European Journal of Medical Genetics 59 (2016) 5–10

Contents lists available at ScienceDirect

European Journal of Medical Genetics

journal homepage: http://www.elsevier.com/locate/ejmg

Letter to the Editor

Renal dysfunction in sibs with band like calcification with simplified gyration and polymicrogyria: Report of a new mutation and review of literature

Keywords:
Occludin
Band like calcification with simplified gyration and polymicrogyria
Renal dysfunction
Pseudo TORCH syndrome

A B S T R A C T

Band like calcification with simplified gyration and polymicrogyria (BLC-PMG) is a distinct neuroradiological phenotype initially reported as a pseudo-TORCH syndrome and known to result from biallelic mutations in the Occludin(*OCLN*) gene. This is report of a family of Indian origin with two affected sibs and segregation of a homozygous novel *OCLN* mutation in the exon 3(NG_028291.1(OCLN_v001):c.252delC). A literature review suggests that renal dysfunction may be an unrecognized phenotypic manifestation of *OCLN* mutations and monitoring for the same should form part of the clinical care of these individuals.

1. Introduction

Band-like calcification with simplified gyration and polymicrogyria (BLC-PMG) caused by mutations in Occludin(*OCLN*) gene is a discrete phenotype belonging to the heterogeneous group of entities initially described as Pseudo-TORCH syndromes [Baraitser et al., 1983, Briggs et al., 2008, Abdel-Salam et al., 2008]. BLC-PMG is characterized by specific radiological findings in the form of dense band like calcification involving the deep cortical layers, white matter, basal ganglia, with polymicrogyria and simplified gyral pattern involving frontal & parietal lobes and in some cases cerebellar hypoplasia [Abdel-Salam and Zaki, 2009]. First described in 1983 by Baraitser et al., it is clinically characterized by progressive microcephaly, developmental arrest, seizures and spastic paraparesis. Mutations have been reported in a small number of patients, of which six patients have been reported to have renal dysfunction with no apparent genotype–phenotype correlation [Abdel-Salam and Zaki, 2009, O'Driscoll et al., 2010, LeBlanc et al., 2013, Elsaid et al., 2014]. We report an Indian family with diagnosis of BLC-PMG and renal dysfunction with a novel homozygous mutation in *OCLN* gene. On basis of this report and literature review, we would like to suggest that renal dysfunction maybe a common phenotypic component of BLC-PMG.

2. Clinical report

A third degree consanguineous couple attended for preconception counselling in view of death of previous two children affected with a similar neurological phenotype. The first pregnancy had been terminated due to antenatal diagnosis of anencephaly. The second offspring was a male born at term from an uncomplicated pregnancy. Antenatal ultrasonography showed lagging of head growth in the third trimester and scanty liquor. Ultrasound at 36 weeks gestation showed the head circumference lagging by 2–3 weeks. The head size was reported to be small at birth and child developed seizures on day 3 of life, following which the child was admitted in neonatal care for 20 days. Subsequently, despite antiepileptic drug therapy in the form of carbamezapine & lonazepam, the child continued to have 1–2 episodes of seizures every month. Electroencephalogram showed right centro-temporal seizure with secondary generalisation. CT scan brain at the age of 5 days was reported to have agyria/pachygyria and bilateral dense calcification involving the basal ganglia & subcortical areas. Subsequent MRI brain at age of 1 month age demonstrated polymicrogyria involving the temporal lobes and simplified gyration in the frontal & parietal cortex [Fig. 1a & c]. No cerebellar hypoplasia was apparent. TORCH profile (Serological test for detection of IgG and IgM antibodies against *T*oxoplasma,, *R*ubella, *C*ytomegalovirus and *H*erpes simplex viruses) done on day 4 showed positive IgG titres for rubella and cytomegalovirus, but normal IgM levels. CSF evaluation was not done. No developmental milestones were achieved except for light perception and following objects since the age of 3.5 years. The child developed generalised spasticity since infancy which the parents felt was non-progressive in course. Ophthalmic and auditory evaluations were unremarkable as per the parents, however no records were available. Feeding difficulties were present and the child accepted only liquid and semi-solid diet, though a gastrostomy feeding was not required. Following an acute episode of gastroenteritis at the age of 4.5 years, the child developed respiratory distress and status epilepticus and expired after an inpatient course

http://dx.doi.org/10.1016/j.ejmg.2015.11.014
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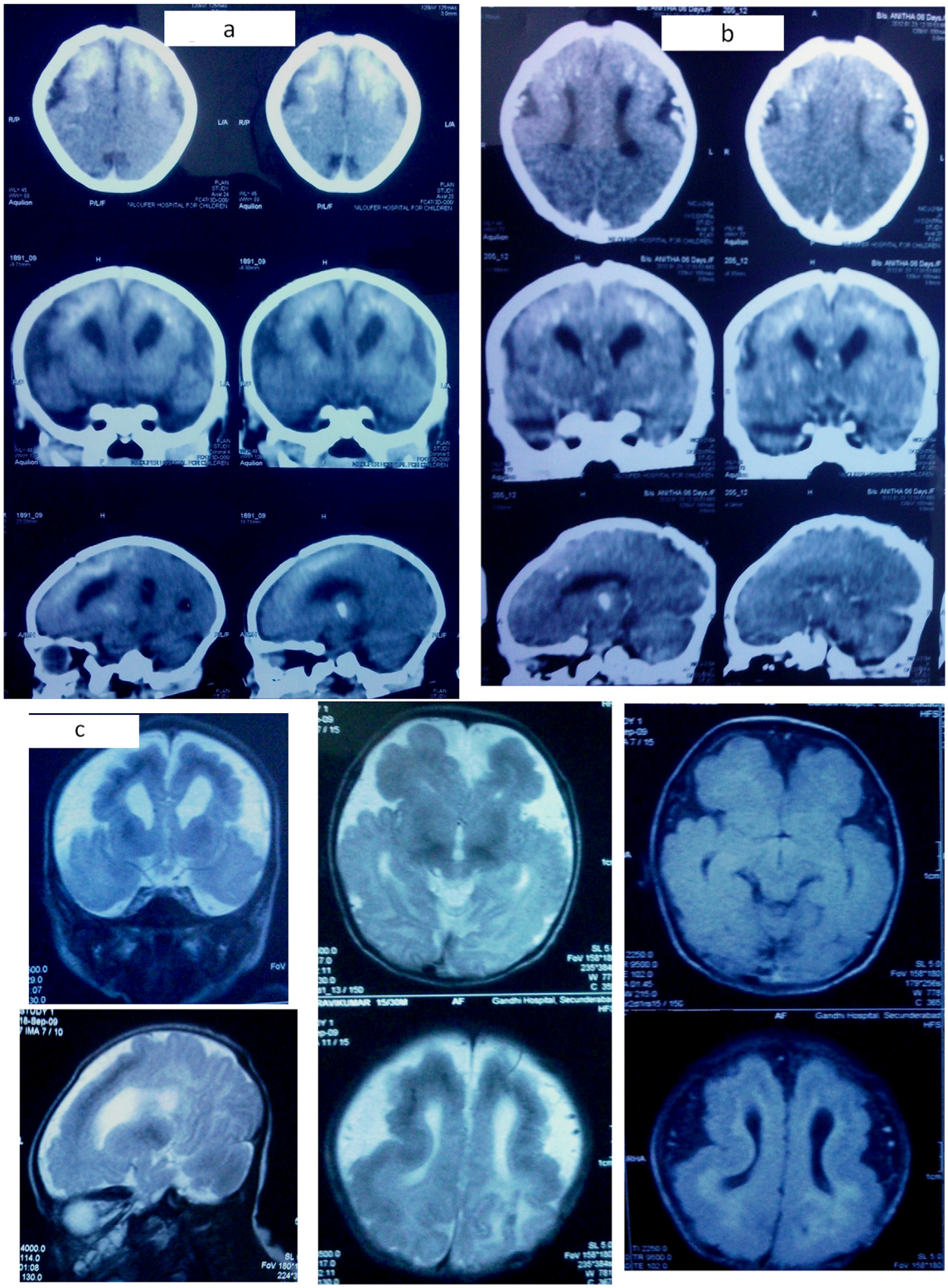

Fig. 1. a: CT brain of male sib showing band like cortical calcification and basal ganglia calcification, b: CT brain of female sib showing multiple cortical (nearly confluent) and basal ganglia calcification, c: MRI brain of male sib showing polymicrogyria and T1 hyperintensity in frontal subcortical white matter suggestive of calcification.

of 10 days. The parents were informed of a terminal diagnosis of renal failure as the immediate cause of death, although no medical records, renal imaging or histopathology findings were available to substantiate the same. The third offspring was a female child born at term of an uncomplicated pregnancy. Antenatal ultrasonography reports showed head size corresponding to gestation till the second