CASE REPORTS

“FAMILIAL SPASTIC PARAPLEGIA” (STRÜMPELL-LORRAIN SYNDROME)

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ABSTRACT

Familial spastic paraplegia (FSP) is not a single disease entity; it is a group of clinically and genetically diverse disorders that share a primary feature of progressive and generally severe lower extremity weakness and spasticity. We present a family with uncomplicated FSP from a remote village of Gilgit, Pakistan. Clinical presentation of 6 years of gait disturbance and frequent falls in elder son, led us to the diagnosis of definite FSP in our index patient and one of the siblings and findings consistent with probable FSP in their mother.

Keywords: Familial spastic paraplegia, Hereditary spastic paraplegia, Strümpell-Lorrain syndrome

INTRODUCTION

Familial spastic paraplegia (FSP) is a description for familial disorders with primary presentation of progressive, bilateral, lower extremity spastic weakness. Strümpell first described familial forms of spastic paraplegia in 1883, with Lorrain later providing more extensive detail. FSP is also called hereditary spastic paraplegia and Strümpell-Lorrain syndrome1. The age for onset of symptoms and degree of severity may vary widely within different clinical, inherited and genetic types of FSP. Physical therapy and medications are significantly helpful in decreasing muscle spasticity and improving range of motion of the lower limbs.

CASE HISTORY

Ten year old boy presented to our OPD with complaints of difficulty in walking since 4 years of age. According to the parents the child started walking at the age of 15 months. At around 4 years parents observed that child had difficulty in walking and climbing stairs. They also noticed that he used to walk on his toes, with frequent falls, and inability to run. There was no past history of head injury, meningitis, epilepsy or regression of any other milestones. He achieved age appropriate developmental milestones. He was delivered full term with no antenatal or perinatal complications. He was eldest among the four issues of consanguineous parents with other siblings aged six years, two and a half years and seven months. There was also history of difficulty in walking in younger sibling aged 6 years.

On examination he was an intelligent and a cooperative child. There was no dysmorphism and his height (129 cm) and weight (25 kg) were on the 10th percentile with fronto-occipital circumference of 50 cm, which was normal for his age. His ophthalmological and hearing assessment was unremarkable with normal speech. Examination of the central nervous system revealed normal cognitive functions and intact cranial nerves. There was no sensory deficit and he was continent for urine and stool. Examination of the spine was unremarkable. Motor examination of the lower limbs showed hypertonia, hyperreflexia, ankle clonus and bilaterally up going planters. There was no loss of muscle mass. Upper limbs examination was normal. He had a broad, spastic gait with toe walking. Rest of the systemic examination revealed no abnormality. A normal CT scan brain was followed by MRI of brain and spine, which also revealed no abnormality. Electromyography and nerve conduction studies were normal. Vitamin B12 levels done by radioimmunoassay method were found to be within normal limits. Likewise, other disorders presenting with spastic paraparesis (amyotrophic lateral sclerosis, funicular myelosis, multiple sclerosis, Frederick’s ataxia) were excluded.
In the light of neurological findings, normal imaging studies and family history of difficulty in walking in a sibling, suspicion of familial spastic paraplegia was made and family’s neurological assessment was requested. There was nothing significant in the antenatal, postnatal, past and developmental histories of all siblings. The 6 years old male also had spastic gait with hypertonia, hyperreflexia and positive Babinski with unremarkable rest of the central nervous system and systemic examination. However, examination of the two and half and seven month old siblings was unremarkable. Physical examination of father, who was a soldier in active service revealed no abnormality. Mother was asymptomatic, but examination revealed increased muscle tone in both lower limbs with exaggerated reflexes. The family belonged to a remote village of Gilgit and there was a strong history of consanguinity for many generations but despite our extensive inquiring, no evidence of similar cases was found in other closed relatives.

In the light of progressive gait disturbance, neurological manifestations of hyperreflexia and extensor planter responses in lower limbs, exclusion of alternative diagnoses, and evidence of familial inheritance pattern, final diagnosis of “Familial Spastic Paraplegia” was made. Genetic counseling of family was done, however, genetic type of our index patient and affected family members could not be found due to non-availability of genetic analysis facility. Regular physiotherapy and muscle relaxants (tizanidine) were advised to decrease spasticity and to improve muscle strength.

**DISCUSSION**

FSP is classified according to the mode of inheritance as autosomal dominant, autosomal recessive, and X-linked or on the basis of clinical presentation as “uncomplicated” and “complicated”. FSP can also be classified according to the specific genetic locus (SPG) as “SPG1” through “SPG 48”. Uncomplicated FSP is a syndrome of gradually progressive spastic weakness of legs, frequently accompanied with urinary urgency and mild impairment of vibratory sensation in the lower limbs. In complicated FSP, in addition to symptoms of uncomplicated FSP there are additional neurologic abnormalities such as seizures, dementia, cataracts, amyotrophy, extrapyramidal disturbance, cutaneous abnormalities, or peripheral neuropathy.

Primary symptom of uncomplicated FSP is disturbed gait mainly because of spasticity with or without weakness. Gait disturbance can present from anytime between early childhoods to adolescence. The lower extremities are always symmetrically involved and if unilateral findings are present, it warrants a search for an alternative diagnosis particularly multiple sclerosis. Other symptoms include urinary urgency and paresthesias in lower limbs. Motor examination of lower limbs in patients with uncomplicated FSP reveals weakness, spasticity, hyperreflexia, and extensor plantar responses. Weakness is mostly seen in iliopsoas, hamstring, and tibialis anterior muscles. Upper extremity examination is normal in uncomplicated FSP. Muscle bulk is usually preserved in uncomplicated FSP.

According to Fink et al criteria for diagnosis of FSP; subjects are diagnosed as ‘definitely affected’ if all alternative disorders have been excluded; the family history supports an inherited disorder; subjects report a progressive gait disturbance; and neurological examination shows a frank corticospinal tract deficit in the lower limbs, including grade hyperreflexia and extensor plantar responses. Our patient fell into this category. ‘Probably affected’ subjects include asymptomatic individuals with lower limb hyper-reflexia and extensor plantar responses. ‘Possibly affected’ members are asymptomatic at-risk subjects who have a normal gait, but who show possible corticospinal tract deficits on examination (mild hyper-reflexia, a few beats of unsustained ankle clonus, but with flexor plantar responses). Mother of our index patient can be considered as “possibly affected” as she was asymptomatic but had hyper-reflexia.

Laboratory workup including vitamin B12,
lactate, pyruvate, serum long chain fatty acids, and cerebrospinal fluid examination are normal in uncomplicated FSP. Neuroimaging studies which comprise magnetic resonance imaging (MRI) of the spinal cord may be normal or show atrophy in thoracolumbar segments. MRI of the brain is usually normal in uncomplicated FSP. In patients with autosomal recessive FSP linked to chromosome 15q have thin corpus callosum. Electromyography and nerve conduction studies are usually normal in uncomplicated FSP. All the above investigations were normal in our patient so he was labelled as uncomplicated FSP. The exact chromosomal location could not be identified in our case due to lack of facilities for chromosomal analysis.

The differential diagnoses of FSP include treatable disorders like B12 deficiency, dopa-responsive dystonia, tethered cord syndrome, spinal cord compression, multiple sclerosis, tertiary syphilis, amyotrophic lateral sclerosis, primary lateral sclerosis, spinal cord arteriovenous malformation, tropical spastic paraparesis and Friedreich’s ataxia. With the help of history, clinical examination and detailed investigations we were able to exclude all the above mentioned conditions.

Neuropathologic examination of FSP reveals axonal degeneration in the terminal portions of the spinal cord affecting corticospinal tracts and dorsal column fibers with little involvement of the spinocerebellar tracts. Studies also concluded that myelin loss found on histopathology is consistent with primary axonal degeneration rather than a primary demyelinating disease. However, dorsal root ganglia, posterior roots and peripheral nerves are normal in uncomplicated FSP.

Till date, more than 40 genetic loci (designated SPG1 through SPG48, in order of their discovery) have been identified for 18 autosomal dominant, 17 autosomal recessive, and 3 X-linked types of FSP. Most cases of uncomplicated FSP are autosomal dominant, whereas complicated forms tend to be autosomal recessive. With regard to uncomplicated, autosomal dominant FSP, SPG4, SPG3A, and SPG6 account for 70-80% of families. SPG5, SPG7, and SPG11 are responsible for most cases of autosomal recessive FSP. Genetic counseling sessions must consider the prevalence of significant variability in the age of clinical presentation and the extent of disability in a single kindred gene defect. This explains the co-existence of individuals with progressive severe paraplegia and only mild gait disturbance in same family members. Different genetic forms of uncomplicated FSP are undistinguishable clinically except for the average age of presentation of symptoms.

Currently, the treatments are only symptomatic. Physical therapy targeting muscle stretching and strengthening exercises of the lower limbs is significantly helpful in decreasing muscle spasticity and improving range of motion. Medications available to decrease spasticity and improve effectiveness of weakened muscles include baclofen, dantrolene, botulinum toxin and tizanidine. We referred our patient to the rehabilitation department and currently he is under-going physical rehabilitation.

REFERENCES