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CASE REPORT

Thanatophoric dysplasia type 1 with tectal plate dysplasia and aqueductal stenosis

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Abstract

Introduction Skeletal dysplasias are a heterogeneous group of disorders comprising of more than 300 entities, many of which manifest in the prenatal period, emphasizing the importance of accurate prenatal diagnosis. Detection of a lethal skeletal dysplasia via prenatal ultrasound is often straightforward. However, establishing the specific diagnosis and detailed evaluation of intracranial anomalies are often challenging. Fetal magnetic resonance imaging (MRI) is superior to ultrasound in the detection of abnormal sulcation pattern, corpus callosal agenesis, and posterior fossa anomalies. Hence, it has the potential of delineating neuroimaging features that may not be fully elucidated by ultrasound. The objective of this article is to describe an unusual case of thanatophoric dysplasia (TD) with dysplastic tectal plate and resultant aqueductal stenosis diagnosed on fetal MRI. To the best of our knowledge, this has never been reported before in the literature. A comprehensive review of literature pertaining to TD-associated CNS abnormalities will also be included.

Conclusions Our reported case adds to the current limited knowledge of this rare entity and emphasizes the crucial role of fetal MRI in expanding the neuroimaging phenotypes of TD

Keywords Thanatophoric dysplasia · Tectal plate dysplasia · Aqueductal stenosis

Introduction

Skeletal dysplasias are suspected when severe long bone shortening and narrow thoracic cavity are detected prenatally on ultrasound (US). Most affected neonates do not survive beyond the first day of life due to severe pulmonary hypoplasia. Detection of a lethal skeletal dysplasia via prenatal ultrasound is often straightforward. However, establishing the specific diagnosis and detailed evaluation of intracranial anomalies are often challenging, especially in the context of a complex disorder with variable phenotypes such as thanatophoric dysplasia (TD). Fetal magnetic resonance imaging (MRI) allows better anatomical delineation and has the potential of expanding the neuroimaging phenotypes of TD [1]. Herein, we describe an unusual case of TD with dysplastic tectal plate and aqueductal stenosis, diagnosed on fetal MRI.

Case report

Routine prenatal US in a 34-year-old gravida four para three female revealed features suggestive of an underlying skeletal dysplasia; marked shortening of long bones with curved femora (classic telephone handle appearance of type I TD) and narrow thoracic cage. Ventriculomegaly was also detected, involving the lateral and third ventricles.

She was referred to our facility for further evaluation and a fetal MRI was performed at 22 weeks of gestation (Fig. 1). An abnormally shaped cranial vault (cloverleaf deformity) and megalencephaly were noted, along with frontal bossing. There were also hyperplasia and abnormal sulcation pattern of the occipito-temporal lobes, most prominent at the inferomedial aspects. The brain stem was hypoplastic with abnormal thickening of the inferior tectal plate, resulting in narrowing of the cerebral aqueduct. In addition, there was

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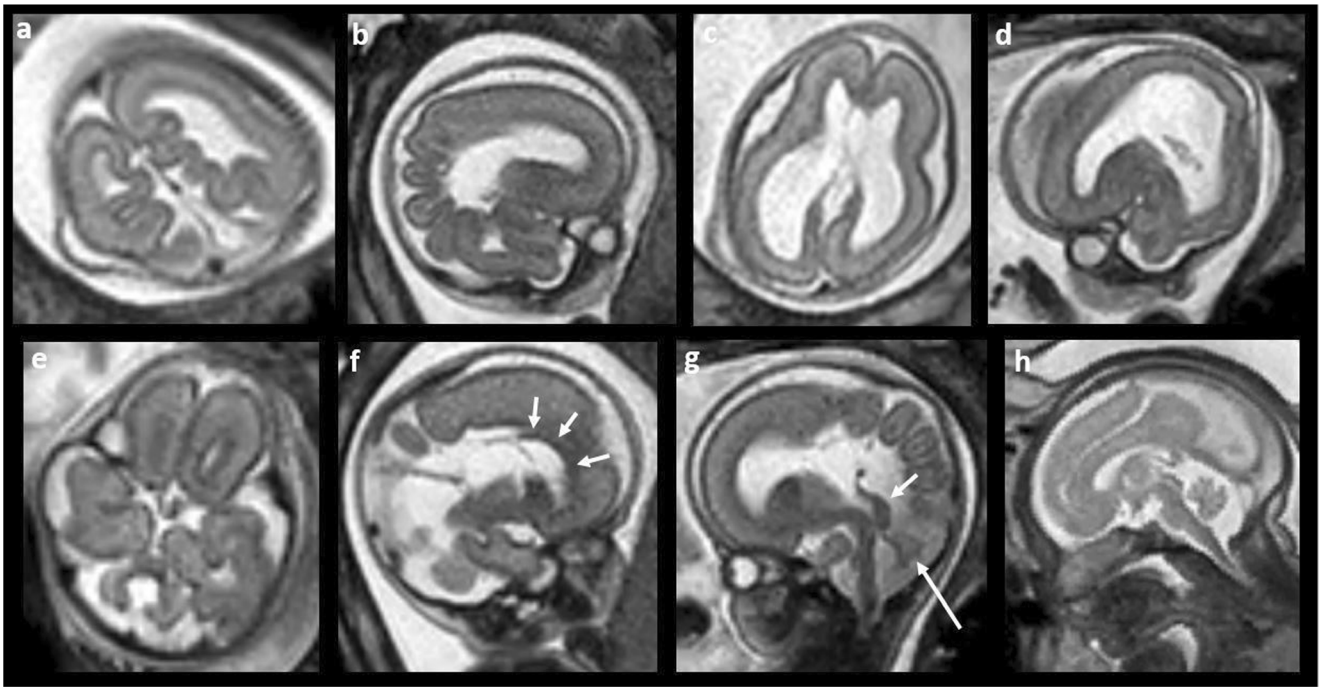

Fig. 1 Coronal (**a**) and sagittal (**b**) T2-weighted fetal MRI brain images showed abnormal sulcation in the occipital and temporal lobes. Bilateral ventriculomegaly (**c**) and macrocephaly with frontal bossing (**d**) are also observed. Cloverleaf deformity of the skull is seen, with hyperexpansion of the temporal lobes (**e**). There is partial agenesis of the corpus callosum with absence of the splenium (**f**). The anterior corpus callosum (short white arrows in **f**) also appears thin and dysplastic. The brainstem has an abnormal morphology with abnormal thickening of the tectal plate (short white arrow in **g**) and narrowing of the inferior aspect of the cerebral aqueduct. The vermis is small and is rotated superiorly (long white arrow in **g**). Normal appearance of the brainstem and vermis in another 22-week fetus for comparison (**h**)

partial agenesis of the corpus callosum. Enlargement of the lateral and third ventricles was noted, more than expected for the degree of temporal lobe dysplasia and partial corpus callosal agenesis, likely due to concurrent aqueductal stenosis. The 4th ventricle was normal in size and this excludes obstruction of cerebrospinal fluid (CSF) flow at the level of the foramen magnum. In thanatophoric dysplasia, ventricular enlargement is typically confined to the temporal horns.

Discussion

TD is one of the most common neonatal lethal skeletal dysplasias. It can be divided into two subtypes; types I and II, which can be differentiated by shape of the cranial vault and femur morphology. Type I TD, the more common subtype, is characterized by micromelia with bowed femurs and metaphyseal flaring, giving rise to the characteristic "telephone receiver" appearance and, uncommonly, the presence of cloverleaf skull deformity. Type II TD on the other hand is characterized by micromelia with straight femurs and moderate-to-severe cloverleaf skull deformity. Previously described intracranial abnormalities associated with TD include temporal lobe dysplasia, megalencephaly, cloverleaf skull deformity, ventriculomegaly, holoprosencephaly, encephalocele, corpus callosal dysgenesis, brainstem hypoplasia, malformations of cortical development, maldevelopment of the inferior olivary, and cerebellar dentate nuclei [2–10].

Temporal lobe dysplasia (TLD) is a characteristic neuroimaging feature of TD, described as deep, radially oriented sulcation affecting the inferomedial surfaces of the temporal lobes, possibly related to *FGFR3* mutation-induced disturbances in neuronal proliferation [11, 12]. Wang et al. reported that the detection rate of TLD by US is low (only 25% of cases were identified on US). This emphasizes the importance of fetal MRI as a complementary imaging modality in the assessment of fetuses with suspected skeletal dysplasia. TLD is present in 100% of cases by 18 weeks of gestation, and earlier in some cases [10–12]. In a normal fetus, temporal lobes do not demonstrate sulcation prior to 20 weeks of gestation.

Cloverleaf skull deformity is thought to be secondary to premature closure of cranial sutures. However, megalencephaly involving predominantly the dysplastic temporal lobes may also contribute to secondary deformation of the overlying cranial vault. Cloverleaf skull deformity may also be seen in severe cases of Apert, Crouzon, and Carpenter syndromes.

Ventriculomegaly is a common finding that has been postulated to be secondary to obstruction of CSF flow due to platybasia and foramen magnum stenosis. However, in our

opinion, the etiology of ventriculomegaly in TD is more likely to be multifactorial. As it is frequently limited to the temporal horns, ventriculomegaly can be related to cisternal deformation and obstruction due to the cloverleaf skull deformity. Ventriculomegaly may also be associated with corpus callosal dysgenesis, present in some cases of TD. In our reported case, there is brainstem hypoplasia and abnormal thickening of the tectal plate, a feature that has never been reported before in association with TD. The enlargement of the lateral and third ventricles was also more than expected for the degree of temporal lobe dysplasia and partial corpus callosal dysgenesis. The authors hypothesized that this may be in part due to the dysplastic tectal plate and resultant aqueductal stenosis. As the 4th ventricle was normal in size, obstruction of CSF flow due to platybasia and foramen magnum stenosis can be excluded.

Encephaloceles and holoprosencephaly are infrequent intracranial abnormalities associated with TD, the prior postulated to be secondary to an expansile dysplastic brain and ventriculomegaly as well as cranial vault compression from craniosynostosis [4]. FGFR3 mutations may play an important role in brain rostral signaling, a possible explanation for the association between TD and holoprosencephaly [4]. Commissural dysgenesis has been reported in patients with TD, but its occurrence is extremely rare. Kalache et al. speculate that the same mechanism of deficient bone marrow seen in skeletal dysplasia also causes insufficiency of guiding glial cells, resulting in callosal dysgenesis [13]. Although uncommon in TD, callosal dysgenesis has been found in patients with Apert and Crouzon syndromes (due to FGFR2 mutations) and in achondroplasia–hypochondroplasia (due to FGFR3 mutations) [14].

Conclusion

Fetal MRI has the potential of delineating neuroimaging features of TD that may not be fully elucidated by ultrasound. It also has the potential of expanding the neuroimaging phenotypes of TD and providing additional information for prognostication, antenatal prediction of lethality and early parental counseling. To the best of our knowledge, TD with dysplastic tectal plate and cerebral aqueductal stenosis had never been reported before in the literature.

Compliance with ethical standards

Conflict of interest None.

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