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A 35 Yr Female with Progressive Breathlessness: Rare Presentation of a Rare Disease

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Abstract: *Pseudoxanthoma elasticum is a rare inherited multisystem disorder that is characterized by a pathological mineralization of the elastic connective tissue, which involves predominantly the skin, eyes and cardiovascular system. Its cause lies on mutations in the ABCC6 gene, which lead to reduction or absence of the transmembrane transport ADP dependent protein (MRP6), causing an accumulation of extracellular material and subsequent deposition of calcium and other minerals in the elastic tissue. We report a case of 35 year old female presented with progressive breathlessness and sings of right heart failure diagnosed with pseudoxanthoma elasticum, emphasizing its major clinical features and the importance of early diagnosis of the disorder, aiming for adequate therapeutic management of associated complications. With our best search of literature we could not found any case report which suggestive of ventricular wall calcification and patient presenting with symptoms of heart failure in PXE. Probably this is the first reported case in world until now.*

Key words: *Connective tissue; Elastic tissue; Pseudoxanthoma elasticum*

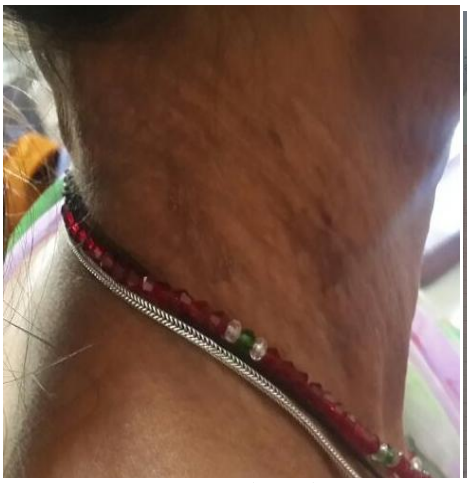
I. Introduction-

Pseudoxanthoma elasticum (PXE), also known as Grönblad–Strandberg syndrome, is a genetic disease that causes fragmentation and mineralization of elastic fibres in some tissues. The most common problems arise in the skin and eyes, and later in blood vessels in the form of premature atherosclerosis.PXE is caused by autosomal recessive mutations in the ABCC6 gene on the short arm of chromosome 16 (16p13.1) . This is between 1 in 70,000 and 1 in 100,000 but milder cases occur and are not diagnosed. Presentation can be highly variable and phenotypic penetration may be incomplete. It affects females twice as often as males and affects all races. Modes of inheritance are both autosomal dominant and autosomal recessive. 90% of cases are thought to be recessive but some may be new mutations.

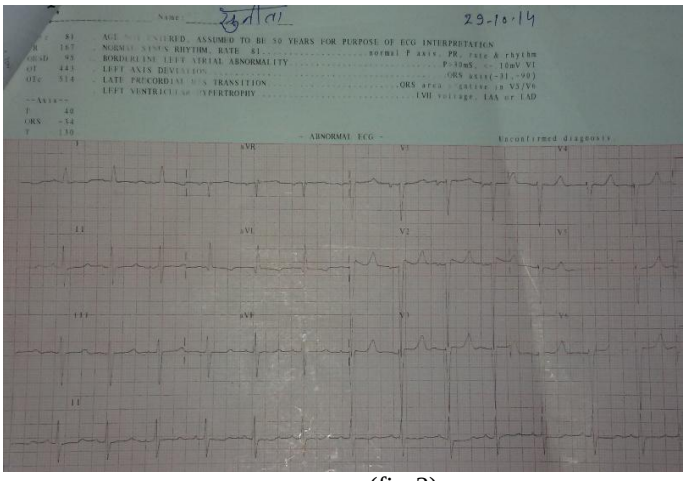
II. Case Report:

A 35 year old female came to emergency department with complaint of dyspnoea on exertion since last one year, which was progressed from NYHA 1 to 3, she also gives history of bilateral pedal oedema on and off for past 6 months, there was history of chest pain on exertion for 6 months which was non radiating. There was history of vascular claudication.There was no other significant past medical history. Patient was non smoker and non Alcoholic.

On examination her pulse rate was 82beats/min,regular,BP was 86/60mm hg in right arm supine position, BP was non recordable in left arm, respiratory rate was 24 bpm, JVP raised, B/L pitting type pedal oedema and tender hepatomegaly present. Cardiac auscultation revealed loud P2 and pan systolic murmur over tricuspid area was present, without radiation, increased on passive leg rising. There were skin lesions which consist of yellow papules that merged to form plaques. They appeared on the flexural areas of the neck (fig.1) and elbows, popliteal spaces and umbilical region, and they were accompanied by loosening of the skin around the inguinal folds and armpits and nape of the neck. Other systemic examination was within normal limit.

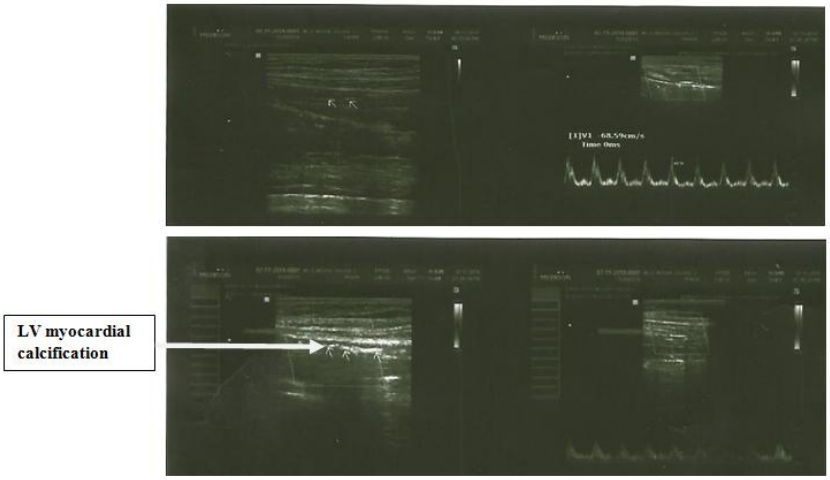


(Fig-1)

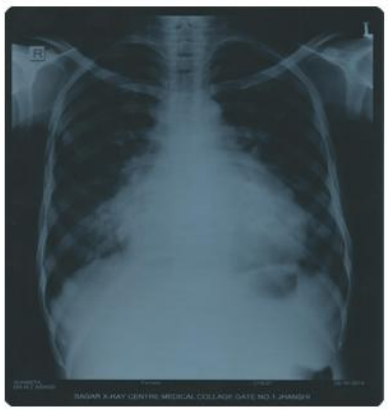


(fig-2)

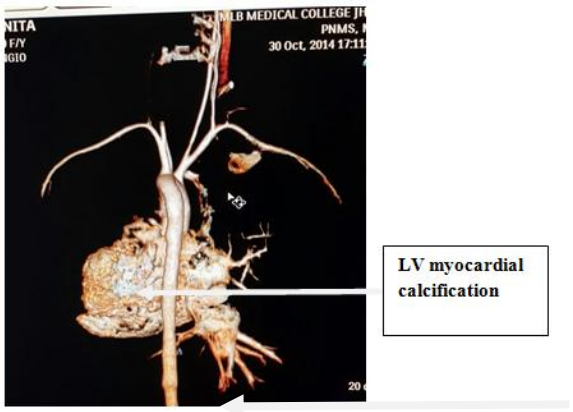
Her ECG was showing left axis deviation with LVH(fig 2), 2D ECHO showed dilated LA,PA,RV,RA,severe TR, Severe PAH(RVSP- 107 mmHg), LV is spongy with severe left ventricular myocardial calcification with normal systolic function(LVEF-59%). (fig.3)



Her PFT was normal, chest x-ray PA view showed cardiomegaly (fig4). Colour Doppler F/S/O Monophasic flow pattern with reduced velocity in all arteries of upper and lower limbs extensive calcification is seen in B/L lower limb arteries. CT Chest showed dilated central pulmonary artery with isolated left ventricular myocardial calcification (Fig-5).

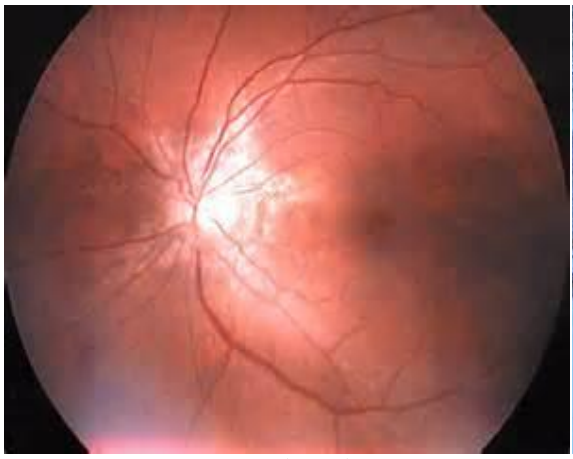


(Fig-4)

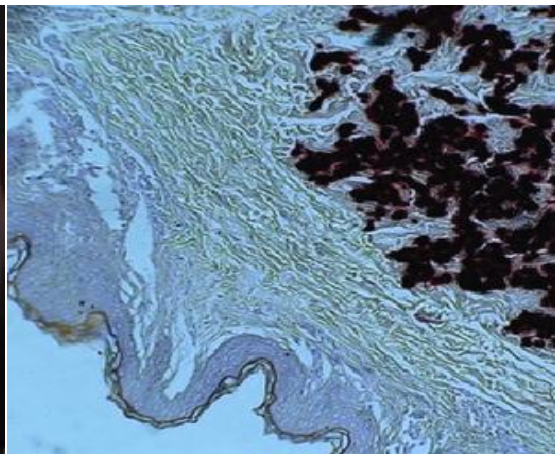


(Fig-5)

Fundus examination showed angioid streaks (FIG-6). USG abdomen showed normal sized kidney with multiple calculi in right kidney.CBC, with GBP S/O microcytic hypo chromic anemia.Hb electrophoresis shows normal Hb pattern. Skin biopsy report s/o PSEUDOXANTHOMA ELASTICUM (fig-7).



(Fig-6)



(Fig- 7)

APCC-6 gene study was refused by the patient. Patient pedigree showed autosomal recessive pattern of disease inheritance.

So it was a case of PSEUDOXANTHOMA ELASTICUM, she was started on diuretics (torsemide 10mg OD), ACE inhibitors (Ramipril 1.25mg BD) and pentoxyphylline 400 mg tds.

III. Discussion

SYNONYMS OF PSEUDOXANTHOMA ELASTICUM (PXE)

- Elastosis dystrophica syndrome (obsolete)
- Gronblad-Strandberg syndrome
- Systemic elastorrhexis (obsolete)

Pseudoxanthoma elasticum is a hereditary disease of the elastic connective tissue with an autosomal recessive inheritance pattern in 90% of the cases, or autosomal Dominant. It is caused by a mutation in gene ABCC6 located in the short arm of chromosome 16(16p13.1), responsible for coding a transmembrane transport ADP dependent protein (MRP6), expressed predominantly in the liver and kidneys, and found in low levels in the tissues involved by pseudoxanthoma elasticum. The mutation in gene ABCC6 causes diminishing or absence of this protein and subsequent accumulation of substances with high affinity for the elastic tissue, resulting in calcium deposition and distortion and fragmentation of the elastic fibres.

Clinical manifestation occurs in skin, eyes, oral mucosa, and gastrointestinal tract and in the arteries. Cutaneous alterations are the most frequent and are characterized by yellowish asymptomatic papules of 1-3 mm in diameter, symmetrically distributed in the neck and flexural areas, especially the axillae. Mucosal lesions of similar aspect can be observed in the oral, genital and gastrointestinal mucosa.

The main ocular manifestation consists in the presence of angioid streaks visualized by ophthalmoscopy, which represent the calcium deposit in the retina Bruch's membrane and may lead to the rupture of vessels, with subsequent neovascularisation that is associated with retinal haemorrhages and may lead to progressive loss of visual acuity. The cases of ocular involvement must be monitored by periodical fluorescein angiography and ophthalmoscopy.

In the cardiovascular system the calcification of artery walls of small and medium calibre is observed, which results in early atheromatosis. It can present itself through gastrointestinal haemorrhages, hypertension, acute myocardial infarction, cerebrovascular accident and peripheral arterial occlusion.

The diagnosis is clinical, associated with anatomopathological examination, which is characteristic and reveals fragmented and distorted elastic fibers in the reticular and deep dermis. These changes are more evident in the Verhoeff, Van Giesson and Calleja stains, specific for the elastic tissue. The calcification of fibers can be clearly identified in stains for calcium, as the Von Kossa.

To this day, there is no specific treatment and the therapeutical management is based in prevention, tracking and monitoring of complications associated with the disease. Complementary exams such as blood count, lipid profile, echocardiogram, and ophthalmologic monitoring should be made whenever necessary. The diet supplemented with magnesium and vitamin K may extend the progression of the disease and improve the quality of life of the patients. Surgery for aesthetic improvement of cutaneous lesions is not routinely performed

due to the risk of complications with formation of keloids, dehiscence and extrusion of calcium particles through the surgical wound.

The reported case presented typical clinical manifestations of pseudoxanthoma elasticum, and the diagnosis was confirmed after anatomopathological examination. In this case there was skin involvement; significant involvement of the cardiovascular system was detected in the case. In conclusion, despite the rarity of this pathology, one must be aware of the need for early diagnosis, recognizing the typical cutaneous manifestations of the disease, for adequate handling and better management of the associated complications when these are present, making periodical ophthalmologic and cardiovascular follow-ups imperative.

References

[1]. Chassaing N, Martin L, Calvas P, Le Bert M, Hovnanian A. Pseudoxanthoma Elasticum: A Clinical, Pathophysiological And Genetic Update Including 11 Novel Abcc6 Mutations. J Med Genet. 2005; 42:881-92.
[2]. Finger Rp, Charbel Issa P, Ladewig Ms, Götting C, Szliska C, Scholl Hp, Et Al. Pseudoxanthoma Elasticum: Genetics, Clinical Manifestations And Therapeutic Approaches. Surv Ophthalmol. 2009; 54:272-85.
[3]. Li Q, Jiang Q, Pfendner E, Váradi A, Uitto J. Pseudoxanthoma Elasticum: Clinical Phenotypes, Molecular Genetics And Putative Pathomechanisms. Exp Dermatology. 2009; 18:1-11.
[4]. Li Q, Török L, Kocsis L, Uitto J. Mutation Analysis (Abcc6) In A Family With Pseudoxanthoma Elasticum: Presymptomatic Testing With Prognostic Implications. Br J Dermatology. 2010; 163:641-3.
[5]. Bressan Al, Vasconcelos Bn, Silva Rs, Alves Mfgs, Gripp Ac. Periumbilical And Periareolar Perforating Pseudoxanthoma Elasticum. A Bras Dermatology. 2010;85-7
[6]. Lee Tk, Forooghian F, Cukras C, Wong Wt, Chew Ey, Meyerle Cb. Complementary Angiographic And Autofluorescence Findings In Pseudoxanthoma Elasticum. Int Ophthalmol. 2010; 30:77-9.
[7]. Jiang Q, Endo M, Dibra F, Wang K, Uitto J. Pseudoxanthoma Elasticum Is A Metabolic Disease. J Invest Dermatol. 2009; 129:348-54.