Is tooth agenesis related to brainstem anomalies in myelomeningocele patients with Chiari II malformations?

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Defects in the prenatal development of the brainstem can result in cranial nerve deficiencies. As the development of tooth germ is dependent on n. trigeminus, which originates from the brainstem, the hypothesis underlying this study was that anomalies of the brainstem would lead to an increased prevalence of tooth agenesis. Twenty-three patients (13 F and 10 M, age range 6–37 years) were studied, all with myelomeningocele and brainstem anomalies (Chiari II). They were examined retrospectively from the data in journals and dental radiographs and compared to available data on the prevalence of tooth agenesis in the Swedish population. Our hypothesis was rejected, since there was insignificant difference in the frequency of agenesis in our material (8.7%) compared with that of the Swedish population (7.4%).

□ *Brainstem anomaly; Chiari; cranial nerve deficiencies; myelomeningocele; tooth germ agenesis*

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Myelomeningocele is a congenital defect in which the meninges, nerves, and spinal cord extend like a sac on the back from the vertebral column and usually localized in the lower thoracic and lumbosacral region. It is a form of neural tube defect in which the vertebral column is open because of failed neural tube closure that normally occurs during the prenatal embryonic period (1, 2). Myelomeningocele is also associated with other central nervous system abnormalities; hydrocephalus, syringomyelia, neuropathic bladder and bowel, scoliosis, limb paralysis, and anesthetic skin. Patients with myelomeningocele invariably have Chiari II malformations in which both the brainstem and cerebellar tissue are displaced to a varying extent into the cervical spinal canal (3–6). These patients also show symptoms and signs of cranial nerve deficits (7), abnormal brainstem auditory evoked potentials (8), and eye movement disorders of central etiology (9, 10). In addition, aplasia of cranial nerve nuclei has been recorded in neuropathological studies (11).

Scoliosis is also associated with congenital brainstem abnormalities in patients without neural tube closure defects (12–14), and it is suggested that patients with idiopathic scoliosis have a primary dysfunction of the brainstem and that the spine deformity may develop secondary to a disturbance of the central postural reflex system (15–18). Scoliosis may also be the first sign of a Chiari I malformation with syringomyelia in young children. This malformation is restricted to a varying but moderate herniation of the cerebellar tonsils into the upper cervical spinal canal and with an origin probably different from the Chiari II malformation.

Tooth and nerve development are closely related and tooth agenesis is most commonly located at the site where innervations take place latest in the development (19, 20). Tooth formation is dependent on both oral epithelium and adjacent mesenchymal cells for development and neural crest cells are synonymous with the mesenchymal cells of the head and neck (21). These cells detach from the neural plate during neuralization, a process of folding in which the neural plate converses into a neural tube and then migrates down the sides of the head and into the jaws, beginning at the cranial end at day 22. The folding of the neural plate, detachment and migration of the cells, occurs in a craniocaudal way. In the jaws, the neural crest cells induce the oral epithelium to proliferate and then form the dental lamina, which is the first sign of tooth development and has been detected in 5–6 week old embryos.

The cranial nerve that innervates all the teeth is n. trigeminus (V); it is a large nerve that subdivides and goes to different parts of the jaws. There are three developmental fields bilaterally in the maxilla and in the mandible with its own innervations. These are: an incisor field, a canine and premolar field, and a molar field (20). Within the fields, it is always those teeth that are the last to be innervated that are the ones most frequently missing.

Huggare et al. (22), reporting on a study of scoliosis patients with malocclusion of the teeth, showed that 25% of these patients had tooth agenesis of the premolars. A recent study of patients with severe scoliosis by Samuelsson et al. (23) confirmed their findings, reporting a prevalence of developmentally missing premolars of 14%, which is twice as high as in the Swedish population and also significantly higher than in a matched control sample. Based on the theory that the etiology and pathogenesis of scoliosis may be neurogenic, tooth agenesis might be a useful predictor for scoliosis.

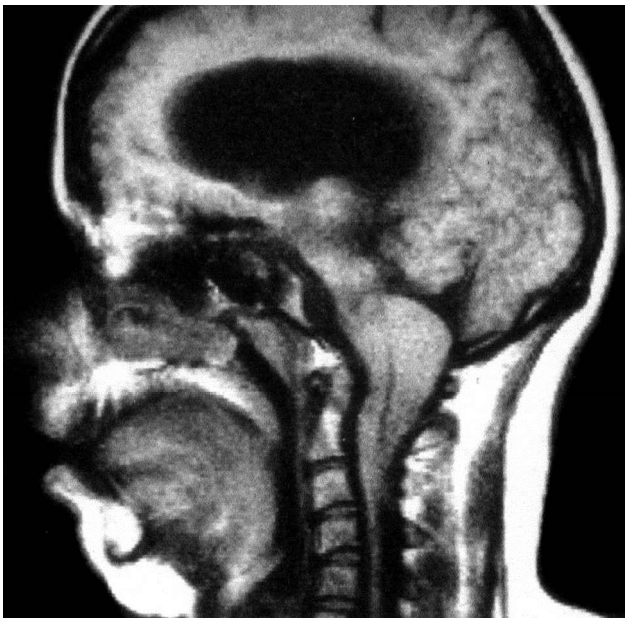

Fig. 1. MRI of the brain and cervical spine in a patient with a typical Chiari II malformation. The brainstem and cerebellar tissue are displaced downward through the foramen magnum into the upper portion of the spinal canal.

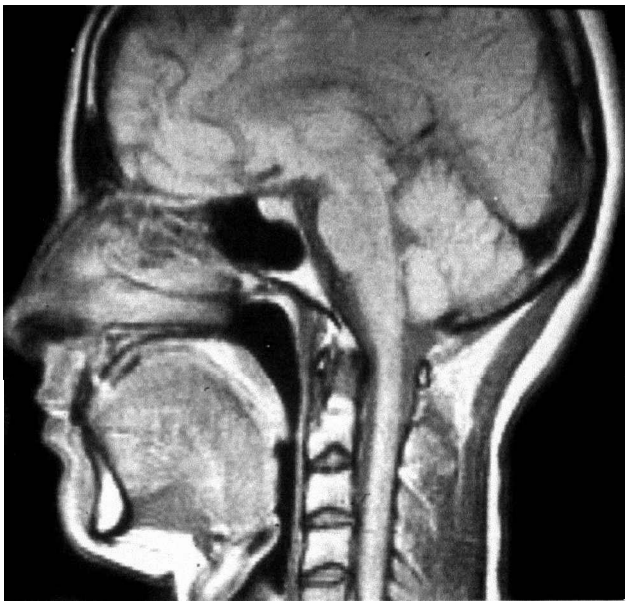

Fig. 2. MRI of the brain and cervical spine in a patient with a normal position of the brainstem and cerebellum.

The aim of our study was to evaluate whether there is a connection between brainstem anomaly and tooth germ development by assessing the prevalence of tooth agenesis in a group of patients with myelomeningocele and Chiari II malformations.

Subjects and methods

Approval for this study was obtained from the Regional Research Ethics Committee of Örebro County Council. Informed consent was obtained before the examination from each patient or from the parents or guardians of each child.

This retrospective study of patients with myelomeningocele and Chiari II malformations is based on examination of dental radiographs and dental journals from their childhood; we evaluated whether these patients have a higher prevalence of tooth agenesis (excluding the third molars) compared to the prevalence reported for the Swedish population in general.

Twenty-nine patients treated and followed-up at the Örebro Medical Centre Hospital were identified, all examined with magnetic resonance imaging (MRI) of the brain and the spine. The characteristic radiographic image of a patient with Chiari II malformation of the hindbrain is shown in Fig. 1 and that of a healthy subject in Fig. 2. Five of the patients refused to take any part in the study and did not want anyone to look through their journals and radiographs, while the parents of a 6-year-old boy did not want the missing radiographs to be obtained. In two children the radiographs did not give enough information why supplementary orthopanomograms (OPG) were obtained. For the remaining patients, there was enough information in their journals and on their previously obtained intraoral radiographs and OPG.

The study thus comprised 23 myelomeningocele patients (79.3%), 13 F and 10 M, with a mean age of 21 years (range 6–37) and with different neurological levels of their back lesion classified according to Lindseth (24). It was located at a high level in the vertebral column, between the lower thoracic (T) and the 1st two lumbar segments (L 1–2) in 4 patients; at a medium level, between the 3rd and 4th lumbar segments (L 3–4) in 13 patients; and in 6 patients at a low level, between the 5th lumbar and the 5 sacral segments (L 5-S). We did not use any control group, but compared our findings with available data on tooth agenesis in the Swedish population based on the data of Bäckman and Wahlin (25), Grahnén (26), and Bergström (27).

Results

Two out of 23 patients (8.7%) had agenesis of the premolars. None of them had agenesis of any other teeth. In one patient, localization of the myelomeningocele was at a medium neurological level (L3) and he had a typical Chiari II malformation. In the 2nd patient, localization of the myelomeningocele was at a low neurological level (L5) and the Chiari II malformation was less pronounced.

Examining the dental journals and radiographs revealed that 40% of the patients older than 13 years (6 out of 15 patients) had had orthodontic correction in the past,

Table 1. The frequency of tooth agenesis, tooth extractions, and level of the neurological deficit of the cele in 23 patients with myelomeningocele according to Lindseth (24). The thoracic (T) and the first 2 lumbar (L1–2) segments are at a high position, the 3rd and 4th lumbar (L3–4) segments are at a medium level, and the 5th lumbar (L5) and the sacral (S) segments are at a low level in the vertebral column

Patient	Sex	Age	Agenesis	Extractions	Level
1	Female	6 years	–	–	L3
2	Female	7 years	34, 35	–	L3
3	Female	10 years	–	–	S
4	Female	10 years	–	–	L4
5	Female	11 years	–	–	L4
6	Female	12 years	–	–	L4
7	Male	12 years	–	–	L5
8	Female	12 years	–	–	L4
9	Male	16 years	–	–	T
10	Female	19 years	–	14, 24, 35, 45	L3
11	Male	20 years	45	15	L5
12	Female	21 years	–	14, 24, 35, 45	T
13	Female	23 years	–	–	S
14	Male	25 years	–	–	T
15	Male	25 years	–	–	L5
16	Male	25 years	–	–	L3
17	Female	27 years	–	24,34	L3
18	Female	27 years	–	14,24	L4
19	Male	28 years	–	–	L3
20	Male	31 years	–	–	S
21	Male	33 years	–	–	L4
22	Female	34 years	–	–	T
23	Male	37 years	–	15	L4

including having their premolars extracted, for proper alignment of their teeth (Table 1).

Discussion

The hypothesis for this study was that congenital anomalies or dysfunction of the brainstem would result in increased prevalence of tooth agenesis. The importance of an intact neurogenic path for the development of the tooth germ renders patients with myelomeningocele and hindbrain herniation with associated Chiari II malformation interesting for our hypothesis. The cranial nerve V (trigeminus), which is of importance for the development of all the teeth in the jaws, has its nuclei in the brainstem, like most of the other cranial nerves.

In a study by Samuelsson et al. (23) of patients with severe idiopathic scoliosis and malocclusion of the teeth, the frequency of tooth agenesis was 14%, more than twice that in age- and sex-matched control subjects. In the present study, 8.7% of the patients had tooth agenesis and 40% of the patients above 13 years of age had to correct their dental malocclusion by extractions of one or more premolars followed by active orthodontic fixed appliance treatment. The figures regarding tooth agenesis correspond with the data given for the Swedish population in general (25–27), while the figures for the demand of extractions as a phase of the orthodontic correction seem rather high (28, 29).

The fact that a relatively high percentage of the patients (20.1%) did not want to participate in the study diminished the study group and thus reduced our possibility of detecting an increased prevalence of tooth agenesis. Another difficulty was that we do not know if the brainstem anomaly in our patients really was congenital or early prenatal, as the study was retrospective. If the hindbrain herniation has developed late prenatal, it should not have any effect on the tooth development, which is an early prenatal event. It has been reported that intrauterine myelomeningocele repair appears to reverse the pre-existing hindbrain herniation normally seen in Chiari II malformations and also limits or reduces hydrocephalus progression (30, 31) by improving cerebrospinal fluid (CSF) hydrodynamics. In postnatal repair of myelomeningocele, the hindbrain herniation persists.

More than 95% of patients with myelomeningocele develop hydrocephalus after birth (2). Although an aberrant craniofacial development has been detected in hydrocephalic patients (32), no obvious dental anomalies, such as shape or number of teeth, were observed (33).

The association between tooth agenesis and idiopathic scoliosis may be an expression of a primary dysfunction of the brainstem causing both conditions (15–18). In myelomeningocele, the Chiari malformation is not restricted to the herniation of the hindbrain and cerebellum, as several studies have shown aplasia of cranial nerve nuclei or cranial nerve dysfunction of central origin (7–11). A recent report on both pre-natal and post-natal neuro-osteological studies of spina bifida and myelomeningocele shows cranial base abnormal bony tissue, suggesting notochordal abnormality in the corresponding area (34). However, these brainstem abnormalities probably differ from those of patients with idiopathic scoliosis, as we could not find an increased prevalence of tooth agenesis in myelomeningocele patients.

The vertebral position of the myelomeningocele was not associated with tooth agenesis, but as we had only two patients with missing premolars (Table 1) and none of these had a lesion at a high level, we cannot tell whether a high location of the back lesion affects the prevalence of tooth germ aplasia.

Our hypothesis was rejected, because we could not show that patients with Chiari II anomalies of the brainstem have a higher risk of developing tooth agenesis as a result of cranial nerve deficiencies. This could be an expression either of tooth innervation commencing locally and independently from central nervous development or of other non-neurogenic mechanisms being important for tooth formation. In fact, family studies have revealed a strong genetic component in the etiology of hypodontia, the mode of inheritance being autosomal-dominant (26, 35). A frenetic search for the localization of the involved gene(s) has been the focus of research for the past decade (36–39).

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