

Recurrent Heart Attacks in a Young Lady

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ABSTRACT

24-year-old woman presented to our hospital with chest pain, new ECG changes and high troponin suggestive of non-ST Myocardial infarction, patient gave history of another two heart attacks at the age of 20 and 21, on both occasions, she was treated with angioplasty and no stenting.

Her past medical history was significant for recurrent meniscal tear on both knees which was treated conservative, when patient was 15-year-old, she was diagnosed as carotid-cavernous fistula and Treated with endovascular therapy, her family history was noted for her sister having small bowel rupture at the age of 18 year; her brother had two strokes at the age of 18 and 19, patient also was known to have recurrent dislocation of right shoulder and delayed wound healing.

Examination showed scattered bruising, blue sclera, hyperelasticity of skin over elbow joints, MRA of whole body showed aneurysm of both internal iliac vessels, coronary CT showed aneurysm in the left anterior descending and right coronary arteries, differential diagnosis was discussed with the patient who gave a consent for genetic study which came positive for COL3A1 and confirmed the diagnosis of Vascular Ehlers Donals Syndrome (formally called Ehlers Donals Syndrome type 4).

Patient agreed for genetic counselling, and first-degree family agreed for genetic testing, in the article we will report the case and discuss the differential diagnosis

Case Report

24-year-old lady presented to ED with central crushing chest pain for 30 minutes, she did not have any risk factors for ischemic heart disease apart from significant family history of heart attacks in a young age as her father died from a heart attack at the age of 40, her mother died at the age of 35 during delivery, her sister had an acute intestinal bowel obstruction at the age of 18, patient did not smoke, drank alcohol or use illicit substance. Patient had significant medical history for occipital lobe stroke with no residual neurologic deficit, two episodes of chest pain and high troponin at that time, diagnosed as non ST- MI and treated with angioplasty at the age of 22, patient presented with acute onset of severe frontal headache, diplopia, red eyes and exophthalmos,

patient was diagnosed as high flow carotidocavernous fistula which was treated with endovascular therapy, patient had recurrent shoulder dislocations and meniscal tears in both knees, patient noted that she easy bruise and skin wound bleeds for longer time.

On examination, patient looks pale with blue sclera, cardiac examination showed dual heart sounds with mitral regurgitant murmur, chest was clear for auscultation, abdomen was distended but not tender and no organomegaly, auscultation revealed bruit over the epigastrium, examination of the lower limbs showed no ankle oedema and bounding peripheral pulse, pulse 70/min regular, Blood Pressure 130/80 with no postural drop, oxygen saturation 100% on room air, normal capillary filling.

Skin over the both elbows was hyperextensible, examination of the skin over the abdomen and the back showed multiple bruises ECG showed depressed ST segment in the inferior leads, Troponin I was 200ng/ml(less than 0.03), full blood count, urea and creatinine, metabolic panel, liver function tests, coagulation screen and inflammatory markers were within the normal range. Patient was started on Clexane, Dual anti platelets, and isosorbide mononitrate, and 1 mg of morphine with good effect and resolution of chest pain, patient was taken for coronary Angio, which showed dissecting aneurism in the right coronary artery. Patient started on Lipitor and metoprolol, patient observed in ICU for 48 hours with no complications.

Daily ECG did not show any new ECG changes and the troponin showed a trend to decrease to 100ng/ml, transthoracic echo showed normal ventricular size and function, left atrium was normal volume, mild mitral incompetence, and normal pressures in right and left sides of the heart.

The following investigation was performed, autoimmune screen including AND, DNA, Complement, RF, ACCP, anti-RO, Anti SM, Anti La, and centromere antibodies, anti ribonucleoprotein antibodies, CK, Lactic acid to exclude mitochondrial disease, hepatitis B surface antigen, hepatitis C serology, vasculitic screen included P and C ANCA, MRA of the whole-body including brain, neck, chest, abdomen and pelvis. CT coronary, genetics for marfan syndrome, homocysteine in blood and urine to exclude homocystinuria, thrombophilia screen, flowcytometry to exclude paroxysmal nocturnal hemoglobinuria, continuous monitoring of the heart rate to exclude arrhythmias. All the above-mentioned investigation ruled out vasculitis, Rheumatoid arthritis, systemic lupus, scleroderma, Marfan syndrome, homocystinuria, inherited thrombophilia, Paroxysmal nocturnal hemoglobinuria, Fibromuscular dysplasia, Kawasaki disease, Takayasu disease, Giant cell arteritis. Polyarteritis Nodosa, Systemic lupus arthrotomies, scleroderma, mixed connective tissue disease. Dermatomyositis, genetics for COL3A1 confirmed Vascular Ehlers Donals Syndrome Type 4.

Diagnosis discussed with the patient, she also offered few sessions with her family to see the geneticist, also regular follow up had been arranged with a multidisciplinary team, which included, cardiologist, neurologist, immunologist, vascular surgeon, general physician with an interest in vasculitis, and a general surgeon.

Discussion

Vascular Ehlers -Donals Syndrome is an autosomal dominant genetic hereditary collagen disease affecting type 111 collagen that is found in abundance in vascular structures like uterus, heart, intestine, liver, carotid vessels. It causes a defect in the Pro-alpha-1 type 111 collagen fibres resulting from mutation in the COL3A1 gene, which in defective type 111 collagen causing spontaneous visceral and vascular rupture, needing urgent surgical interventions with high rate of complications [1-3].

All high vascular organs are susceptible to spontaneous rupture, 10 different types of Ehlers Donals had been described in the

literatures, and most of them are associated with skin hyper elasticity and joint hypermotility, resulting in recurrent bruises and dislocation of the large joints, [4-8].

The diagnosis is often not made until a catastrophic clinical event happened, prevalence of vascular Ehlers – Donald syndrome is 1 per 100,000, disease is relatively common in young females. The diagnosis is quite difficult, not uncommonly if affected children will be misdiagnosed with coagulation disorder and given wrong treatment; Literatures pointed out that 20% [9,10]. Patients had symptoms of EDS before a catastrophic event happen. Hyper elasticity of the skin is common resulting in easy bruising thin transparent skin and sclerae. It can also cause ruptured vessels and viscera in addition to carotid-cavernous fistula without joint hypermobility. Recurrent myocardial infarction in young females with no risk factors for atherosclerosis is a warning sign and should be taken seriously. Medical practitioners should have a very low threshold to investigate young females with heart attacks and no risk factor for vascular Ehlers Donals syndrome; it is a vascular hereditary genetic disease not to miss because of the fatal complications. It is characterized by arterial intestinal and uterine fragility causing thin skin, blue sclera, easy bruising, micrognathia, pinched nose, prominent eyes, aged appearance, thin lax skin hyperextensible joints, vascular dissection and rupture including hollow viscus, uterus, spontaneous dissections of the coronary arteries which makes angioplasty and stenting quite challenging, arterial rupture might cause carotid-cavernous A-V fistula, in rare occasions, cerebral vessels might dissect and rupture causing a large vessel stroke, new bleed formation had not been described before in the literatures but it is something to be observed for if patient will have recurrent strokes [11-13].

Diagnosis of Vascular EDS is confirmed by identification of a heterozygous pathogenic variant in COL3A1 mutation, patients with the classic phenotype and negative proband and molecular genetic testing should offered histologic biopsy for Biochemical assessment of type 111 procollagen from cultured fibroblast. Patients with confirmed diagnosis of vascular EDS should have strict control of blood pressure and heart rate. Should avoid heavy lifting, collision sports. Routine colonoscopy in the absent of risk factors should be avoided, arteriography and elective surgery should not be done ,maternal risk with pregnancy and delivery should be discussed with patients, diagnosed pregnant women should have delivery in a tertiary center equipped with all subspecialties including vascular surgeons, interventional cardiologist. Intensive and coronary care unites [14,15].

Pneumothorax, hemothorax and hemopneumothorax in vascular EDS with successful lung transplant, and keratoconus and severe gingival recession had been reported in the literatures before.

Summary and conclusion

Our patient presented with classic phenotype of vascular Ehlers Donald Syndrome type 4, diagnosis had been missed until the patient presented with life threatening heart attack and carotid -cavernous fistula.

Early diagnosis needs a high clinical suspicion when young patients presented with spontaneous arterial rupture, patient should have indefinite follow up with multidisciplinary team. Family of the patient should offer genetic assessment to avoid catastrophic complications in the future.

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