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RESEARCH ARTICLE

INTERRELATION BETWEENCARDIAC CONDUCTION ANOMALIES AND RADIOLOGICALFEATURES OF FAHR'S SYNDROME: AFACT OR COINCIDENCE? CASE REPORT AND REVIEW OF THE LITTERATURE

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Abstract

Introduction:Fahr's syndrome is a rare, slowly progressive, neurodegenerativedisorder, characterized by extensive, bilateral, and symmetrical basal ganglia calcification. It isassociatedwithneuropsychiatric manifestations and gradually progressive cognitive impairment. Fahr's syndrome is the secondaryform of brain calcification thatiscaused by variousmetabolic, infectious, or degenerativediseases.

Case report: An old manwasadmittedto ourdepartmentwithrecurrentepisodes of syncope. An electrocardiogramrevealedcomplete AV block.Laboratoryresultsdisclosedhypocalcemia, pseudo hypoparathyroidism, and hyperphosphatemia. Computedtomographyrevealedintracranial calcifications suggestiveofFahr's syndrome.

Conclusion: Fahr's syndrome is a rare anatomo-clinical and radiologicalentity, with multiple clinical and etiological aspects. The pathophysiologicalmechanism of the lesionsremainspoorlyunderstood, even more cardiacfeaturesthatmaycause, but is set to benefitfromadvances in functionalneuroimaging.

Introduction:-

Fahr's syndrome (FS), initiallydescribed by Germanneurologist Karl TheodorFahr in 1930,is a rare sporadicgeneticneurodegenerativedisorderwith a prevalence of < 1/1,000,000, characterized by neurologicaldisorders resultingfromabnormal intracranial , non-arteriosclerotic, bilateral and symmetricalcalcification deposits in the basal ganglia, dentate nucleus, cerebral cortex and otherbrain structures (1). It is a rare condition whosepathophysiologicalmechanisms are controversial. The clinical manifestations of FS are highlypolymorphicincludingseizures, cognitive impairment, parkinsonism, tremor, dystonia, ataxia, chorea, dysarthria, headache, and otherneuropsychiatricsymptoms in addition to cardiacirritability, and decreasedcardiaccontractility (2). Itsetiologies are dominated by disorders of phosphocalcicmetabolism(3)(4), and maybe due to variousmedical conditions includinginflammatory, metabolic, autoimmune, and geneticdisorders (5).

Hypoparathyroidism (HP) is an endocrine disorder, caused by aheterogeneous group of conditions, in whichlow calcium and high phosphate levelsoccur as the result of insufficientparathyroid hormone (PTH) secretion. Idiopathichypoparathyroidismis a term for a rare deficient PTH secretionwithoutdefinitive cause and

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maybegeneticallyinherited or may have an autoimmune cause. Radiologically, this state may cause calcifications, predominantly in globuspallidus of the basal ganglia. The association of basal ganglia calcifications withchronic HP, wasdescribed for the first time by Eaton et al. in 1939 (6).

Variousgene mutations werediscoveredassociatedwith the disease, allowing a more precisediseasecharacter (7). A locus on chromosome 14q has been identified as associatedwithbilateralstriatopallidodentatecalcinosis (BSPDC)(8). Familial type of the syndrome has been previouslydescribed(9). Calcium deposits are the major elementresponsible for the radiologicalappearance of this syndrome. Hypoparathyroidism and disturbance of calcium metabolismcanberesponsible for BSPDC development, but cases of patients with normal parathormone levels have also been reported(10) as in ourpatient's case. Pseudohypoparathyroidismassociatedwith production of biologically inactive form of parathormone canalsobeconnectedwith BSPDC pathology. It is possible thatdisturbance of blood flow through basal gangliaassociatedwitharterial malformations cause injury to the blood-brainbarrier. A consequence of thismaybeprecipitation and mineralization of serumproteins. Alkaline phosphatase (AP), whichplays a role in cellular transport, also itmaybeinvolved in pathogenesis of BSPDC.Increase in AP activity in basal gangliawasobserved in patients, whileserum AP activityremainedbeyond normal values. Progressive inflammatoryprocesses in the brainmayalsoberesponsible for calcifications (11).

Fahr’s syndrome isdifferentfromFahr’sdisease, as itiscaused by secondaryfactors, whileFahrdisease arises from a primaryhereditary condition (12).

The symptoms are related to hypocalcemiawithwidespread calcification of the nervous system and vessels. Duringperioperativeperiods, FS alsoraisesconcernsassociatedwithneuromuscularproblems, such as myopathy, abnormalresponse to neuromuscularblocking agents, spasticity, and concerns of hypotension, heartfailure, cardiacarrhythmia, and cerebrovascularattackbecause of hypocalcemia and vessel calcification (13).

Diagnosis of BSPDC isbased on findingpathognomonic basal ganglia calcifications in computedtomography or magneticresonanceimaging(14).

The objective of this case report was to describe an old patientwithcompleteatrioventricular block and bilateralintracranial calcification suggestive of Fahr's syndrome.

Case Report:

A 88-year-old man patient wasreferred to ourdepartment, for pacemaker implantation for completeatrioventricular block, revealed by recurrentepisodes of loss of consciousness, occurring 15 daysbeforehis admission, lasting for 30 minutes, and preceded by atypicalchest pain withblockpnea, eyerevulsionandloss of urine without return to baselineconsciousness.The patienthad nopastmedicalhistory.

The patient also reports diarrhea and therewas no history of fever, rash, head trauma or anydrug abuse.

Physical examinationrevealed a patient with a glascow score of 12 depending on the verbal response (aphasic) withoedemas of the lowerlimbsreachingmid-leg and bilateralsnoringrales.

Hisbaseline ECG showedcompleteatrioventricular block with a ventricular rate of 40 beats per minute (bpm), left bundle branch block with normalQT corrected(Figure 1).

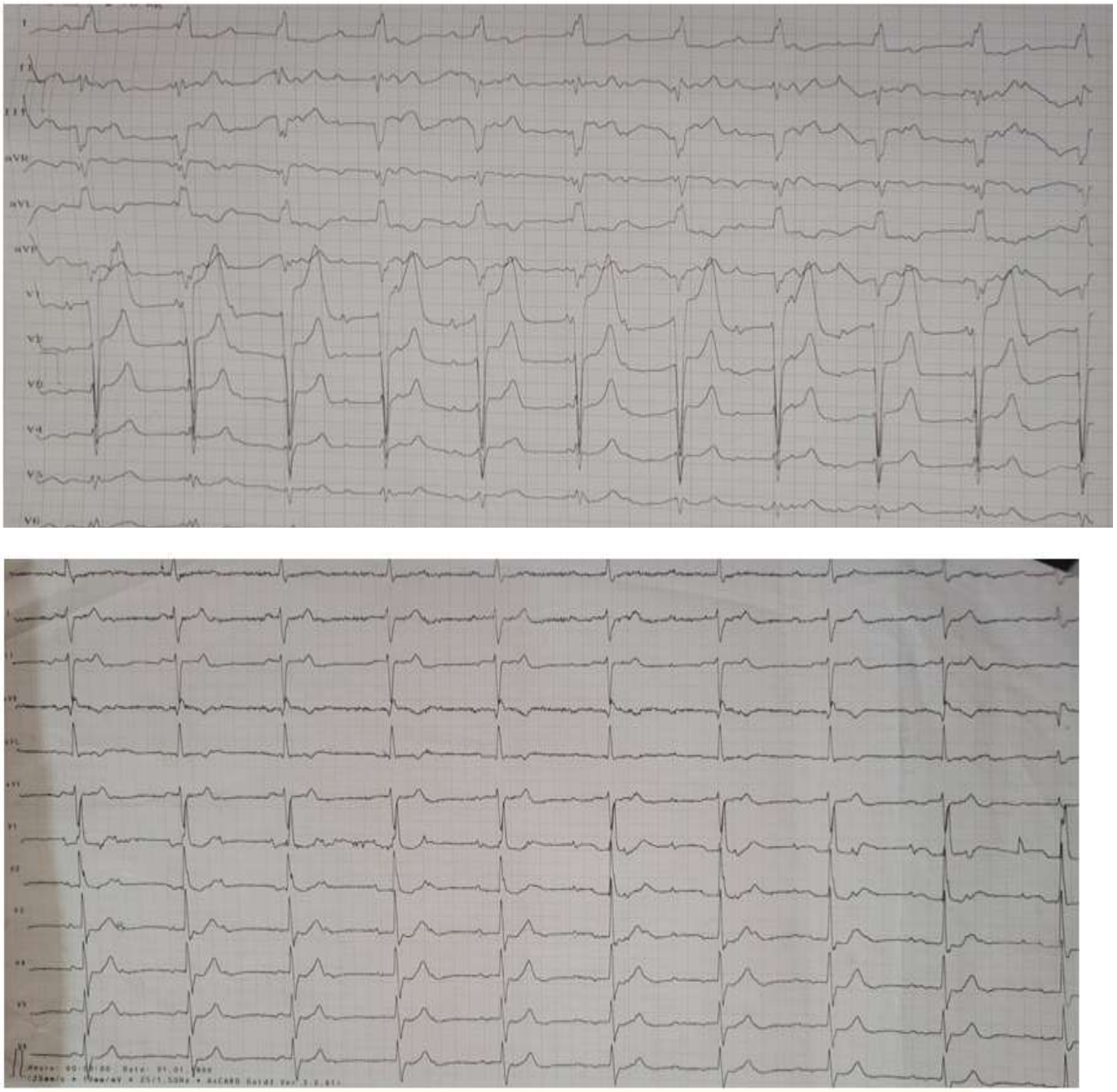

Figure 1:Electrocardiogram of a patient withFahr's syndromeshowingcompleteatrioventricular block with a ventricular rate of 40 beats per minute.

The transthoracicechocardiography has not been done. And hisbrain scan hadshowncalcifications of the choroidplexus and of the brain scythe (figure 2).

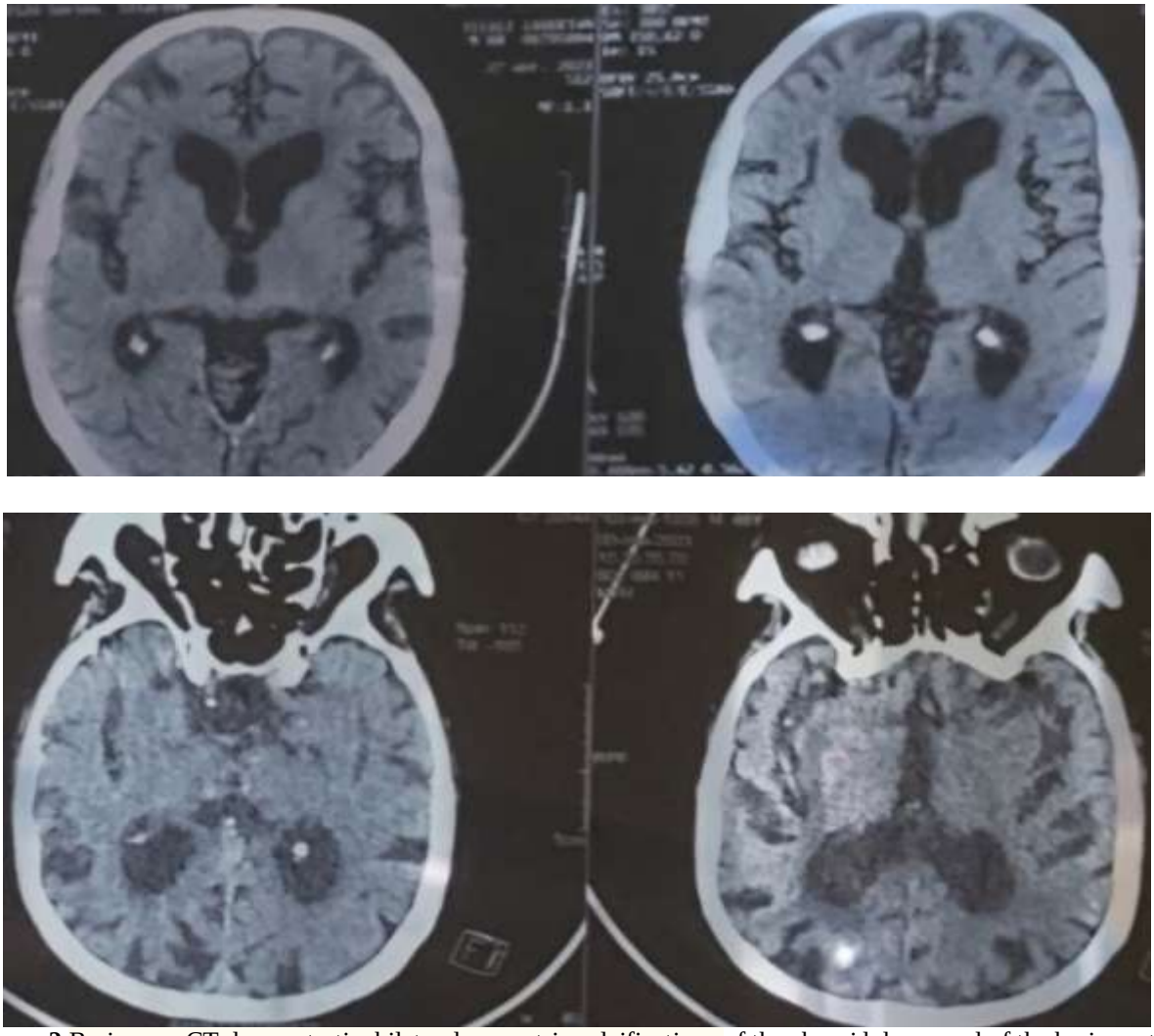

Figure 2:Brain scan CT demonstratingbilateralsymmetric calcifications of the choroidplexus and of the brain scythe in a patient withFahr's syndrome and cardiac conduction anomalies.

Laboratorybloodtestsshowed normal parathormone levelswithhypocalcemia and hyperphosphatemia. Duringhospitalization, the patient presented an increase in his CRP levelwith the identification of E.Coli on cytobacteriologicaltesting of urine, and was put on appropriateantibiotictherapy. This wasfollowedafter a few days of hospitalizationby an asystole cardiac. Immediatecardiopulmonaryresuscitationwasinitiated and maintainedwithoutrecovery of anycardiacactivity.

Discussion:

The termFahr'sdiseaserefers to cases of idiopathic calcifications in the basal ganglia and otherbrainregions, and isclinicallydefined as bilateral BGC in the presence of neuropsychiatric and extrapyramidal disorderswith normal calcium and parathyroidlevels(17)(20). In contrast to thisprimaryform, bilateral and symmetric calcifications of basal ganglia and otherbrainregions, canoccursecondary, as the consequence of variousmetabolic, infectious, or degenerativedisease. Theseincludes endocrine disorders, mitochondrial myopathy, somedermatologicaldisorders, brucellosis, toxoplasmosis…etc(16)(17)(21). And this condition isknown as Fahr's syndrome.

The mostcommonreportedmetabolicdisordersthat cause Fahr's syndrome are HP and pseudohypoparathyroidism(12)(22)(23)(24). HP couldbeiatrogenic, as the consequence of surgicalremoval or radiotherapy, or couldbeidiopathic(12)(19)(21).

There is no clearexplanation for the mechanism of brain calcification and hypocalcemia association. It issuggestedthatincreased calcium-phosphoruscomplex formation plays an important role(19)(21)(23).

The impact of changes in calcium levels in the QT interval in ECG recordingiswell-known. In our case, electrocardiogramrevealedcomplete AV block comparedwitha studyconducted by Dejan M. Marinkovićet al, whereECG has shownepisodes of sinus tachycardiawith first degree AV block and prolongeddepolarization, fullyretreatedwith normal serum calcium levels. Cardiac conduction diseasewas alsoobserved in some cases of FD (25), laboratoryblood tests showedelevatedinflammatorybiomarkers, decreasedserum calcium and parathyroid hormone levels, and serumphosphoruslevelwashigherthan normal range. The results of all other hormone tests were normal(26), as is the case for our patient and for otherstudies (23)(24).

Furtherstudieshave revealed the presence of prolonged QT interval on ECG as for PrashanthPanduranga et al (25), Ahmed S Mohammedin et al (27)andPark, Suyong MD (13).

An ECG examinationtaken on admission in patients withfahr's syndrome revealedflattened T-waves in limb leads, biphasic T-waves in precordial leads V3-V5 and prolongedQTcinterval (531ms). Laboratoryresultsdisclosedhypocalcemia and hyperphosphatemia(28).

Patients with FS are prone to cardiovascularproblems, such as, prolonged QT on ECG and hypocalcemiacardiomyopathy. Furthermore, because calcium is essential for myocardial contractile function, permanent hypocalcemiamayresult in cardiacdysfunction. In severe cases, hypocalcemiamay cause heartfailurewhenaccompanied by renal sodium reabsorption and sodium retention.Therefore,anesthesiologistsshouldpay strict attention to cardiovascular monitoring includingblood pressure, heart rate, CVP,ECG, and a preoperativeechocardiographicexaminationis essential (13).

There isstilllimited data regardingsignificancebetweenFahr'sdisease or Fahr's syndrome and cardiovascularor cerebrovasculardisease (CVD). Some case reports (incidence of stroke in young patient withFahr's disease) and literaturereview supports the pathogenicrole of Fahr's diseasewith CVD due to extensive calcium and mineraldeposits in affectedvesselsleading to reduction of vascularelasticity and hemodynamic changes, although the exact pathogenicmechanismsstillunclear(29)(30). Another case report found the incidence of Fahr's syndrome withcardiomyopathy, calcium isnecessary for myocardial contractile function, whileparathyroid hormone has a positive inotropiceffect on the heart muscle, thushypocalcemia and hypothyroidism in Fahr syndrome may lead to cardiomyopathy (31). A causal linkbetweenFahrdisease and CVD needsfurther investigation.

To date, thereis no standard course of treatment for Fahr's syndrome/disease. A recent prospective study has foundthatincreasedrisk for BGC progression issignificantlyassociatedwithlow calcium/phosphorus ratio, and withhyperphosphatemia. Interestingly, withevery 1% increase in the calcium/phosphorus ratio, progression of basal ganglia calcification decreased by 5% (19)(21)(32).

Conclusion:

Wepresentedthe case of a patient withimagingfeatures suggestive of FS in association withcardiac conduction anomaliesthat have beenfewlyreportedto date. The intriguing question of whetherthereis a reallygenetic association or justcoincidencebetween FD and cardiac conduction system diseaseneedsfurtherstudies.

In conclusion, whenintracranial calcifications are presented, itisimperative to make a careful distinction betweentheirphysiological and pathologicalorigins. For radiologicalapproach, the presence of symmetric, bilateral, and multiple calcifications in brain CT scan raisedconsideration of Fahr's syndrome or Fahr'sdisease.

Everyintracranial calcification, incidentallydetectedduringradiographicimaging, needsthoroughneurologicalexamination and biochemical tests. Timely recognition of thesetwoentitiesallowsappropriatetreatmentthatcanpreventclinical manifestations of the disease and potentially slow its progression.

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