



An Extremely Rare Syndromic Form of Intellectual Disability: Temtamy Syndrome; About a Clinical Case

M. Akhrif^{1*}, R. Abilkassem¹, A. Elyajouri¹, H. Ennouali²,
N. Amsigine² and A. Agadr¹

¹Department of Pediatric, Mohamed V Military Training Hospital, Rabat, Morocco.
²Department of Radiology, Mohamed V Military Training Hospital, Rabat, Morocco.

Authors' contributions

This work was carried out in collaboration among all authors. Author MA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author RA managed the analyses of the study. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Temtamy syndrome is a congenital syndrome. It was first described by Temtamy et al. in 1991. Characterized by mental retardation, ocular coloboma, seizures, variable craniofacial dysmorphism, and brain abnormalities, including abnormalities of the corpus callosum and thalamus. The extreme clinical and genetic heterogeneity of these phenotypes posed a major diagnostic challenge until the advent of genomic tests that scan a large number of genes with little bias by the clinical phenotype.

Materials and Methods: We reporting the case of a male child aged followed since the age of 3 months for epileptic seizure with corpus callosum agenesis, and clinical examination found craniofacial dysmorphism, mental retardation, strong myopia, an irian coloboma, chorioretinal atrophy. The aim of this study is to highlighting the specific features of temtamy syndrome and show the points of divergence with other similar syndromes.

Keywords: Temtamy syndrome; agenesis of the corpus callosum; optic coloboma.

*Corresponding author: Email: akhrif2510@gmail.com;

1. INTRODUCTION

Temtamy syndrome is an extremely rare disorder. It was first described by Temtamy et al. In 1991 and later published in 1996. Consider as a syndromic form of intellectual disability, characterized by ocular involvement, epilepsy and dysgenesis of the corpus callosum. Although the autosomal recessive inheritance is clearly suspects, it wasn't until 2013 that Akizu and al and others identified pathogenic bialyl variants in the mischaracterized gene C12orf57 as the cause of this syndrome [1].

2. CASE REPORT

18 month old boy was admitted to our clinic for evaluation of craniofacial dysmorphism. Pregnancy was complicated by ultrasound discovery of omphalocele. He was the 2900-g product of a 38-week gestation to a 33-year-old G4P3 woman by cesarian delivery with Apgar scores of 8 and 10 at 1 and 5 minutes, respectively. He was operated on the second day of life for omphalocele. He has poor psychomotor development: holding his head at 6 months, sitting at 12 months, standing with support at 17 months, walking at 22 months. Family history was remarkable in that the parents are consanguin and her sister was died at six hours of life from an unknown etiology. There was no similar case in the family.

On physical examination, he was an alert, healthy-appearing boy. Weight and height was in the 15th percentile. head circumference was greater than 97 percentile. Pulse was 80, respiratory rate was 23, blood pressure was 100/50 mm Hg. Craniofacial dysmorphia: dolicocephaly, macrocephaly, long face, prominent forehead, pointed eyebrows, micrognathia, bulging eyes, low implanted ears. HEENT exam was unremarkable, Lungs were clear, neurologic examination: he wos tonic, sitting and standing with assistance, no motor deficit. The rest of the somatic examination was unremarkable. Ophthalmologic examination showed strong bilateral myopia, an irian and lower crystalline coloboma, rupture of the lower zonular fibres with ectopy of the crystalline lens, beginning posterior cataract. The fundus showed chorioretinal atrophy with enlarged and pale papillae of strong myopia. The auditory evoked potentials showed bilateral cophosis. Brain MRI revealed total agenesis of the corpus callosum with separation of the ventricular bodies and lowering of the interhemispheric fissure. The

ocular globes are greatly increased in volume responsible for bilateral exophthalmos. Rock MRI showed that the acoustic-facial packages are thin, normal. A filling of the mastoid cells and the left middle ear.

Pertinent laboratory tests included : hemoglobin 11.7 g/dL with normal white blood cell differential and platelet count, Serum chemistries were unremarkable, urinalysis was normal, thyroid check-up was normal, normal karyotype, the chromatography of amino acids in blood and homocysteine levels were normal. TORCH (toxoplasmosis, other infections, rubella, cytomegalovirus, and herpes simplex) virus and parvovirus titers were negative. Bone x-rays were normal, abdominal and cardiac ultrasound were normal, normal electroencephalogram. Bone x-rays were normal.

Temtamy's syndrome was retained in front of the association of psychomotor retardation of the dysmorphic syndrome, data from ophthalmological examination (irian and crystalline coloboma, chorioretinal atrophy), congenital sensorineural deafness and corpus callosum agenesis). The patient received a cochlear implant at the age of 3 years.

3. DISCUSSION

Temtamy syndrome characterized by mental retardation, ocular coloboma, seizures, variable craniofacial dysmorphism and brain abnormalities, including abnormalities of the corpus callosum and thalamus [2]. Temtamy et al. In 1991 observed a boy and 2 girls with a syndrome consisting of craniofacial dysmorphism, iris coloboma and absent corpus callosum. The affected male and his father had a satellited long arm of the Y chromosome (Yq).The craniofacial anomalies consisted of macrodolichocephaly, arched eyebrows, antimongoloid slant of the eyes, low-set and simple lop ears, beaked nose, long philtrum, short upper lip, and micrognathia, the lenses were dislocated upward and there was myopia and hypertelorism. Two of the 3 sibs had aortic regurgitation with aortic dilatation, and one had moderate mental retardation .The sister, who died at age 22 years from heart failure, had myocardial impairment, moderate dilatation of the aorta, and bulbous thumbs [3]. Diverses studies have reported similar results , Chan et al. Chan et al. concluded in 2000 that the main clinical manifestations of the newly described syndrome include corpus callosum agenesis,

ocular coloboma, hypertelorism and relative macrocephaly [4]. Another study was described in 2007 by Li et al. reported a brother and sister, born of consanguineous parents of Middle Eastern origin, noted that both had severe mental retardation, intractable seizures, and interhemispheric colloid cyst, the difference with the patients originally described by Temtamy et al. that neither had cardiac anomalies, and Linkage analysis did not identify a candidate disease locus [5]. In 2013 Akizu et al. reported 10 patients from 4 consanguineous families with Temtamy syndrome. The phenotype included hypotonia and moderate to severe intellectual disability with features of autism. Eight patients had brain imaging, which revealed absent corpus callosum or hypoplasia of the corpus callosum,

thalamic hypoplasia, and reduced white matter. Eight patients had epilepsy, 7 had dysmorphic craniofacial features, 5 had spasticity, and 4 had variable eye abnormalities, including esotropia and optic atrophy. One patient had microphthalmia and coloboma [6]. In 2013 Salih et al. reported a study which 4 of 6 sibs had features consistent with Temtamy syndrome, the study revealed that patients have motor and cognitive retardation with seizures in early childhood., iris and chorioretinal colobomas, posterior staphyloma, microcornea with corneal opacity and dense cataract, and chorioretinal coloboma and posterior staphyloma. Magnetic resonance imaging of the brain was abnormal with agenesis, thickening, or dysgenesis of the corpus callosum [7]. Platzer et al. reported in



Fig. 1. Axial section showing an agenesis of the corpus callosum

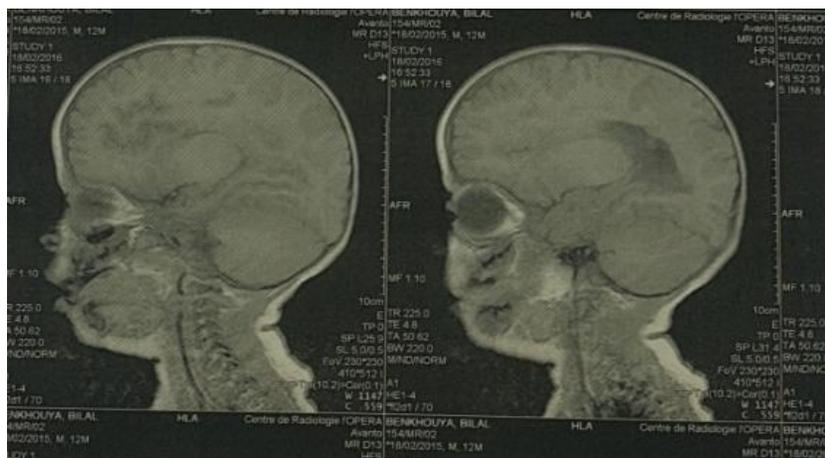


Fig. 2. Sagittal section showing anagenesis of the corpus callosum

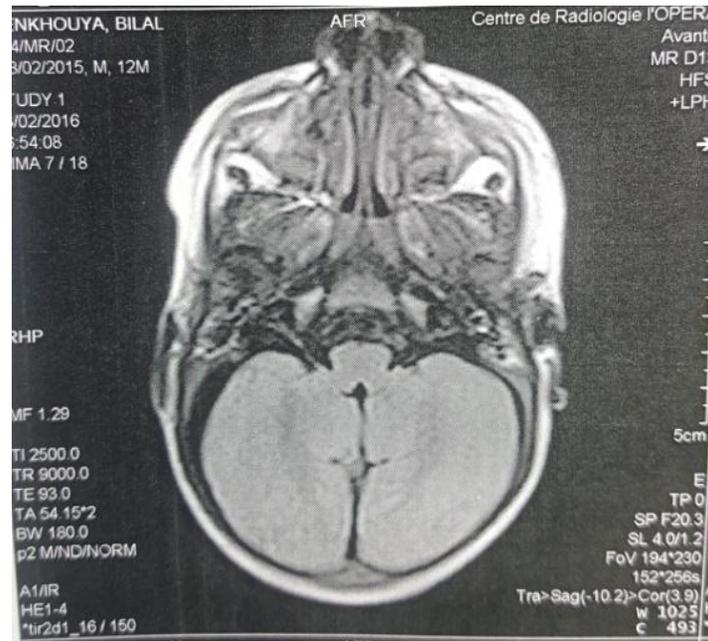


Fig. 3. Axial section showing the acoustic-facial packages are thin, normal



Fig. 4. The recent image of our patient when he was 5 years old

2014, 2 sibs born of unrelated German parents, with severe intellectual disability, lack of speech acquisition, early-onset intractable seizures, and visual impairment. One child had bilateral chorioretinal coloboma and the other had an atrial septal defect, hypoplasia of the corpus callosum, short stature, and ataxic gait [8]. Our case has many features consistent with the initial patients reported in the literature including agenesis of the corpus callosum, irian and crystalline coloboma, chorioretinal atrophy, dysmorphism cranio-facial, mental retardation and epileptic seizures. However our patient lack the cardiac anomalies previously identified in the family described by Temtamy et al., comprising enlargement of the left ventricle and aortic dilation and regurgitation. It corroborates with most of the cases described in the literature.

The differential diagnosis for agenesis of the corpus callosum (ACC) and optic colobomata is mainly represented by Aicardi syndrome, Donnai–Barrow syndrome and Baraitser– Winter syndrome, each of these syndromes has features that distinguish them from Temtamy syndrome. The features in Donnai–Barrow syndrome include diaphragmatic hernia, omphalocele, myopia, and sensorineural deafness and Aicardi syndrome includes infantile spasms, and is inherited as a sporadic condition that only occurs in females or XXYmales. In Baraitser–Winter syndrome, the cerebral malformations include evidence of abnormal neuronal migration such as pachygyria, agyria, or subcortical band heterotopia and microcephaly, without evidence of callosal agenesis [9]. Comparison of the different conditions associated with ACC and colobomata indicated that the case we report here most closely resembles Temtamy syndrome, but may constitute a new or unique syndrome in this family.

The genetic etiology of Temtamy syndrome is unknown. Talisetti et al. reported in [2003] a 5-year-old female with features similar to the cases of Temtamy et al. This girl had a novo balanced chromosome translocation [karyotype 46, XX, t(2; 9)(p24; q32)]. Physical mapping of the break points has revealed two zinc-fingers like genes, ASXL2 and ZNF462. There is evidence for the production of a novel fusion transcript from the conjunction of these two genes [9]. It can be suggested that a different gene is probably responsible for CCA in this family, and possibly also Temtamy's syndrome [9].

Alrakaf et al in their study concluded that The combination of corpus callosum anomalies, the disability intellectual, colobomatous, microphthalmia, epilepsy, appears to be specific to Temtamy's syndrome. Although they cannot speculate on the positive predictive value of this constellation of characteristics as written subjects are found solely on the basis of the presence of C12 or f57 mutations, the absence of reports from any other location for Temtamys emblems support this notion. As with other syndromes, the study by alkaf et al shows that Temtamys syndrome has variable expressivity and that the C12orf57 biallelic mutations are also compatible with a phenotype limited to non-specific intellectual disability [1]. Zahrani et al. (2013) identified a homozygous mutation in the C12ORF57 gene. The mutation was identified by exome sequencing of 1 of the patients. An unrelated Saudi girl with a similar disorder was compound heterozygous for the 1A-G mutation and another C12ORF57 mutation [6].

The poorly understood function of C12orf57 makes it difficult to speculate on the mechanism of pathogenesis, including its pleiotropy and highly variable phenotypic expression. The variable expressivity of Temtamy's syndrome, despite its limited allelic heterogeneity, suggests a significant role played by stochastic factors rather than genetic modifiers, especially considering the variable expressivity even among siblings of highly inbred pedigrees [10].

4. CONCLUSION

Temtamy syndrome is a rare and congenital syndrome, recently described by temtamy et al in 1991; it encompasses mental retardation, ocular coloboma, seizures, variable craniofacial dysmorphism and brain abnormalities, including abnormalities of the corpus callosum and thalamus. It genetic etiology is unknown, studies incriminate the participation of C12orf57, but the poorly understood function of the latter, makes it difficult to speculate on the mechanism of pathogenesis

CONSENT

As per international standard or university standard, patient's parents' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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