Frontoethmoidal encephaloceles. A study of their pathogenesis

Hoving, Eelco Wieger

Summary

Chapter 1

The frontoethmoidal encephalocele is a congenital anomaly of the central nervous system with a relatively high incidence in South East Asia. The reasons for this characteristic geographical distribution are not understood, since the etiology and the pathogenesis are unknown. This study was focused on the pathogenesis of frontoethmoidal encephaloceles. First a hypothesis was developed, based on data of the literature and on an embryological study. Subsequently, a prospective study was carried out in order to find clinical support for this hypothesis. Thirty cases of frontoethmoidal encephaloceles were collected in Surabaya, Indonesia. Clinical features of these cases were listed, and a radiological evaluation was performed preoperatively. After surgical dissection, 29 specimens could be investigated with special reference to the relationship between cerebral tissue (neural ectoderm) and epidermis (surface ectoderm) within the wall of the celes. Finally, the results of the prospective clinical research are discussed in relation to the proposed hypothesis about the pathogenesis of frontoethmoidal encephaloceles.

Chapter 2

An encephalocele is defined as a protrusion of cranial contents beyond the normal confines of the skull. A variable terminology is found in the literature, but the term encephalocele is preferred this study. Encephaloceles are classified on the basis of the location of the defects in the cranium. Frontoethmoidal encephaloceles are characterized by an internal skull defect between the frontal and ethmoidal bones, either in the midline in the anterior fossa corresponding to the foramen caecum, or on either side of the midline just anterior to the cribriform plate. On the basis of the different locations of the external defects in the facial skeleton, while sharing the same location of the internal skull defect, a subdivision can be made into: a. nasofrontal b. naso-ethmoidal c. naso-orbital or d. combined nasoethmoido-orbital encephaloceles. Several theories about the pathogenesis have been proposed. Sternberg's study about the closure of the rostral neuropore in human embryos, and his ideas about a possible relationship between a developmental disturbance at the

site of final closure of the rostral neuropore and the genesis of frontoethmoidal encephaloceles, provided the theoretical basis for the subsequent embryological study.

Chapter 3

The separation of neural and surface ectoderm after closure of the rostral neuropore in the head region was studied by investigating the integrity of the basement membranes of these epithelia in 11- to 27-somite rat embryos. The basement membranes were visualized with polyclonal antibodies against laminin. Furthermore, cell degeneration was investigated in relation to neural crest activity and discontinuities of the basement membrane in 9- to 30-somite mouse embryos. The separation of the basement membranes of neural and surface ectoderm in the midline is the final phase during the fusion of the neural folds, which takes place between the closure of the rostral neuropore, at the 19-somite stage and the 27-somite stage (rat embryos), and which occurs focally with variation in the midsagittal and transverse planes. In the prosencephalon, neural crest activity is absent during the separation phase of both epithelia, but cell degeneration may contribute to the separation of the initially connected basement membranes. A disturbance in the separation of neural and surface ectoderm may be the pathogenic basis of midline skull defects and of frontoethmoidal encephaloceles in particular. The outgrowth of the nasal septum and the concomitant formation of the nose may act as herniating force if epidermis (surface ectoderm) and cerebral tissue (neural ectoderm) do not separate at the site of final closure of the rostral neuropore between the nasal fields. Subsequently a frontoethmoidal encephalocele may arise.

Chapter 4

Frontoethmoidal encephaloceles manifest themselves clinically as congenital, skin-covered masses near the root of the nose. Differential diagnoses are dermoid cyst, hemangioma, teratoma and nasal glioma. Additional anomalies of patients with frontoethmoidal encephaloceles include hydrocephalus, microcephalus, microphthalmia and mental retardation. Adequate treatment of frontoethmoidal encephaloceles consist of surgery aimed at 1. excision of the encephalocele, 2. watertight closure of the dura mater, 3. closure of the internal skull defect and 4. reconstruction of the

medial orbital walls. Different surgical techniques can be used namely, the extra-, sub- and transcranial approaches, respectively. Patients with frontoethmoidal encephaloceles appear to have a better prognosis than patients with encephaloceles in parietal or occipital locations. A series of 30 patients with frontoethmoidal encephaloceles was collected in Surabaya during the first three months of 1990. The clinical data like case and family histories, physical examination, psychomotor examination, additional investigations (except for radiological evaluation), treatment and outcome are presented and discussed. Twenty nine patients received surgical treatment of their encephalocele. In 28 patients the extracranial technique was used, and one patient was treated transcranially. Postoperative complications occurred in 8 patients. The outcome was scored as good in 17 patients, fair in 9 patients and poor in 3 patients.

Chapter 5

The aims of the radiological evaluation were: 1. to demonstrate the presence, location and size of the skull defect, 2. to define the shape and tissue characteristics of the herniated mass and 3. to provide information on additional anomalies of the brain and its CSF compartments. All patients were examined by means of CT scan and plain radiography of the skull. All nasoethmoidal, naso-orbital and nasoethmoido-orbital encephaloceles had the internal skull defect located at the site of the foramen caecum. In the nasofrontal encephaloceles the internal skull defect was located in the midline just superior to the nasal bones. The configuration of the skull defects varied in size and shape. The final subdivision of the frontoethmoidal encephaloceles based on the CT scan and location of the celes differed from the subdivision made on clinical grounds. The bony interorbital distance was enlarged in all patients, while the outer orbital distances were within the normal range. This means that all patients had interorbital hypertelorism. In addition, all patients had a lowered level of the cribriform plate. On the basis of 2-dimensional reconstructions in the sagittal and coronal planes, most celes were found to be connected with the inferior part of one or both frontal lobes. In 22 out of 30 patients additional intracranial anomalies were be found. In most patients the presence of additional anomalies could not be predicted, and the nature of the anomalies was often difficult to assess. Therefore, an extensive radiological evaluation of the intracranial contents is mandatory in patients

with frontoethmoidal encephaloceles.

Chapter 6

The goal of the histological investigation of the 29 specimens obtained was to determine whether the pathogenesis of frontoethmoidal encephaloceles might be related to a disturbance in separation of surface ectoderm (epidermis) and neural ectoderm (cerebral tissue) in the fourth week of gestation. If epidermis and cerebral tissue do not separate, an intimate relationship between these layers would be expected to be present in the wall of the celes. Three objectives were formulated: I. To investigate the presence of an intimate epidermis-cerebral relationship in the walls of the celes, II. To identify the different layers in the wall of the cele, with special reference to the presence of dural and/or pia-arachnoid layers, III. To determine the presence of cerebral tissue within the cele. In the specimens of 10 patients GFAP staining was used in order to confirm the presumed presence of glial tissue.

In 15 out of 29 specimens a close relationship between epidermal structures (epidermis and epidermal appendages) and glial tissue was found. The outcome of these findings were considered supportive of the non-separation theory. The outcome may have been influenced by the age of the patients and the method of obtaining the specimens. The younger the patient, the better the chance of finding close relationships between glial and epidermal tissues in the wall of the celes.

Although collagenous connective tissue was identified in most specimens, a continuous layer of supposedly dural collagen could was never found. A vascular or arachnoid layer was present in 9 specimens, and glial tissue was identified in all specimens. Considering the descriptions of the pathological findings of nasal gliomas as presented in the literature, several histological similarities with our series were evident. Supposedly characteristic histological features of encephaloceles could not be identified in our series. Therefore, the value of defining two entities concerning neural tissue in the nasal region may be questioned. Nasal gliomas and frontoethmoidal encephaloceles may be different terms for varying expressions of the same entity.

Chapter 7

Embryological considerations

Embryological findings in human embryos, as described in the literature, contain important features in relation to the hypothesis about the pathogenesis of frontoethmoidal encephaloceles: Firstly, the connection between surface and neural ectoderm at the situs neuroporicus appears to be stronger and lasts longer than in the dorsal part of the neural tube. Secondly, degenerated cells are found at the situs neuroporicus, and disturbances of programmed cell death may represent a mechanism of teratogenesis. Thirdly, the description of the situs neuroporicus as two parallel rows of cells between telencephalon and surface ectoderm may provide an additional explanation of the herniation of sagittal cranial structures (frontal lobes) through a midline skull defect.

The skull defect

The consistency in the location of the skull defect in the midline strongly supports the theory of primary non-separation between neural and surface ectoderm in the fusion zone of the rostral neuropore. Some variation in the site of final closure of the rostral neuropore seems probable, since its location is the result of a bidirectional process. The extent of non-separation between neural and surface ectoderm may determine the size of the mesodermal skull defect.

Herniation

The substantial growth process of the nasal septum can explain the herniation of frontoethmoidal encephaloceles, which occurs before the development of the bone centres in the neurocranium. This process of outgrowth of the nasal septum must have occurred in a normal fashion in the patients of this series, since all patients had a normal nose, and the bony outer orbital distances were within the normal range.

Additional intracranial anomalies

The concomitant presence of intracranial anomalies in a majority of the patients with frontoethmoidal encephaloceles in this series illustrates the presence of extensive neurectodermal developmental disturbances, and stresses the importance of an adequate radiological evaluation of these patients.

Neuropathology

The relationship between epidermis and glial tissue appears to become more remote

with time. The epidermal appendages might be considered as remnants of early developmental stages before the expansion of the skin during the third month of gestation.

Conclusions

The hypothesis

The hypothesis concerning the pathogenesis of frontoethmoidal encephaloceles is based on a primary disturbance in the separation of neural and surface ectoderm at the site of final closure of the rostral neuropore. This will result secondarily in a mesodermal defect at this site. The subsequent outgrowth of the nasal septum may act as herniating force.

This study has lead to the following conclusions:

1. A disturbance in the separation of neural and surface ectoderm should be considered as a neurulation disorder.
2. This separation process occurs focally with variation in the sagittal and transverse planes in mouse and rat embryos.
3. The disturbance in separation could be caused by the insufficient occurrence of cell death.

Clinical findings supportive of the hypothesis are:

4. The consistency in the location of the internal skull defect.
5. The close relationship between epidermal structures and glial tissue in 15 out of 29 specimens.
6. The presence of a normal nose in combination with interorbital hypertelorism in all patients.