating and non-communicating cystic lesions of varying sizes with septations and debris in intramuscular plane with subcutaneous extension. These lesions showed thick peripheral contrast enhancement. An abnormal dilated vein was noted bilaterally in the subcutaneous plane which was not draining into the femoral vein. No abnormal flow voids occurred within these lesions. Other superficial and deep veins, arteries and their branches were normal in course and caliber. There was thickening of skin and subcutaneous tissue. Sacral, pelvic, inguinal and gluteal regions, hemiscrotum, thigh and lateral aspect of both lower limbs were involved. Viscera, bones, spinal canal, gastrointestinal and genitourinary tracts were not involved. Tissue sampling could not be done for fear of torrential bleeding. A diagnosis of Klippel-Trenaunay syndrome was made.

The 26-yr-old mother had a gestational trophoblastic neoplasm 4 yrs. back. She was treated with EMA/CO (etopside, methotrexate, actinomycin D, cyclophosphamide and vincristine) regime. Serum beta-HCG values at diagnosis, after treatment, and at one year and two year follow-ups were 60031 mIU/mL, 3.5 mIU/mL, 0.1 mIU/mL and 1.4 mIU/mL, respectively (normal pre-pregnant value <5 mIU/mL). During the present pregnancy, ultrasonogram revealed a large soft tissue tumor in the fetus at 29 weeks of gestation. Acute myeloid leukemia (AML) in mother was diagnosed at 33 weeks of gestation and chemotherapy was given.

The infant was regularly followed up till 8 months of age. He had steady weight gain with malformations increasing in size progressively and proportionately without signs of involution. There was no evidence of consumption coagulopathy. Profuse spurting of blood occurred every week which required packed cell transfusions and tight pressure bandages. Steroids were tried and stopped. He was on propranolol from 6 weeks of age. Interventional procedures were deferred due to limited access in the diffusely scattered lesion with no marked arterial plane.

DISCUSSION

A primary mesodermal abnormality in fetal development leads to persistence of microscopic arteriovenous communications. Failure of regression of these channels (which occurs normally by 8 weeks) leads to limb hypertrophy, varicosities, nevi and persistence of lateral venous channels leading to Klippel-Trenaunay syndrome [1].

Hyperglycosylated human chorionic gonadotropin (HCG-H) with its beta subunit is a variant of HCG secreted by gestational temphoblastic neoplsma [2]. It stimulates angiogenesis [2,3]. Klippel-Trenaunay

syndrome in the fetus is associated with relatively higher level of maternal serum beta HCG than that in normal pregnancy [4]. Acquired uterine arteriovenous malformations have been reported in patients with this neoplasm [5,6], but vascular malformations in newborns born to mothers with history of gestational trophoblastic neoplasm have not been reported. In this case, beta-HCG values were normal during yearly follow-ups done post-chemotherapy. As beta-HCG values rise exponentially even in normal pregnancies, a rise due to fetal Klippel-Trenunay syndrome *per se* could not be appreciably demonstrated in our mother. As the specific investigation HCG-H was not freely available, it was not done.

Long-term toxicity of EMA/CO regimen, including second malignancies like AML in the mother are well described [7]. Even after a gap of four years, present pregnancy was complicated with AML in mother. Klippel- Trenaunay syndrome in connection with a possible teratogenic effect of butobarbital has been reported [8]. Though other malformations are reported with EMA/CO regime, vascular malformations are not yet reported [7].

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