Original Article

Clinical and Outcome Analysis in Head Injury Patients with Fahr's Disease

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Abstract

Context: Fahr's disease (FD) is a rare neurodegenerative disorder. Head injury in patients with FD is an uncommon occurrence. **Aim:** The aim is to evaluate clinical and outcome characteristics in traumatic head injury patients with FD. **Settings and Design:** Retrospective cohort study. **Materials and Methods:** This retrospective cohort study includes 13 patients of FD presenting as head injury in neurosurgical emergency between September 2018 and February 2021. Each patient was evaluated in terms of demographic profile, Glasgow coma scale (GCS) at admission, severity of head injury, type of head injury, preexisting clinical features of FD, radiological findings, Glasgow outcome score (GOS), family history of FD, and biochemical abnormalities. Patients were also evaluated for dichotomized outcome (Good recovery: GOS 5–4 versus Poor recovery: GOS 1–3) and gender differences in FD presentation. **Statistical Analysis Used:** Fisher's exact test and unpaired *t*-test were used. $P < 0.05$ was considered statistically significant. **Results:** Neurological symptoms (69.2%), neuropsychiatric manifestations (46.1%) and extrapyramidal features (38.5%) were preexisting in these patients. Seizure (61.5%) was the most common neurological manifestation. Depression (23.1%) and anxiety disorder (15.4%) were common psychiatric disorders seen. Akathisia (23.1%) followed by tremor (15.4%) were predominant extrapyramidal presentations. On dichotomized outcome analysis, preexisting neurological, neuropsychiatric, and extrapyramidal manifestations due to FD were not associated significantly with outcome following head injury. GCS at admission, severity of head injury and pupillary changes were significantly associated with outcome ($P < 0.05$). Neuropsychiatric features ($P = 0.0210$) were significantly more in females suffering from FD. **Conclusions:** Neurological features in FD predominate over neuropsychiatric and extrapyramidal symptoms. FD does not affect outcome following head injury.

Keywords: *Clinical presentation, Fahr's disease, head injury, outcome analysis*

Introduction

Fahr's disease (FD) is a rare disorder with characteristic presence of idiopathic bilateral calcification in striopallidodentate (SPD) area.[1] In FD calcification is due to calcium carbonate/phosphate deposition in the basal ganglia, thalamus, hippocampal formation, cerebrum, cerebellum, subcortical white matter, and dentate nucleus.[2] It mostly shows an autosomal dominant transmission, but may be autosomal recessive or sporadic.[3] Chromosome 14q is a susceptible locus for FD.[4] FD is reported in about 0.3%–1.2% of computed tomography (CT) of the brain.[5]

The diagnosis of FD is heralded by the presence of bilaterally symmetrical SPD calcification in absence of biochemical abnormalities and the presence of family history (in nonsporadic cases).[6] In case of the presence of biochemical abnormalities, the term Fahr's syndrome is used. FD presents with neurological, extrapyramidal, and psychiatric manifestations or may remain asymptomatic with incidental diagnosis on CT scan of the brain done for some other reason.[7]

Preferred radiological imaging for FD is noncontrast CT (NCCT) and magnetic resonance imaging (MRI) brain [Figures 1 and 2]. NCCT of the brain is more sensitive in detecting SPD calcification seen in FD than MRI brain.[8]

Management of FD is focused on symptomatic relief. Prenatal genetic counseling in families with history of FD should be done to prevent affection in babies.

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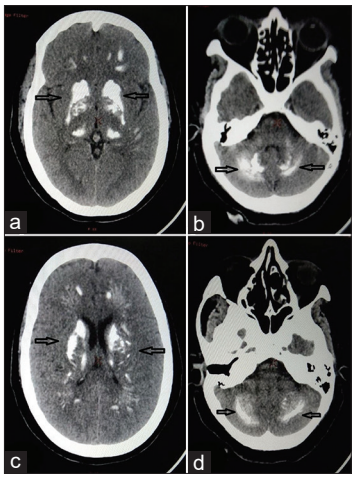

Figure 1: (a-d) Noncontrast computed tomography scan brain axial cuts showing bilateral symmetrical calcification in strio-pallido-dentate area

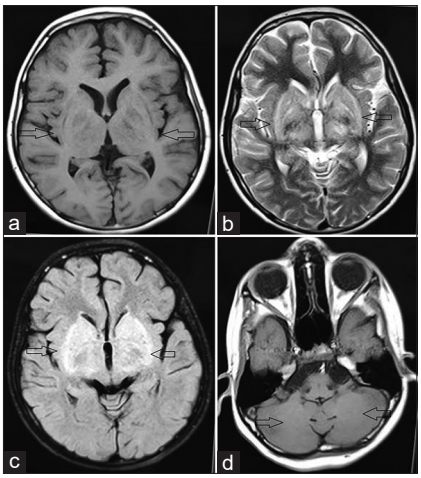

Figure 2: Magnetic resonance imaging brain axial cuts, (a) T1 image (calcified areas are of high signal), (b) T2 image (calcified areas demonstrate low to isointense signal), (c) fluid-attenuated inversion recovery image and (d) T1 image showing bilateral symmetrical strio-pallido-dentate calcification

This study aims to study the impact of FD on the outcome of head injury sustained in such patients and to evaluate the clinical manifestations of FD in symptomatic patients.

Materials and Methods

This retrospective cohort study includes 13 patients of FD presenting to neurosurgical emergency as head injury in our neurosurgery department between September 1, 2018, and February 2, 2021.

Diagnostic criteria for Fahr's disease[6]

1. Bilaterally symmetrical SPD calcification;
2. Progressive neurological dysfunction;
3. No biochemical alterations in blood, infection, trauma, or toxicity; and
4. History of FD in family (in case of nonsporadic FD).

To rule out biochemical alterations in calcium metabolism, serum levels of Ca^{2}+, Mg^{2}+, PO_4^{3-}, parathyroid hormone, Vitamin D, and calcitonin were done. Ellsworth–Howard test was done for evaluation of hypoparathyroidism. To rule out heavy metal toxicity, their levels in blood and urine were evaluated. Cerebrospinal fluid examination was done to rule out infectious and autoimmune causes.

Each patient was evaluated in term of demographic profile, Glasgow coma scale (GCS) at admission, severity of head injury, type of head injury, preexisting clinical features of FD, radiological findings, Glasgow Outcome Score (GOS) at discharge, family history of FD, and biochemical abnormalities. Patients were also evaluated for dichotomized outcome (good recovery: GOS 5–4 vs. poor recovery: GOS 1–3) and gender differences in FD presentation.

Data were collected retrospectively by analyzing medical and radiological records of these 13 patients. Follow-up data were collect from outpatient department records. Nine patients of FD at the time of presentation were having preexisting symptoms for which they were taking treatment from either a neurologist or a psychiatrist. These patients were already diagnosed as FD by the treating physician. Four patients were having incidental finding of FD at presentation. We repeated and performed all the biochemical evaluation of patient and radiological evaluation of relatives at the initial visit only.

Since genetic testing for FD is not available at our center and due to poor socioeconomic conditions of the patients genetic testing was not done. Management of FD was done based on symptoms in collaboration with psychiatry and neurology department. Eight patients were having isolated head injuries, whereas three patients were having orthopedic injury and two patients were having maxillofacial injuries in addition to head injury.

Unpaired *t*-test and Fisher's exact test were used according to the type of data analyzed. $P < 0.05$ was taken as statistically significant. GraphPad Prism version 8.3.0 for Windows, (GraphPad Software, San Diego, California USA) software was used for statistical analysis.

Results

Of 7344 brain CT scans done for head injury patients in 2 years, 13 (0.18%) patients were found to have bilateral symmetrical SPD calcification.

Patients of FD that presented to the emergency department as head injury were having history of neurological symptoms (n = 9, 69.2%), neuropsychiatric manifestations (n = 6, 46.1%), and extrapyramidal features (n = 5, 38.5%).

Most common preexisting neurological feature was seizure (61.5%) followed by episodes of loss of consciousness (23.1%), dementia (23.1%), and gait disorder (15.4%) [Table 1].

Most common preexisting neuropsychiatric features were depression (23.1%) followed by anxiety disorder (15.4%) and psychosis (7.7%) for which these patients were already taking treatment under a psychiatrist [Table 1].

Most common preexisting extrapyramidal feature was akathisia (23.1%) followed by tremor (15.4%) [Table 1].

On the NCCT brain, bilateral SPD calcification was present in all patients. No biochemical abnormality of calcium metabolism was found in any patient. On evaluating the NCCT brain of first-degree relatives of the patient, similar radiological findings were present relatives of three patients. No radiological similarity was present in relatives of four patients. Family relatives of six patients did not consented for performing NCCT head [Table 1].

Most patients presented with mild head injury (61.5%) followed by moderate (30.8%) and severe (7.7%) head injury. Concussion (53.8%) followed by DAI (30.8%), small parietal EDH (7.7%) and frontal contusion (7.7%) were types of head injury sustained in these patients [Table 1].

Mean age of the patients was 34.5 years. Females (61.5%) were predominantly more than males (38.5%) [Table 2], with male-to-female ratio of 1:1.6. Mean duration of follow-up was 5.8 months to address for head injury.

Most of FD patients presenting as head injury were having GOS of 5 (69.2%) followed by GOS 4 (15.4%), GOS 3 (7.7%), and GOS 1 (7.7%) [Table 3].

On dichotomized outcome analysis, preexisting neurological, neuropsychiatric, and extrapyramidal manifestations due to FD were not associated significantly with outcome following head injury [Table 4].

GCS at admission, severity of the head injury and pupillary changes were significantly associated with outcome ($P < 0.05$) [Table 4].

Among the preexisting neurological, neuropsychiatric and extrapyramidal features, neuropsychiatric features ($P = 0.0210$) were significantly more in females suffering from FD as compared to males [Table 5].

Table 1: Clinical presentation of patients with Fahr's disease (*n*=13) presenting with head injury

Clinical presentation	Number of patients, *n* (%)
Neurological features	
Seizure	8 (61.5)
Episodes of LOC	3 (23.1)
Dementia	3 (23.1)
Gait disorder	2 (15.4)
Absent	4 (30.8)
Neuropsychiatric features	
Depression	3 (23.1)
Psychosis	1 (7.7)
Anxiety disorder	2 (15.4)
Absent	7 (53.8)
Extrapyramidal features	
Akathisia	3 (23.1)
Tremor	2 (15.4)
Absent	8 (61.5)
Imaging findings (NCCT head)	
B/L strio-pallido-dentate calcification (SPD)	13 (100)
Biochemical abnormality	
Present	0
Absent	13 (100)
Severity of head injury	
Mild (GCS 13-15)	8 (61.5)
Moderate (GCS 9-12)	4 (30.8)
Severe (GCS 3-8)	1 (7.7)
Similar radiological findings in family	
Present	3 (23.1)
Absent	4 (30.8)
Data not available	6 (46.1)
Type of head injury	
Concussion	7 (53.8)
Right frontal contusion	1 (7.7)
Small parietal EDH	1 (7.7)
DAI	4 (30.8)

LOC - Loss of consciousness; NCCT - Noncontrast head computed tomography; SPD - Striopallidodentate; GCS - Glasgow Coma Scale; DAI - Diffuse axonal injury; EDH - Extradural hematoma

Table 2: Age and gender distribution

Characteristic	Number of patients, *n* (%)/value
Age (years)	
Mean±SD	34.5±5.7
Gender	
Male	5 (38.5)
Female	8 (61.5)

SD - Standard deviation

Discussion

FD is a rare disorder with bilateral symmetrical SPD calcification reported in 0.5%–10% of CT scans of the brain.[9-11] In our study, 0.18% of CT brains showed bilateral SPD calcification. Radiologically prevalence of SPD calcification is more in children (15%) as compared to adults.[12]

Neurological manifestations FD vary from 0% to 20% of patients.[9,13] Involvement of frontostriatal motor fibers may result in motor neurological manifestations. Neurological manifestations of FD commonly consist of epilepsy, Parkinson such as features, speech disturbances, dystonia, and dementia.[14,15] Extrapyramidal symptoms are seen in 30%–55% of patients.[7,16] In our study, the most common presentation of FD was neurological symptoms (69.2%) followed by neuropsychiatric manifestations (46.1%) and extrapyramidal features (38.5%). Seizure (61.5%) was more common neurological symptom followed by episodes of loss of consciousness (23.1%), dementia (23.1%),

and gait disorder (15.4%). Akathisia (23.1%) was more common extrapyramidal manifestation of FD followed by tremor (15.4%).

Studies have reported schizophrenia-like psychosis (35%) followed by mania and bipolar disorder (22.5% each) and depression (20%) as the common neuropsychiatric manifestations of FD.[7] About 40% of patients with BG calcification show neuropsychiatric manifestations.[7] Cortico-subcortical disconnection due to BG calcification involves frontostriatal and limbic pathways[7,17,18] resulting in psychosis, mood, personality, and cognition disorders. In our study, we found that depression (23.1%) was the most common neuropsychiatric manifestation in FD followed by anxiety disorder (15.4%) and psychosis (7.7%).

Table 3: Glasgow outcome score of patients of Fahr's disease patients presenting with head injury

Glasgow outcome score	Number of patients, *n* (%)
1	1 (7.7)
2	0
3	1 (7.7)
4	2 (15.4)
5	9 (69.2)

In our study, mean age of the patients was 34.5 years. According to reported series, FD manifests in fourth to fifth decades of life.[2,19] Studies have shown male predominance with male-to-female ratio of 2:1.[20] In our study, females were predominant than males, with male-to-female ratio of 1:1.6.

Most of FD patients in this study, presenting as head injury were having good recovery (GOS of 5 and 4). On dichotomized outcome analysis, preexisting neurological, neuropsychiatric, and extrapyramidal manifestations due to FD were not associated significantly with outcome following head injury ($P > 0.05$). There is paucity of literature with regards to outcome following head injury in FD patients. In our study, GCS at admission, severity of head injury, and pupillary changes were significantly associated with outcome ($P < 0.05$).

In our study, neuropsychiatric features ($P = 0.0210$) were significantly more in females suffering from FD than males. There is paucity of literature in this regard.

Since, the sample size taken is small owing to rarity of the FD, the statistical analysis used is having limitations in evaluating potential association with the outcome. Further large size samples may be required for strong statistical validity of results.

Table 4: Dichotomized outcome analysis of Fahr's disease patients presenting with head injury (good recovery: Glasgow outcome score 5-4, poor recovery: Glasgow outcome score 1-3)

Characteristics	Good recovery (11)	Poor recovery (2)	*P*
Neurological features			
Present (9)	7	2	>0.9999
Absent (4)	4	0	
Neuropsychiatric features			
Present (6)	4	2	0.1923
Absent (7)	7	0	
Extrapyramidal features			
Present (5)	3	2	0.1282
Absent (8)	8	0	
Severity of head injury			
Mild (8)	8	0	0.0268*
Moderate (4)	3	1	
Severe (1)	0	1	
Type of head injury			
Concussion (7)	7	0	0.1499
Frontal contusion (1)	1	0	
Small parietal EDH (1)	1	0	
DAI (4)	2	2	
GCS at admission	13.09 (SD=2.16)	6.50 (SD=0.7)	0.0016*
Pupillary changes			
Present	0	2	0.0128*
Absent	11	0	
Age (years)	32.8 (SD=7.3)	35.2 (SD=3.5)	0.6660
Gender			
Male (5)	4	1	>0.9999
Female (8)	7	1	

GCS - Glasgow Coma Scale; DAI - Diffuse axonal injury; EDH - Extradural hematoma, * - Significant (P<0.05)

Table 5: Gender differences in Fahr's disease presentation

Clinical presentation	Male (5)	Female (8)	*P*
Neurological features			
Present (9)	4	5	>0.9999
Absent (4)	1	3	
Neuropsychiatric features			
Present (6)	0	6	0.0210*
Absent (7)	5	2	
Extrapyramidal features			
Present (5)	2	3	>0.9999
Absent (8)	3	5	

* - Significant (P<0.05)

Conclusions

FD is a rare neurodegenerative disorder. 0.18% of CT brains show FD features. Neurological symptoms predominate over neuropsychiatric and extrapyramidal symptoms. FD does not affect outcome following head injury. Females are predominantly having more neuropsychiatric manifestations in FD when compared to males.

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Conflicts of interest

There are no conflicts of interest.

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