International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Case Report..

Familial Ataxia with Deaf Mutism and Muscle Wasting

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ABSTRACT

There are very few cases described in literature of familial ataxia with deaf mutism. Although Friedreich's ataxia can present with deafness, but its onset is usually before 25 years. Recently it has been documented that 25% of the cases can present as late onset Friedreich's ataxia (LOFA; 25-39years) and very late onset Friedreich's ataxia (VLOFA; ≥ 40 years). Here we are describing a family in which three members were affected, two having deaf-mutism and one having only ataxia, with onset of ataxia after 50 years of age and there was presence of muscle wasting. The clinical phenotype was not like that of Friedreich's ataxia according to Harding's criteria and Quebec cooperative study on Friedreich's ataxia criteria. The mutation analysis for GAA expansion in the first intron of frataxin gene was also found to be normal. This case opens the discussion for occurrence of this rare association of genetic ataxia with deaf mutism.

Keywords: Familial Ataxia with Deaf-Mutism, Late-Onset Friedreich's Ataxia, Ataxia Deafness and Muscle Wasting.

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Article History:

Received: 08-02-2021, **Revised:** 03-03-2021, **Accepted:** 29-03-2021

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2021.7.2.014	

INTRODUCTION

Very few cases of familial ataxia with deaf mutism have been described in literature. Although the most common autosomal recessive ataxia i.e Friedreich's ataxia (FA) can present with deafness, but its onset is usually before 25 years. However now it has been documented that 25% of the cases can present themselves with a late onset Friedreich's ataxia (LOFA; 25-39years) and a very late onset Friedreich's ataxia (VLOFA; ≥ 40 years). The typical clinical phenotype of FA is of gradually progressive ataxia of limbs and gait, dysarthria, absent deep tendon reflexes, extensor plantar response, distal loss of joint position and vibration sense and electrophysiological evidence of neuropathy.[1]

Matthews (1950) described a family in which four siblings out of seven developed a condition like FA accompanied with muscular wasting of unusual distribution. Three of the affected members were deaf-mute. Ataxia was noted in this family by the age of 30 years.[2] Here we are describing a family in which three members were affected, two having deaf-mutism and one having only ataxia, with onset of ataxia after 50 years of age with presence of muscle wasting.

CASE REPORT

A 55-year male was admitted in our medical college who was deaf-mute since his early childhood. The history of the disease was given by patient's son (who can converse with his father with the help of sign language) and other relatives. Patient was normal at birth and attained all his milestones at appropriate time except the speech. It was only by 4-5 years of age when his parents realized that child is deaf-mute. The patient attended special school where he learned the technique of lip reading.

Patient was apparently asymptomatic 3 years back when he developed swaying while walking which was more in walking through narrow corridor, uneven surfaces and without any difference in daylight or dark. Subsequently, he developed nodding of head, truncal ataxia and dysarthria. In two and a half years' time, the patient became non-ambulatory, confined to bed and required one person support to walk. On examination his blood pressure was 140/80 mm of Hg without any postural drop. There was no scoliosis, and no deformity of the feet.

In cranial nerve examination positive findings were slow saccades and broken pursuits with full extra ocular movement and no

nystagmus. For practical purposes he was completely deaf. Eighth cranial nerve examination revealed bilateral sensorineural deafness. Motor examination revealed presence of fasciculation's and wasting of bilateral quadriceps and left first dorsal interossei (Figure 1). There was detectable weakness of bilateral quadriceps, tibialis anterior and first dorsal interossei. Deep tendon reflexes were uniformly exaggerated and plantar's were bilaterally extensor. Sensory examination was normal and cerebellar examination showed presence of both upper and lower limb in coordination with ataxic gait.

Routine blood investigations including complete blood counts, renal function test, liver function test, thyroid function test, HIV ELISA, VDRL, serum B12 level were all normal. Nerve conduction studies were normal, and electromyography showed presence of fasciculation's, large amplitude, prolong duration polyphasic MUAP's in bilateral vastus lateralis and left first dorsal interossei with incomplete interference pattern suggesting neurogenic pattern. ECG, EEG and somatosensory evoked potentials were normal and MRI brain showed presence of cerebellar and diffuse cerebral atrophy (Figure 2). Mutation analysis using triplet primed PCR (TP-PCR) was done to detect GAA expansion in the first intron of frataxin gene which was found to be normal (6/8 GAA repeats).

On detailed family history, it was found that a total of three members were affected in the family including this patient. Patient's mother was also deaf-mute, and she developed ataxia at around 50-55 years of age. She died at 68 years of age and it was a natural death. Patient's elder brother is 75 years of age with normal hearing and speech, developed ataxia at around 52-53 years of age. He is now bedridden and not brought to this hospital, so we were not able to examine this patient. The inheritance pattern seems to be autosomal recessive (Figure 3).

Figure 1: Showing wasting of A. Left first dorsal interossei B. Bilateral quadriceps.

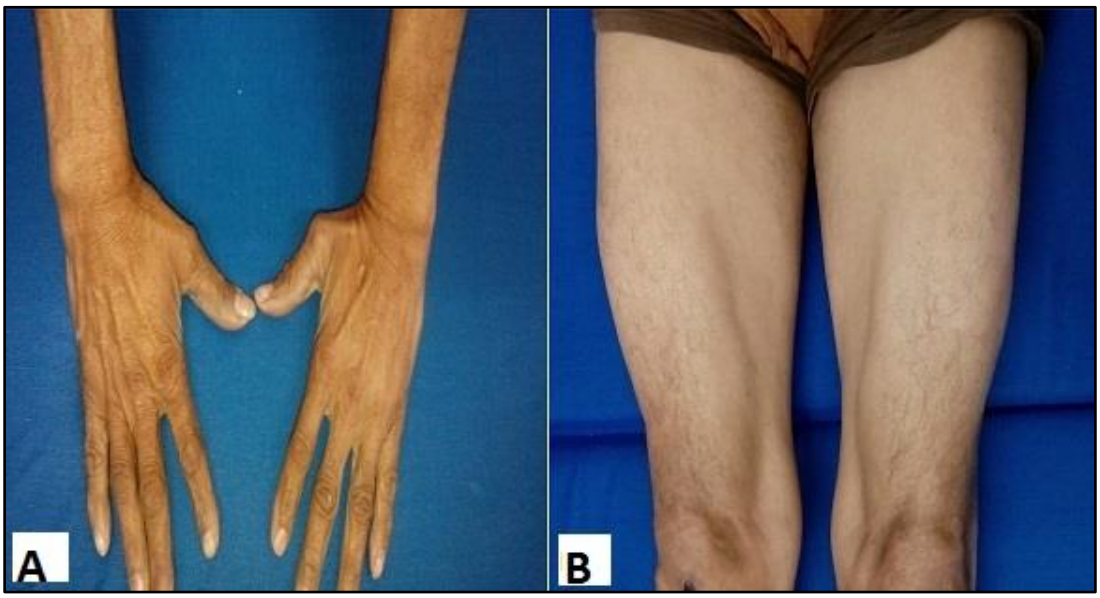


Figure 2: MRI brain T 2 axial image showing diffuse cerebral and cerebellar atrophy.

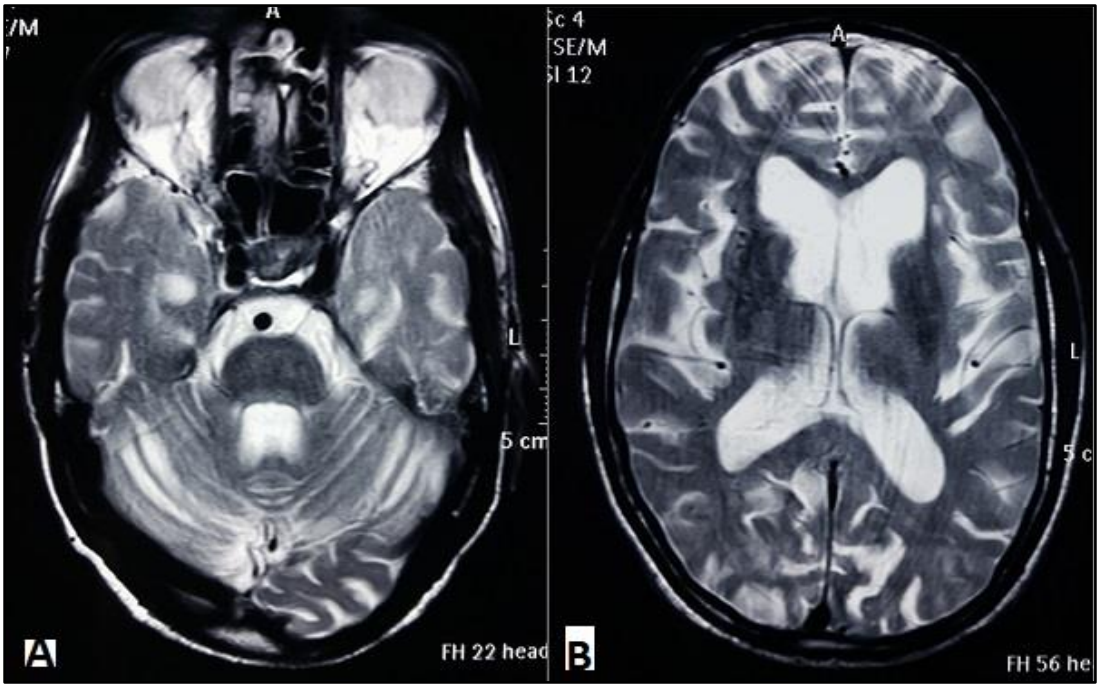
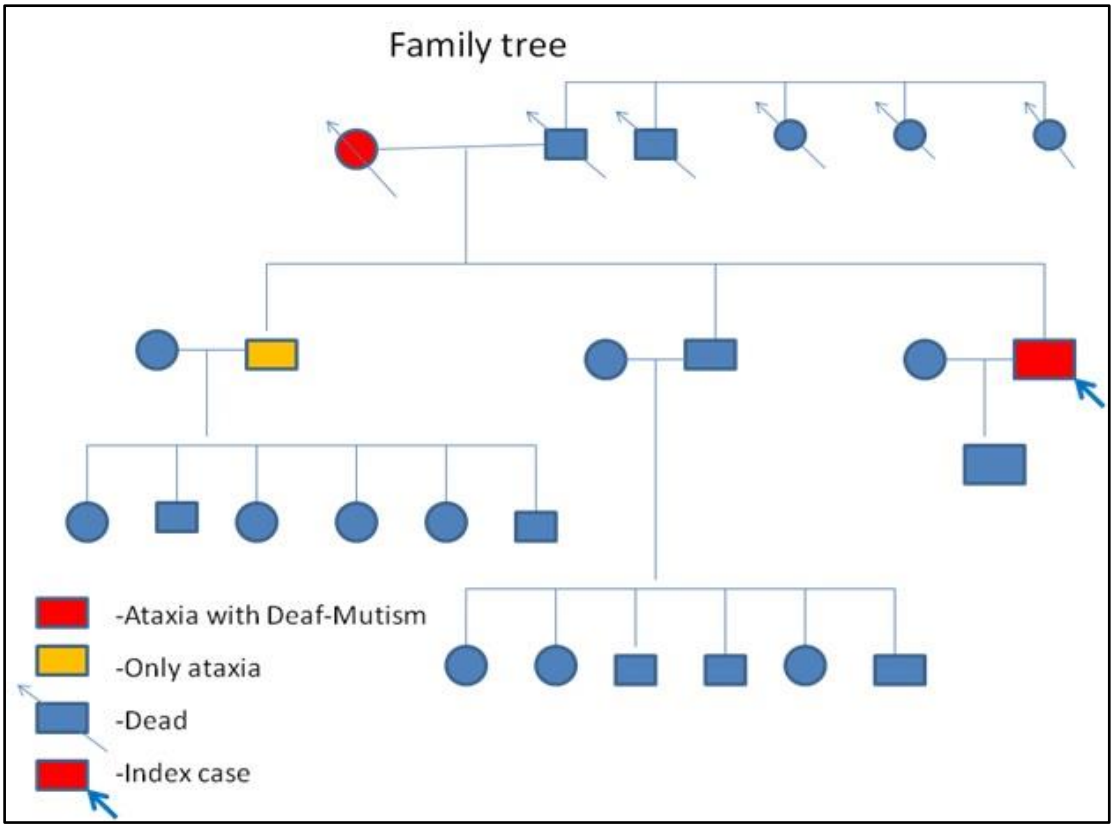


Figure 3: Family tree



DISCUSSION

Association of familial ataxia and deaf mutism has been described rarely in literature. The triad of early onset deafness with ataxia and mental retardation has been reported by Jenne et.al (1963) and Berman et.al (1973).[3-5] Jenne and colleagues described a brother and sister who developed progressive hearing loss, cerebellar ataxia and mental deterioration at about the age of 6 years. They also had pigmented skin lesions, depressed tendon reflexes and extensor plantar response. The three brothers described by Berman et.al had mental retardation, sensorineural deafness (that was detected in infancy) and ataxia. There was mild spasticity in legs with extensor plantar response. There was presence of distal neurogenic atrophy in limbs which was confirmed electromyographically and histologically. Inheritence was probably autosomal recessive but could have been X-linked.

Another family grouped under Harding's classification of ADCA type IV is described by May and White (1968) and Baraitser et.al (1984).[6,7] This disorder is characterized by deafness developing in the first to third decades, followed by progressive cerebellar ataxia in the third to sixth decades associated with photosensitive myoclonus and electrophysiological evidence of sensory neuropathy.

Matthews (1950) described a family in which 4 members were affected. Three individuals had severe congenital deafness. Ataxia was noted in two by the age of 30 years, along with wasting of small hand muscles and quadriceps femoris, depressed tendon reflexes and sensory loss in the lower limbs. Concluding his paper Matthews considered this as familial disorder reminiscent of FA, without pes cavus or scoliosis, but with the addition of deaf mutism in three and of selective muscular wasting in all.[2]

FA is the most common form of hereditary ataxia. The typical clinical phenotype is of gradually progressive ataxia of limbs and gait, dysarthria, absent deep tendon reflexes, extensor plantar response, distal loss of joint position and vibration sense and electrophysiological evidence of neuropathy. Deafness has been relatively rarely reported in cases of FA. Harding (1981 a) found that 9 out of 115 patients had sensorineural deafness, which was moderate to severe in three.[3] There has been considerable controversy as to whether distal amyotrophy occurs in FA. Friedreich (1876) observed it in all four limbs in some of his patients in late stages of disease. Spillar (1910) commented on severe atrophy of the small hand muscles in one of his cases and considered it to be a late sign. Three of Whyte's (1898) patients had "main en griffe" deformities of the hand.[8] Nevertheless Symonds and Shaw (1926) firmly stated that distal amyotrophy never occurred in the disease and Gilbert (1962) said: When distal muscular atrophy appears in the course of what might have appeared to represent FA, that diagnosis should be seriously questioned.[9] In Harding's (1981a) series wasting of the small hand muscles was present in nearly half of the patients.[5]

Unfortunately, we got the chance of examining only one member because one is dead and the other one is now 75 years of age, bedridden and could not be brought to our institute. Onset of ataxia in all three cases was after 50 years of age. The inheritance pattern seems to be autosomal recessive. This index case was deaf-mute with onset of ataxia at around 52 of years and had dysarthria, wasting of bilateral quadricep femoris and left first dorsal interossei, exaggerated deep tendon reflexes, extensor plantar response, normal sensory examination, and normal nerve conduction studies. There were phenotypic differences from what has been described for FA according to Harding's criteria and Quebec cooperative study on Friedreich's ataxia criteria like age of onset, deaf-mutism, brisk reflexes, normal sensory examination, absence of any skeletal deformity, presence of wasting and

normal nerve conduction studies. MRI brain showed cerebellar and diffuse cerebral atrophy which too, is not a characteristic of FA. Mutation analysis for GAA expansion in the first intron of frataxin gene was found to be normal. This family closely resembles the family described by Matthews but the major difference between the two was presence of sensory involvement and absent deep tendon reflexes in lower limb in the latter.

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Source of Support: Nil.

Conflict of Interest: None Declared

Cite this article as: Rajendra Kumar Pandey, Prithpal Singh Matreja. Familial Ataxia with Deaf Mutism and Muscle Wasting. Int J Med Res Prof. 2021 Mar; 7(2): 56-59.
DOI:10.21276/ijmrp.2021.7.2.014