ELSEVIER

Brain & Development xxx (2018) xxx–xxx

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Case Report

Fazio-Londe syndrome in siblings from India with different phenotypes

Vykuntaraju K. Gowda [a,*,1], Tamilarasan Udhayabanu [b], Perumal Varalakshmi [c], Varunvenkat M. Srinivasan [a], Balasubramaniem Ashokkumar [b,*,1]

[a] *Department of Pediatric Neurology, Indira Gandhi Institute of Child Health, Bangalore, India*
[b] *Department of Genetic Engineering, School of Biotechnology, Madurai Kamaraj University, Madurai 625021, India*
[c] *Department of Molecular Microbiology, School of Biotechnology, Madurai Kamaraj University, Madurai 625021, India*

Received 26 July 2017; received in revised form 14 February 2018; accepted 14 February 2018

Abstract

Background: Fazio-Londe syndrome also called progressive bulbar palsy of childhood is a very rare motor neuron disease of pediatric age group characterized by progressive paralysis of lower cranial nerves.

Objective: To describe Fazio-Londe syndrome in sibling with different phenotype.

Methods: A 6 years old female child presented with inability to close eyes, difficulty in swallowing, respiratory muscle weakness and voice change since 5 yr of age. Examination showed lower motor neuron facial nerve palsy, absent gag reflex, tongue atrophy, fasciculation, limb wasting and exaggerated deep tendon reflexes. An 11 year old boy, elder sibling of the above child presented with similar complaints at 10 years of age, other than later onset and lack of respiratory problem. Genetic testing in both cases confirmed the diagnosis of Fazio-Londe Syndrome.

Conclusion: In any child who presents with progressive bulbar palsy with lower motor neuron facial palsy a diagnosis of Fazio-Londe Syndrome should be considered and family members should also be screened.

Keywords: Fazio-Londe syndrome; BVVLS; Ponto bulbar palsy; Riboflavin; RFVT-3

1. Introduction

Fazio-Londe Syndrome (FLS) and Brown-Vialetto-Van Laere Syndrome (BVVLS) are progressive disorders affecting motor neurons which are riboflavin dependent and clinically distinguished by deafness in the latter [1,2]. Fazio-Londe syndrome, characterized by progressive bulbar palsy and respiratory compromise, affects children and young adults [3]. It is inherited in an autosomal recessive manner caused by mutations in *SLC52A3* gene that encodes intestinal riboflavin transporter (hRFVT-3) [4]. Here we report siblings with FLS from India having variable age of onset with different severity and without deafness.

2. Case-1

A 6 year old female child born to a second degree consanguineously married couple with normal birth his-

* Corresponding authors at: Bangalore Child Neurology and Rehabilitation Center, No 8/A, First Cross, First Main, Near Adhichunchanagiri choultry, Vijayanagar, Bangalore 560104, India (V.K. Gowda).

E-mail addresses: drknvraju@hotmail.com (V.K. Gowda), rbashokkumar@yahoo.com (B. Ashokkumar).

[1] Shares equal contribution as corresponding authors.

https://doi.org/10.1016/j.braindev.2018.02.010

tory was brought with history of difficulty in breathing and change of voice since 1 year duration. The patient developed pneumonia and respiratory distress for which she required mechanical ventilation and tracheotomy care. The patient had difficulty in closing eyes since 5 years of age. Later she also developed difficulty in swallowing. Developmental milestones were attained up to date.

On examination, height, weight and head circumference were appropriate for age. Neurological examination showed bilateral lower facial weakness, absent gag reflex, and wasting of tongue muscles with fasciculation (Fig. 1). Motor system examination showed normal tone, wasting of muscles and exaggerated deep tendon reflexes bilaterally. Sensory and cerebellar systems were normal. Initial baseline investigations including complete hemogram, liver function, renal function, serum electrolytes, and serum creatine kinase were all normal. Motor, sensory and F wave nerve conductions studies were done in bilateral median, ulnar, posterior tibial, common peroneal and sural nerves. Compound muscle action potential, sensory nerve action potential, distal latency, conduction velocity and F wave latency were normal in above tested nerves. Electromyography of facial muscles showed fasciculation (Fig. 2A). MRI of brain and spine was normal. Patient was put on 200 mg of Riboflavin per day. On follow up after 2 years residual facial weakness with some difficulty in swallowing was present. Her respiratory muscle function improved and she is on and off tracheostomy care.

3. Case-2

An 11 year old boy, elder sibling of above child presented with history of difficulty in closing eyes since 10 years of age and difficulty in swallowing. On examination, all anthropometric parameters were normal. There was bilateral lower facial weakness, absent gag reflex, and atrophy of muscles of tongue with fasciculation (Fig. 1). Motor system examination showed normal tone, wasting of muscles with exaggerated deep tendon reflexes. Table 1 shows various clinical features of both siblings.

Initial baseline investigations including complete hemogram, liver function, renal function, serum electrolytes, and serum creatine kinase were all normal. Nerve conduction study was normal. Electromyography of facial muscles showed fasciculations (Fig. 2B). MRI of brain was normal. Patient was put on 200 mg of riboflavin and is on regular follow up. His facial muscle power and bulbar muscle weakness improved, and he didn't develop respiratory muscle weakness.

In view of presence of bulbar palsy with facial nerve and upper motor neuron signs, genetic testing for motor neuron disease was performed, which evidenced a pathogenic mutation in *SLC52A3* (c.A > 62G; p.Asn21-Ser) at homozygous condition in the sibling and thus confirming the diagnosis of Fazio-Londe syndrome (Fig. 3). Genetic testing in parents for carrier status revealed that both the parents were asymptomatic heterozygous carriers of the identified mutation (Fig. 3). Ethical clearance was obtained from institutional review board.

Fig. 1. Clinical photographs of both siblings showing bilateral facial weakness and wasting of facial muscles. Informed consent obtained from parents to publish photograph of face from parents.

Please cite this article in press as: Gowda VK et al. Fazio-Londe syndrome in siblings from India with different phenotypes. Brain Dev (2018), https://doi.org/10.1016/j.braindev.2018.02.010