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A case of cerebellar hypoplasia in a Chinese infant with osteogenesis imperfecta

We report a unique case of unilateral cerebellar hypoplasia in a young Chinese girl with osteogenesis imperfecta type IV. Magnetic resonance imaging showed mild basilar invagination and impression. Although unilateral cerebellar hypoplasia and osteogenesis imperfecta may have been coincidental diagnoses, we propose possible mechanisms for unilateral cerebellar hypoplasia secondary to osteogenesis imperfecta. For example, cerebellar hypoplasia may have been because of vascular disruption or direct compression to the posterior circulation in utero. Foetuses with osteogenesis imperfecta are more susceptible to the above risks compared to the normal foetus because of associated craniocervical anomalies and a poorly ossified skull.

Introduction

Osteogenesis imperfecta (OI) is a hereditary systemic bone disease that results from abnormal production of type-I collagen. The disease is characterised by fragile bones, blue scleras, dentiogenesis imperfecta, and early loss of hearing. According to Sillence, there are four types of OI, each further subdivided on the basis of salient characteristics. Type I is the mildest form, and patients tend to live near-normal lives. In contrast, type II is invariably fatal before birth or in the perinatal period. Type III is less severe than type II but more severe than type IV, such that the order of decreasing severity of OI is type II, type III, type IV, and type I.

Osteogenesis imperfecta is associated with spinal deformities, including craniocervical anomalies such as basilar impression and basilar invagination. Posterior fossa lesions that have been associated with OI are brainstem compression, and Chiari-I malformation with syringomyelia; there has also been an isolated report of Dandy-Walker malformation.

In this article, we report a case of unilateral cerebellar hypoplasia in a young child with OI, and discuss the possible aetiology of cerebellar hypoplasia in this patient. To the best of our knowledge, cerebellar hypoplasia in a patient with OI has not been reported previously.

Case report

A 28-month-old Chinese girl known to have type IV OI, presented to the Queen Mary Hospital with repeated spontaneous fractures of her clavicles and limb bones. She was the first child of a non-consanguineous Chinese couple born...
vaginally at 42 weeks’ gestation. There were no antenatal or birth complications. Her birthweight was 2.9 kg; body length, 50.5 cm; and head circumference, 33.5 cm. Apgar scores were 7 and 9 at 1 and 5 minutes, respectively. Physical examination at the time of birth showed white sclera in both eyes and normal deciduous dentition. Cytogenetic study revealed a normal karyotype; however, molecular analysis and genetic mutational studies were not available. Subsequent follow-up revealed recurrent fractures after minor injuries in her first year of life. There was progressive scoliosis and the patient’s gross motor development was delayed. Her head circumference, body length, and weight fell below the third centiles. Tests for autoimmune markers at the age of 2 years gave negative results. By 28 months of life, the patient could stand only with support, and sit independently for a short period of time. At the recent presentation, she was found to have generalised, non-paralytic hypotonia, as well as third cranial nerve palsy over the left eye. Cerebellar signs were otherwise absent, and she did not experience any seizures. 

Magnetic resonance imaging (MRI) demonstrated hypoplasia of the left cerebellar hemisphere and vermis. The left cerebellar hemisphere was small and medially rotated (Fig a). The fissures were of normal size when compared with the those of the folia. The right cerebellar hemisphere was also normal in size. Although the fourth ventricle was asymmetrical and distorted, it was not enlarged. There was also no enlargement of the posterior fossa, and no posterior fossa cyst was detected. No associated anomaly of the corpus callosum and cerebral hemispheres was noted. The ventricles were normal in size. In addition, MRI revealed mild basilar impression and invagination (Fig b) with the Klaus height index measuring 28 mm (i.e., the height of the posterior fossa—a line drawn perpendicular from the tip of the dens to Twining’s line, which is itself a line drawn between the tuberculum and the internal occipital protuberance; normal level, >30 mm). The tip of the dens projected 5 mm above Chamberlain’s line (posterior hard palate to opisthion).

Discussion

We describe focal cerebellar hypoplasia and vermian hypoplasia in a child with OI. Cerebellar hypoplasia has not been previously reported in patients with OI or with basilar invagination or impression from other causes. On the other hand, basilar invagination or impression is common in OI and is estimated to occur in about 25% of patients with OI, most commonly in those with type-IV OI. The pathogenesis of skull base deformities in OI has been proposed to be because of the fact that the weight of the cranium and its contents exceed the weight-bearing capacity of “soft” bones at the skull base; the resulting recurrent microfractures in the region of the foramen magnum with upward translocation of the rostral cervical spine and into the posterior fossa.

In this case, we could not determine if cerebellar hypoplasia and OI were associated with each other, or if these were two isolated processes. Hypoplasia of the cerebral hemispheres is found in a wide range of conditions,
including cytomegalovirus infection, chromosomal abnormalities, genetically determined hypoplasias, metabolic disorders, and complex malformations. Some cases of unilateral cerebellar hypoplasia are due to unexplained prenatal vascular disruption. In the patient in our case, injury to the posterior circulation may have been secondary to direct compression or vascular disruption related to some event during pregnancy. Reported vascular complications of craniocervical anomalies leading to posterior fossa lesions include vertebral artery dissection, cerebellar infarction, and cerebellar atrophy. Although it is unlikely that basilar invagination or impression per se occurs to a significant degree in utero, it is possible that there is added trauma from minor transient displacement of posterior fossa structures in utero, especially in view of the closely packed neuroanatomical structures of the posterior fossa. Another possibility is localised trauma in utero from direct compression of the cerebellar hemisphere in foetuses with poorly ossified skulls. Injury to the cerebellum may be compounded by underlying excessive vascular fragility associated with OI.

Recent postmortem studies in fatal (type-II) OI have shown an association between mutations in type-I collagen and malformations in the central nervous system. These malformations include neuronal migration anomalies, such as lissencephaly and abnormal cortical laminations. It has been suggested that type-I collagen may help guide neurone migration during the development of the central nervous system by acting as a guide for outgrowth of neuronal processes. The above-mentioned cerebral malformations have not been reported in the less severe types of OI. In the patient in our case, there was no MRI evidence of an abnormal folia pattern or the presence of heterotopic nodules of grey matter in the cerebellum to suggest cerebellar dysplasia.

References