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Case Presentation

Fabry's Disease: A Case series report of a Libyan family

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Abstract:

Introduction Fabry's disease (FD) is a rare disorders due to the very low residual function of alphagalactosidase enzyme causing chronic kidney disease (CKD), with the incidence of 1/40,000 males. Heterozygous females may be asymptomatic. We hereby report a patient having CKD and other clinical findings like, dermatological , neurological and cardiological manifestations and pedigree analysis were strongly suggest the diagnosis of Fabry Disease.

Case Presentation: A 40 year old man with high renal profile The patient is normotensive, non-diabetic, in 2013 had history of left ophthalmoloplagia which resulted from acute ischemia in midbrain, In 2014 had bilateral sensory neural hearing loss. In 2019 was noticed that he had a skin rash in a "bathing-trunk" distribution, they are small angiomas, by physical examination patient looks pale, he has mild pedal edema , CNS examination showed 7th , 8th and 9th cranial nerve palsy, his investigations showed raised s. creatinine 3.2 mg/dl, Urine protein++, eGFR 22.4/min/1.73m2. Ultrasound abdomen showed small kidneys and echocardiography showed LVH. A pedigree analysis showed recipient was third in birth order and has two brothers a known case of CKD on regular hemodialysis, The CKD of the brothers was a result of Fabry Disease, was evaluated for a-galactosidase activity which was found markedly decreased (12.10; normal enzyme activity level >60). According to clinical manifestations and strong family history of FD,

Conclusion & Recommendations: This case report highlights the importance of careful evaluation of cases of CKD due to unusual causes, particularly when there's positive family history, in order to avoid misdiagnosis and also for early and proper therapy.

Key words: Fabry's Disease, a-galactosidase, chronic kidney disease, Enzyme Replacement Therapy.

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Introduction

Fabry's disease (FD) is one of those rare disorders which are highly undiagnosed. Thereported incidence of this disorder is 1/40,000 males.[1] FD being a rare cause of end-stage renal disease (ESRD), accounts for 0.0167% of all causes of ESRD.[2] Manifestationsof FD are often more severe in men due to the very low residual function of alpha-galactosidase. Heterozygous females may be asymptomatic except for corneal opacities ordepending on lyonization or random X-inactivation, they may be as severely affected ashomozygousmales.[3]

We hereby report a patient having CKD , andhadother clinical findings such asdermatological, neurological and cardiological manifestations and pedigree analysiswerestrongly suggestthediagnosisof FabryDisease.

Thiscase reporthighlightsthe importanceofcarefulevaluationofcases ofCKDdueto unusual causes, particularly when there's positive family history , in order toavoid misdiagnosisandalsoforearlyandpropertherapy.

CasePresentation:

A 40 year old man referred to our nephrology clinic with history of generalized fatigueassociatedwithhighrenalprofile.

The patient historically normotensive, non-diabetic,but in 2013 had history of leftophthalmoloplagia whichresulted fromacute ischemiainmidbrain.

In2014startedfollowupatENTclinicbecausehehasbilateralsensoryneuralhearing loss.In 2019 it was noticed that he had a skin rash in a “bathing-trunk” distribution.,They aresmall angiomas,probablyangiokeratomas.fig1.

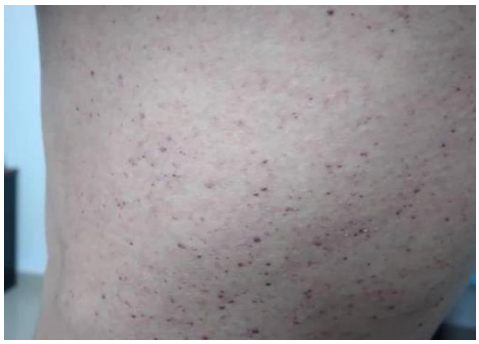

fig1. Angiokeratoma

Onphysical examination patient looks pale , he has mild bilateral mild pedal edema , vitalsignswithinnormalrange,CNS examinationshows7th, 8thand9thcranial nervepalsy.

Tab.1 Atthistimehis bloodtestswere asfollows:-

Sodium	135mmol/L
Potassium	4mmol/L
Bicarbonate	16mmol/L
Urea	80mg/dl
Creatinine	3.2mg/dl
Urineprotein	++
Haemoglobin	10g/dl
Normalwhitebloodcells	
PTH	94pg/ml
HBA1C	5.8%
eGFR	22.4/min/1.73m2

Ultrasound examination of the abdominal cavity showed that the liver, biliarysystem, spleen, bladder and prostate appeared to be normal, with no ascites and nolymphadenopathy. His kidneys appeared to be somewhat small (with a bipolardiameterof8.0cm)and in creaseinechogenisity.

An electrocardiogram showed lateral T-wave inversion and left ventricularhypertrophy. and echocardiography showed LVH , moderate Aortic regurgitationwithEF65%.

A pedigree analysis showed recipient was thirdin birth order and has two brothersa known history of ESKD on regular hemodialysis , the first one on hemodialysissince 2011 and the other since 2013 . the ESKD of the brothers was a result of FabryDisease , was evaluated for alpha-galactosidase activity which was found markedlydecreased (12.10; normal enzyme activity level >60), and was diagnosed as FD withrenalfailure.

According to clinical manifestations and strong family history of FD we suggest themost likely cause of the CKD in this case is Fabry Disease and our planning is for biochemical investigation of aná-galactosidase -Aactivity. And ERT.

Discussion

Our case series is important because of following reasons FD is under-diagnosed andscreening of high-risk groups is important for case finding and (2) this case reporthighlights the importance of screening those patients for CKD who have unexplained renalfailure.

Fabry nephropathy is one of the most severe manifestations of FD. It had been one of theunknown causes of morbidity and

mortality before the widespread availability of dialysisand kidney transplantation. Like most aspects of FD, kidney disease is thought to resultfrom GL-3 accumulation in glomerular endothelial, mesangial and interstitial cells, podocytes, and renal vasculature. Progressive intracellular accumulation of GL-3 is thought to cause glomerulosclerosis and interstitial fibrosis[8] as well as its urinary excretiontogether withotherlipids.[9]
Diagnosismaybepresumptivebasedonobservationofsymptomsandlaboratoryfindingswithfamily history and medical pedigree. Definitive diagnosis is made by enzyme assay and genemutationanalysisorlinkageanalysis.

Conclusion

Fabry's diseasebeing a rare cause of chronic kidney disease, more severe in men due to the very low residual function of alphagalactosidase.
CKD, dermatologica , neurological, cardiological manifestations and pedigree analysis strongly suggest the diagnosis of Fabry Disease .

Treatment includes ERT and RRT in the form of dialysis or kidney transplantation. The use of ARBshas been shown to be nephro-protective in other protein uric renal diseases, and could thus beimportantinFDaswell.[13]
Kidney Disease Improving Global Outcomes guidelines suggest that in patients with CKD Stages 3–5,Vitamin Ddeficiencybecorrected. VitaminDcan reduceproteinuriaoralbuminuria.[14]Newer modalities under research include gene therapy substrate deprivation. Studies onERT of FD patients on dialysis are warranted, as this may be the only hope as thesepatientshavetoimprovesurvivalondialysis.

Definitive diagnosis is made by enzyme assay and gene mutation analysis or linkage analysis.
Enzyme Replacement Therapy and Renal Replacement Therapy in the form of dialysis or kidney transplantation treatment option . Newer modalities under research include gene therapy.

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