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Case Report

Paediatrics Section

Filippi Syndrome: Report of a Rare Case

LATA GOYAL[1], JAGDISH PRASAD GOYAL[2], BHANU KIRAN BHAKHRI[3], ASHI CHUG[4]

ABSTRACT

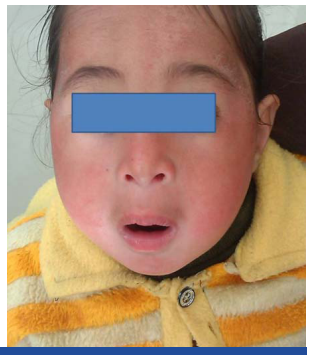
Filippi syndrome is an autosomal recessive condition characterized by syndactyly of fingers and toes, microcephaly, growth retardation and abnormal facies. We are describing a boy who presented with syndactyly, mental retardation, microcephaly, depressed nasal bridge and growth retardation. In addition he had some dental abnormalities like missing bilateral lateral incisors and delayed eruption of teeth. We concluded it to be Filippi syndrome by studying pathognomic clinical features and reviewed the literature. This is the second case report from India.

Keywords: Growth Retardation, Mental Retardation, Syndactyly

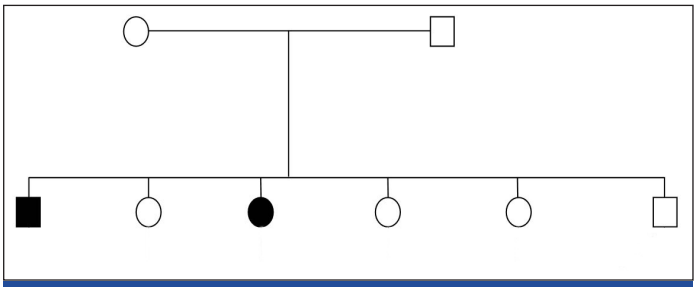
CASE REPORT

A four-year-old male child was brought by his parents with the chief complaint of abnormal facies, hearing and speech impairment. The child was born by vaginal delivery at term and had normal birth weight according to parents. He was started on breast feeding soon after birth.

He had syndactyly of fingers for which he was operated by surgeon [Table/Fig-1]. He had developmental delay. Child presented to us at 4 years of age. His head circumference was 42 cm (<3rd centile), height 79cm (<3rd centile), and weight 9 kg (<3rd centile). He had broad/depressed nasal bridge, syndactyly, micrognathia, obliterated philtrum and high hairline [Table/Fig-2]. His developmental milestone corresponded to 1 year of age. He also had hearing impairment. Examination also showed cryptorchidism and generalized hypotonia. He had additional dental findings like delayed eruption of teeth, carious upper deciduous central incisors, bilateral maxillary and mandibular lateral incisors were clinically missing which was not confirmed radiographically. Magnetic resonance imaging (MRI) and mutational analysis was not done due to financial constraints. His two of the sibling had similar clinical features like syndactyly, facial dysmorphism and developmental delay. As, it was not possible to carry out their clinical examination due to their non availability, we were relying on history given by their parents. Detail pedigree chart is shown in [Table/Fig-3].



[Table/Fig-1]: Patient showing syndactyly of hand.
[Table/Fig-2]: Patient showing facial anomalies as described in text



[Table/Fig-3]: Pedigree Chart of index case showing two sibs with similar illness

DISCUSSION

Filippi syndrome is an extremely rare genetic disorder which is characterized by mild to severe mental retardation, syndactyly of the fingers and toes, microcephaly, pre and postnatal growth retardation and unusual facies. It is transmitted as autosomal recessive condition. It was first of all described by Filippi in three Italian siblings (two boys and one girl) comprising of syndactly of the 3rd and 4th fingers, 2nd, 3rd and 4th toe, microcephaly, unusual facies, short stature and mental retardation [1].

Author	Cases and sex	Features
Present case	1 M	Head circumference 42 cm (<3 SD), height 79 cm, weight 9 kg, broad/depressed nasal bridge, developmental delay, syndactyly, micrognathia, mental retardation, obliterates philtrum, impaired hearing/speech, high hairline, short stature, delayed eruption of teeth, upper deciduous central incisor carious, bilateral maxillary and mandibular lateral incisors.
Sandhu M [2] et al., (2013)	1 F	Syndactyly of hands, mental retardation, short stature, Loss of vision in left eye, Dental findings includes Congenital absence of all third molars, Horizontal bone loss, Shortened crown root length in multiple teeth, Enlarged pulp chambers in molars.
Battalagia A [3] et al., (2008)	1 M	Syndactyly of hands and feet, prominent nasal root and hypoplastic alae nasi, intrauterine growth retardation, diffuse enlargement of subarachnoid spaces, and lateral ventricles; megacisterna magna on MRI, partial symptomatic epilepsy, mental retardation, Normal karyotype, FISH 4p-, 7-DHC, telomere analysis, aCGH, and GJA1 (Cx43) gene analysis.

Sharif and Donai [4] (2004)	2 M	Syndactyly of hands and feet, broad prominent nasal bridge, hypoplastic alae nasi, seizures, intrauterine growth retardation, Normal HRB,FISH 22q11 and 16p13.3, and telomere analysis.
Schroderet [5] et al., (2002)	2 M	Syndactyly of hands in one case and feet in both the cases, seizures, cerebellar atrophy and arachnoidal cyst on MRI, severe mental retardation, Normal HRB, 7-DHC, and telomere analysis.
Franceschini [6] et al., (2002)	1 F	Syndactyly of hands and feet, broad protruding nasal bridge, thin alae nasi, normal karyotype and telomere analysis, CT scan and MRI normal, severe mental retardation.
Walpole [7] et al., (1999)	3 M	Syndactyly of hands in 2 cases and feet in all the cases, normal IQ in two cases and mental retardation in one case, normal standard karyotype.
Williams [8] et al., (1999)	3 (2 M)	Syndactyly of hands in 2 cases and feet in all the cases, mental retardation, normal MRI, normal standard karyotype. Accommodative esotropia with possible type 1 Duane syndrome, brachycephaly and mild ptosis in one case, small pinched nasal bridge, deviated nasal septum and high arch palate, indistinct palmar creases, epicanthic folds, small palpebral fissures (1.9 and 2.1 cm right and left) that slant up, prominent glabella, broad, flat nasal base, moderate micrognathia, inability to open the mouth, and mild skin redundancy of the neck in third case.
Orrico and Hayek [9] (1997)	1M	Syndactyly of hands and feet, broad nasal bridge, intrauterine growth retardation, severe mental retardation, normal CT scan, normal standard karyotype.
Fryer [10] (1996)	2 M	Syndactyly of hands in one case and feet in both the cases, depressed nasal bridge, flaring alae, intrauterine growth retardation, mental retardation.
Herons [11] (1995)	1 M	Syndactyly of feet, major microcephaly, severe mental retardation with speech involvement, dislocation of the elbows with hypoplasia of the radial heads and carpal synostosis. prominent root, intrauterine growth retardation, normal standard karyotype, normal CT scan.
Toriello and Higgins [12] (1995)	1 M	Syndactyly of hands and feet, severe mental retardation, thin alae, broad nasal bridge, high frontal hairline, long eyelashes, long philtrum, thin upper lip, overfolded left ear, cleft soft palate, mild micrognathia, bilateral single palmar crease intrauterine growth retardation, normal standard karyotype.
Meinecke [13] (1993)	3 (2 M)	Syndactyly of hands and feet, severe mental retardation, prominent root, hypoplastic alae, seizures, intrauterine growth retardation, normal standard karyotype.
Woods [14] et al., (1992)	3 (2M)	Syndactly of hands and feet, severe mental retardation, normal karyotype, intrauterine growth retardation, broad bridge, thin alae nasi, growth retardation, seizures.
Zerres [15] et al., (1992)	1(M)	Syndactyly of hands and feet, severe mental retardation, seizures, ventricular enlargement on CT scan, normal standard karyotype.
Filippi [1] et al., (1985)	3 (2 M, 1 F)	Syndactly of hands and feet, mental retardation, normal karyotype, intrauterine growth retardation, unusual facies.

[Table/Fig-4]: Clinical features of published cases

There are mainly 6 syndromes which present with similar clinical presentation namely Scott craniodigital Syndrome, Chitayat syndrome, Zerres syndrome, Kelly syndrome, Woods syndrome and Filippi syndrome [1]. Based on prenatal growth retardation, microcephaly and mental retardation, it is possible to differentiate between these clinical conditions. Filippi syndrome is characterized by syndactyly of hands and feet, developmental delay, mental retardation, microcephaly but clinical heterogeneity is possible. Most prominent feature is the syndactyly of hands and feet and 3-4 finger syndactyly being the most common. To date less than 30 cases of Filippi syndrome have been reported worldwide [Table/Fig-4] out of which one case was from India [2]. This is second case report of Filippi syndrome from India. There is male predominance but no classical X linked inheritance has been reported. This disease occurs in both the sexes suggesting its autosomal recessive mode of inheritance. Our patient presented with dental findings which has been earlier reported in only one case. Case reported by Sandhu M showed congenital absence of third molars, shortened crown root length in multiple teeth and enlarged multiple pulp chambers [2]. In our patient bilateral maxillary and mandibular lateral incisors were missing. Syndactyly is the most common feature present in Filippi syndrome as present in our case also. Growth retardation, present in our patient, has been reported in nearly half the cases by Sharif and Donnai [4]. All, but two of the three patients described by Walpole et al., have shown severe developmental delay and mental retardation [7]. Neuroimaging and genetic analysis could not be performed due to financial constraints. The pathogenesis of this disorder is unknown. Mutational analysis is area of future interest as possibility for developing brain and limb by mutation in gene expression is there. Regarding treatment, supportive care and therapy is provided to patients with disabilities. Surgical corrections of physical deformities and speech therapy for those having hearing loss are the other options. In the present case, parents counselling was done and speech therapy was suggested but they never came back for further investigations and followup. Currently there are no methods to prevent this disease but genetic counselling will be helpful in assessing risk before planning the child. With timely treatment it can be managed successfully but still some children suffer from mental retardation.

CONCLUSION

Filippi syndrome is an extremely rare genetic disorder which is characterized by mild to severe mental retardation, syndactyly of the fingers and toes and unusual facial appearance. Till now there is no means to prevent this condition but genetic counseling is helpful in risk assessment. Symptomatic treatment, supportive therapy and care are the only viable option.

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PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Dentistry, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.
2. Assistant Professor, Department of Pediatrics, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.
3. Assistant Professor, Department of Pediatrics, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.
4. Assistant Professor, Department of Dentistry, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Jagdish Goyal,
Address: Department of Pediatrics, All India Institute of Medical Sciences, Rishikesh, Uttarakhand, India.
E-mail: jpgoyal@rediffmail.com

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