

Holoprosencephaly In A Nigerian Cadaver: An Original Case Report

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Citation

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Abstract

Forebrain abnormalities include cases of abnormally large or small brain volume (Megalencephaly and Microencephaly), abnormally formed gyri (agyria and polymicrogyria), abnormal migration of neurons (neuronal heterotopias), incomplete separation of the cerebral hemispheres (Holoprosencephaly) and agenesis of the corpus callosum. During a routine dissection of formalin-fixed cadavers in our Gross laboratory, a partial fusion of the cerebral hemispheres in the precentral cortex was encountered in a male adult cadaver. The falx cerebri was incomplete with crescentic inferior margin overlying the fused part. Agryria and abnormally formed gyri were also noticed.

INTRODUCTION

The division of prosencephalon into a diencephalon and two telencephalons is essential in the formation of two cerebral cortices, corpus striatum, thalamus, hypothalamus and related structures. Failure of separation of any part of prosencephalon results in a congenital case known as Holoprosencephaly (HPE).

Suggested risk factors include maternal diabetes, infections during pregnancy (syphilis, toxoplasmosis, rubella, herpes, cytomegalovirus), and various drugs taken during pregnancy (alcohol, aspirin, lithium, thiorazine, anticonvulsants, hormones, retinoic acid) (Moore & Persaud; 2003). Mildly affected children may exhibit few symptoms and may live a normal life.

Holoprosencephaly has been categorized into 3 types (from most severe to least severe):

- (1) Alobar HPE or complete absence of midline forebrain division resulting in a monoventricle and fused cerebral hemispheres
- (2) Semilobar HPE or incomplete forebrain division resulting in partial separation of cerebral hemispheres, typically posteriorly; and
- (3) Lobar HPE or complete ventricular separation with focal areas of incomplete cortical division or anterior falcine hypoplasia.

Neuroradiologic studies have provided detailed characteristics of these three major types of Holoprosencephaly and added another one called middle interhemispheric variant (Jin & Lauren; 2004).

HPE occurs every 1 in 250 conceptuses and 1 in 16,000 live-born infants (Golden, 1998; Ming & Muenke, 1998). HPE is aetiologically heterogeneous, with both environmental and genetic causes (Barr et al, 1983; Roessler & Muenke, 1998). So far, three human HPE genes are known: Sonic hedgehog (SHH) at chromosome region 7q36 (Roessler et al; 1996); ZIC2 at 13q32 (Brown et al; 1998); and SIX3 at 2p21 (Wallis et al; 1999). In animal models, genes in the Nodal signalling pathway, such as those mutated in the zebrafish mutants cyclops (Sampath et al; 1998; Rebaglianti et al; 1998), squint (Feldman et al. 1998) and one-eyed pinhead (Gritsman et al 1999), cause HPE. Mice heterozygous for null alleles of both Nodal and Smad2 have cyclopia (Nomura & Li; 1998) Karen et al (2000) reported that Mutations in TG-interacting factor (TGIF,) a homeodomain protein, in human HPE, cause holoprosencephaly and link NODAL signaling to human neural axis determination. SIX3, which is considered to be the functional orthologue of Drosophila genes sine oculis (so) and optix, has been found to be mutated in the homeodomain, in some patients with HPE (HPE2 on Chromosome 2p21) (Pasquier et al, 2000)

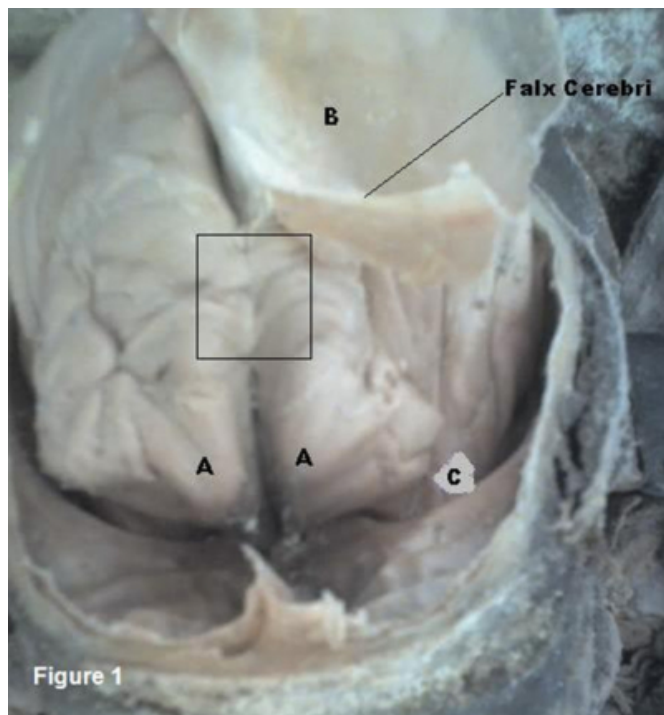
In this report, we present a case study of Holoprosencephaly in a Nigerian adult cadaver.

CASE REPORT

During the head and neck dissection of a formalin-fixed adult male cadaver for the training of 300 level medical students of Igbinedion University, Okada, Nigeria, we came across a brain with partial fusion of the frontal lobes of the cerebral hemispheres [Figure 1]. The fused parts possess continuous gyri and fissures. The fusion also extended to the corpus callosum. The cerebral cortex in general had few gyri which were irregular in outlines. Abnormally deep fissures were observed. The falx cerebri was very short over the fused area with a crescentic margin.

Figure 1

Figure 1: Photograph of Holoprosencephaly showing- A-Frontal lobe; B-Dura mater; C-Temporal lobe; Boxed area-Fused part.



DISCUSSION

Holoprosencephaly is usually associated with anomaly such as hypotelorism (Moore & Persaud; 2003), cebocephaly, cleft lip and/or palate, single maxillary central incisor, cyclopia (Nomura, M. & Li, 1998), proboscis, microcephaly, hydrocephalus, mental retardation, epilepsy, endocrine abnormalities, cardiac, skeletal, genitourinary, and gastrointestinal abnormalities.

HPE was reported in Nigerian population before the present case (Austin & Wilson, 2006), though rare, it has been reported in literatures as a congenital anomaly associated with mental retardation, dementia and agyri (Cotran et al;

1994). We could not correlate the present case with mental retardation, dementia but agyri. This is because the case was found in cadaver and not in the living. The cerebral hemispheres possess few abnormally formed gyri (Fig. 1). Studies in the past have indicated that 3% of all fetuses with Holoprosencephaly survive to delivery and the vast majority of these infants do not survive past the first six months of life, however current statistics are not available. This is at variance with the present study in which the cadaver was an adult meaning that the case was in the category of Lobar (mild)--where the brain is divided and there are some mild abnormalities (there is a well developed interhemispheric fissure however there is some fusion of structures).

Incomplete falx cerebri separated between the hemispheres. It possesses in the anterior part a crescentic inferior margin overlying the fused part. The inferior sagittal sinus begins posterior to this margins. In alobar Holoprosencephaly, falx cerebri is always absent.

In conclusion, the true spectrum of HPE, its clinical manifestations, and underlying etiologies require further elucidation. Applying this knowledge to individuals and their families is of utmost importance.

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