Alobar Holoprosencephaly, Craniosynostosis and Microcephaly: A Constellation of Abnormalities in a Neonate with Frontonasal Encephalocele

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Citation

Abstract
A female neonate who was born with a frontonasal ulcerated protrusion. On examination, she had a frontonasal ulcerated protrusion, microcephaly and pancraniosynostosis. Computerized tomography scan revealed alobar holoprosencephaly. The combination of craniosynostosis with frontonasal encephalocele is rarely described in the literature, and more so is the combination with alobar holoprosencephaly. Problems in syndrome diagnosis can arise when previously unreported findings are seen in usual conditions. We describe our patient with an unusual constellation of conditions.

1. Introduction

Frontonasal encephalocele is an anterior neural tube defect and is rare, constituting 15% of all cases. It presents as a dysplastic mass of brain tissue at the root of the nose. It is very unusual for the protruding mass to be described as cavernous angioma histologically. Holoprosencephaly is the result of absent or incomplete cleavage of the fetal prosencephalon. The alobar type of holoprosencephaly is even rarer as it is said to be incompatible with life. The combination of frontonasal encephalocele and alobar holoprosencephaly is hardly described in the literatures; the presence of microcephaly and craniosynostosis completes this rare presentation. We describe our patient with this unusual presentation and subsequent management.

2. Case Report

A term female neonate delivered to a 32 year-old healthy Nigerian mother, who was gravida 3, para 0, from a non-consanguinous marriage. Gestation was complicated in the 1st month with high grade fever managed only with paracetamol. There was unremarkable family history. At birth, the neonate was noted to have ulcerated frontonasal protrusion without cerebrospinal fluid (CSF) leak and a dysmorphic face
with associated microcephaly, and pancraniosynostosis. There was hypertelorism and a shallow orbit but no syndactyly. She weighed 2.0 Kg, and had an occipitofrontal circumference (OFC) of 27cm. A cranial CT scan showed features of alobar holoprosencephaly with a monoventricle, absent basal ganglia and corpus callosum, a frontonasal defect with an encephalocele. On the 5th day of life she had excision of the frontonasal encephalocele and repair of the frontal defect, as well as performance of the craniosynostosis π procedure and excision of the metopic suture.

Histologically, the excised tissue was described as cavernous angioma. Postoperatively, she did well with no new neurological or feeding problems.

The anomalies are as illustrated below;
At 3 months of age she was yet to fixate her eyes on objects or achieve neck support. The OFC was 32cm with mild hypotonia of the limbs. There was a good cosmetic outcome of the skull.

3. Discussion

Craniostenosis is a condition in which the growth pattern of the skull changes as a result of premature fusion of the skull sutures. Craniosynostosis is part of a syndrome in 15 – 40 % of patients, but it usually may occur in isolation. Our patient had pancraniosynostosis (figure 4) and phenotypic syndromic facie (figure 1) i.e. hypertelorism and shallow orbit. There was a frontonasal encephalocele with minimal intracranial brain mantle of 12 -13 mm, suggesting that the microcephaly maybe of the primary type, where absence of growth of the brain renders the sutures of the cranial vault useless. This is corroborated by the enlarged subarachnoid spaces (figure 2).

In alobar holoprosencephaly, both lateral ventricles and third ventricle become confluent. This is usually accompanied by classical facies of cyclopia, ethmocephaly, cebrecephaly or cleft lip. Hypotelorism is also an accompanying feature. Our patient though has a dysmorphic facie, did not present with any of this classic pattern. This may imply a less distinction towards midfacial dysplasias of the frontonasal dysplasias. Hypertelorism is, equally, more likely to be present in the setting of a frontonasal encephalocele. The exact etiology of alobar holoprosencephaly is unknown. Environmental factors such as maternal diabetes mellitus, alcohol use as well as use of the teratogen – retinoic acid have been implicated, as has been mutation of some genes like Sonic hedgehog and ZIC2 on chromosome 13q32. Our patient was a product of a non-consanguinous marriage and the mother had none of these risk factors. The majority of holoprosencephaly are said to be sporadic. Our patient’s mother had a febrile illness of high grade fever which was treated with only paracetamol in the 1st month of gestation and the genetic abnormalities of holoprosencephaly occur at the 4th week of intrauterine life. Cyto megalovirus infection in pregnancy is known to cause holoprosencephaly. This incidence may have been of infective origin, given an unremarkable family history. Genetic studies were not conducted in our patient due to unavailability of same in our environment; there has been known associations to trisomy 13 or 18. The cost of conducting MRI also precluded our patient and us from its untold benefits.

Surgery had to be conducted on an emergency basis as a result of the ulcerated frontonasal encephalocele. The herniating brain tissues were excised via a cranial approach. The dura defect repaired with pericranium and the frontonasal defect sealed with an autologous parietal bone graft. The skin of the root of the nose was re-fashioned.

At the same setting, a craniosynostotic procedure was performed and metopic suturectomy done (figure 5) and the bones were tacked in place. These were considered as having
corrected the frontonasal encephalocele, immediate brain growth would have been hampered by the fused cranial sutures\(^1, 2,3,5,6\). All considered, though, our patient had an extensive procedure, good anaesthesia, astute surgical haemostasis, prompt blood transfusion as required; the procedure was well tolerated by the neonate. The immediate postoperative period was uneventful. The histology result of cavernous angioma (figure 8) was surprising. The frontonasal protrusion did not look like the brain (figure 1) but was earlier thought to be attenuated cerebral matter from exposure to prolonged extracranial environment. MRI and genetic studies would have assisted with further evaluation\(^5,6\).

There was good cosmetic outcome at age 3 months with a good re-contouring of the skull (figures 6 and 7). However, developmental milestones of fixation of eyes on moving objects, social smiles and neck controls were lacking. This may not be unconnected to the underlying brain pathology.

4. Conclusion

Neonates with encephaloceles must be worked up for underlying structural abnormalities like alobar holoprosencephaly; more so, in the setting of microcephaly. Though, no syndrome may have encompassed all the anomalies seen in our patient, a better understanding of the constellation of abnormalities will help to identify specific syndromes, and this will aid counseling and prognostication. Lastly, in the emergency setting of an ulcerated encephalocele with craniosynostosis, simple craniosynostosis procedures appear well tolerated and give good outcomes.

References