Review / Derleme

Fahr's Disease
Fahr Hastalığı

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ABTRACT

Fahr's disease refers to sporadic or familial idiopathic basal ganglia, cerebral and cerebellar calcification. Patients may remain symptom-free but approximately two-thirds of the patients are symptomatic. Typical presentation starts in the 4th to 5th decades of life. Patients present with pyramidal, extrapyramidal, cerebellar, psychiatric and cognitive manifestations. Various diagnostic studies can be used to detect Fahr's disease and associated abnormalities. There is no specific treatment other than symptomatic support. In this review, clinical features and different types of presentations of Fahr's disease are discussed under the light of current literature.

KEY WORDS: Fahr's disease, Clinical features, Presentation

ÖZET

Fahr hastalığı, ailesel veya sporadik olabilen, idiopatik bazal ganglia, serebral ve serebellar kalsifikasyonla seyreden bir hastalıktır. Hastalar hiçbir belirti vermeyebilir, ancak hastaların yaklaşık olarak üçte ikisi semptomatiktir. Tipik prezentasyon dördüncü ve beşinci dekatlarda başlar. Hastalar piramidal, ekstrapiramidal, serebellar, psikiyatrik ve kognitif bulgularla başvurur. Bir çok tanısal çalışma hem Fahr hastalığının hem de ilişkili hastalıkların tanısını koymada kullanılabilir. Semptomatik tedavi dışında spesifik bir tedavisi yoktur. Bu derlemede Fahr hastalığının klinik özellikleri farklı prezentasyon şekilleri mevcut literatür eşliğinde incelenmiştir.

ANAHTAR SÖZCÜKLER: Fahr hastalığı, Klinik özellikler, Prezentasyon

Introduction

Fahr's disease is a rare clinical neurodegenerative entity with familial or sporadic presentation (1,2). It is charactarized by symmetrical and bilateral calcifitaion over basal ganglia, dentate nucleus and white matter of cerebral cortex (3,4,5). Fahr's disease leads to neurological, psychiatric and cognitive abnormalities (6,7).

Fahr's disease is a rare neurodegenerative disease characterized by almost symmetrical widespread calcification in brain and cerebellum in the absence of any systemic calcium disorder (1,6,7). Many different names are used in literature for the same condition and the nomenclature has been criticized for including heterogeneous etiology but 'Fahr's disease' is still the most commonly preffered term for this entity (2,8).

Background

In 1855, Bomberger described the presence of bilateral symmetrical calcifitation of the basal ganglia histologicaly and in 1930; Karl Theodor Fahr described an adult case with typical clinical and histological findings of this sydrome (5).

In Fahr's disease extensive and almost symmetrical calcifications are present at globus pallidus, putamen, caudate nucleus, internal capsule, lateral parts of thalamus, dentate and lenticular nuclei of cerebellum, white matter of cerebral cortex and intracranial vessels supplying the basal ganglia and the cerebellum (3,4,5,9).

Clinical Presentation

Typical presentation starts in the 4th to 5th decades of life although it may also be evident in childhood (3,8). Patients may remain symptom-free but approximately two-thirds of the patients are symptomatic (1,7). Most of the symptomatic cases present with extrapyramidal symptoms (2,5). Clinical signs and symptoms may be variable and include; parkinsonism, chorea, tremor, distonia, disarthria, paresis, speech impairment, seizures, syncope , stroke like events, memory deficits and ataxia (1,2,3,7). Another type of presentation is behavioural dysfunction and psychiatric symptoms such as anxiety, attention deficit, hallucinations, personality disorders , psychosis, mood disorders and dementia (2,3,6,8).

Fahr's disease is a neurodegenerative disease which may present with acute deterioration in the level of conscioness. Sudden onset of loss of conciosness maybe the first symptom of Fahr's disease (7,9). Loss of consciousness in Fahr's disease is usually secondary to seizures (3,5). However this acute condition maybe the result of any accompanying intracranial pathology or metabolic disorder (3,4).

Presentation of Fahr's disease as aneurysmal subarachnoid hemorrhage is extremely rare. There is only one case of Fahr's disease presenting with aneurysmal subarachnoid hemorrhage in the literature (3). When a case of Fahr's disease presents with loss consciosness, aneurysmal subarachnoid hemorrhage should be kept in mind (10).

Diagnostic Studies

Making a clinical diagnosis of Fahr's disease relies on the combination of clinical features, brain imaging, and exclusion of other causes of intracranial calcification (11,12). Skull x-ray can detect intracerebral calcifications to some extent however; Computed Tomography (CT) is considerably more sensitive to detect intracerebral calcifications. The image pattern is not strictly related with etiology, although some differences in dystrophic senile calcifications. CT is a practical, easy imaging modality and has maximum sensitivity and allows diagnosis, contributing to early treatment of many etiologies of Fahr's syndrome (4,13).

Magnetic Resonance Imaging (MRI) supplies better anatomical detail than CT but is less sensitive in detecting calcification. Brain SPECT (Single-photon emission computed tomography) complements anatomical imaging studies such as CT and MRI (14). Brain SPECT abnormalities are often present earlier than the abnormalities seen on anatomical imaging studies. The detection of perfusion abnormalities can lead to an early diagnosis and asist with clinical management. Reduced blood flow to calcified regions was confirmed in Spect of the brain with ^{99m}Tc-hexamethylpropilenamine (^{99m}Tc-HMPAO) by Uygur et al. (9).

The increased levels of Cu, Zn, Fe and Mg was found and it was advocated that this reflects the involvement of metabolism of several metals and/or metal-binding proteins during the progression of Fahr's disease (15).

Associated Diseases

Fahr's disease is related with many etiologies that can be classified as inflammatory

(CMV infection, neurocysticercosis, toxoplasmosis, neurobrucellosis, tuberculosis, HIV infection), tumoral (astrocytomas), hypoxic and vascular (arteriovenous malformations calcified infarct, ischemic encephalophaty), endocrine (hypoparathyroidsm, pseuso and pseudohypoparathyroidism, hyperparathyroidism), toxic (CO and Pb intoxication, hypervitaminosis D, radiotherapy), metabolic and degenerative (senility, mithocondrial encephalopaties, leukodistrophic diseases, idiopathic familial, motor neuron disease, myotonic muscular dystrophy, carbonic anidrase deficit, biopterin deficit) and other (malabsorption, Down syndrome, lupus, tuberous sclerosis, arthrogriposis) (2,4,10,11).

Treatment

There is no specific treatment other than symptomatic support (11,12). The response to levodopa in those with parkinsonian features is poor (16). The use of antipsychotics may be indicated in those presenting with psychotic symptoms or behavioural problems. The choice of atypical antipsychotics or those with less extra-pyramidal side-effects is more prefferable due to co-existence of extrapyramidal symptoms in these patients (7,17). Seizures are treated with antiepileptic drugs (5).

Prognosis

There is no satisfactory data about the prognosis of Fahr's disease in the literature, so definite prognosis for individuals with Fahr's syndrome is unclear. However, progressive neurological deterioration may result in disability and death (2,11).

Conclusion

Fahr's disease is characterized by bilateral almost symmetrical calcification of cerebrum or cerebellum which may be asymptomatic or may present with a variety of neurological and psychiatric conditions. It may be real cause of many neurological and cognitive abnormalities which can be diagnosed easily. It is important to diagnose the Fahr's disease in certain neurological and psychiatric presentations.

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