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A HISTOLOGICAL DIFFERENTIATION OF HUMAN FETAL CEREBRAL CORTEX

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ABSTRACT

Fetal cerebral cortex made up of specialized cell population and circuits that support unique higher-order cognitive functions. The cerebrum of 25 still born human fetuses of both sexes were collected and 5mm tissues of frontal, temporal, parietal and occipital cortices were processed for histological examination using H and E stains. At 20 weeks gestation, cells showed a closely packed stratifications with migrations of the cells from the ventricular zone to pial surface. The rounded cells with deep stained nuclei. At 24 weeks, the process of migration is still on development. Besides the typical laminar pattern is not seen, but the rounded granule cells with deep stained nuclei were well defined. At 30 weeks, arrangement of cells appear laminar pattern with predominance of granule cells ,few pyramidal cells. At 40 weeks, the laminar pattern are well defined. Large pyramidal cells of betz are well recognized in the frontal lobe . The 5 layered fetal laminar pattern with External marginal layer, Cortical plate ,Subcortical layer ,Intermediate zone and Ventricular zone . Finally, we explore the potential of these basic developmental and histological processes to inform our understanding of the emergence of functional neural networks and circuit abnormalities in neurodevelopmental disorders.

Keywords: Human cerebral cortex, neuronal migration, laminar pattern, Betz cells

1. INTRODUCTION

Human fetal brains are often autolyzed by the time of autopsy due to the unavoidable period of time between death and delivery. In addition to this, there will be also a delay between delivery and autopsy contributes further to artefact and autolysis. The immature brain may be extremely soft, even after fixation for several weeks, but this should not intimidate sampling for microscopic examination, which always adds valuable information. Unfortunately, these delicate brains tend to fragment during processing; the cortical surface being particularly vulnerable to mechanical disruption by handling. Careful processing by experienced lab experts can reduce the artefactual damage.

Describing the structural changes of human fetal brain is essential to understand the complex yet highly organized process of brain development. The histogenesis of the cortical wall of cerebral hemispheres has caused an splendid literature since 1930. Characterizing the dramatic structural changes of human fetal brain development is not a young field. It has nearly two centuries of history.

During 1816, there was one of the earliest specific accounts of the prenatal human brain,(1) following this reports based on serial sections by known neuroanatomists .(2,3,4) The atlases based on histopathological slides became available a couple of years ago, histopathology has been a specialized modality and remains to be an important method to study the detailed neural structures of developing brains.

The work presented here is based on experience of examination of the human fetal brain for clinical diagnostic purposes. The use of human material has limitations which do not apply to animal models, but models can never precisely reflect the processes of human brain development and in particular the timing of these events, which shows huge variation between species of differing gestational periods. Study of the developing human brain is essential, but every brain represents a personal tragedy for a family.

The aim of the study is to analyze the anatomical information revealed by histology is important for developmental studies in basic neuroscience. The present study has been undertaken to differentiate and understand the changes in the cortex of fetal cerebral hemispheres. The anatomical information from histopathology can possibly serve as a clinical review in diagnostic radiology.

2. MATERIAL AND METHODS

25 human still born fetuses of various gestational ages ranging from 20 weeks to 40 weeks were collected from Victoria hospital, BMCRI, Bangalore, India.

Tissues of all the four lobes of cerebral hemispheres have been collected. (20, 24, 30, 33, and 40 weeks)

They were processed and stained with H&E, to view the histopathological structure of cerebral cortex.

3. RESULTS

During 20 weeks of gestation, cells showed a closely arranged stratifications with migrations of the cells from the ventricular zone to pial surface. The cell population is rounded in size with deep stained nuclei. (Fig 1)

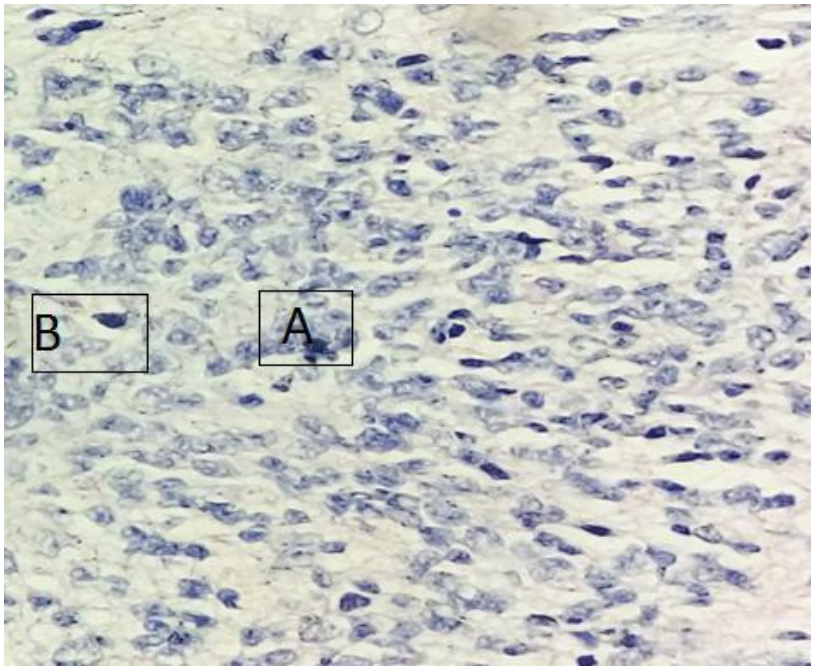
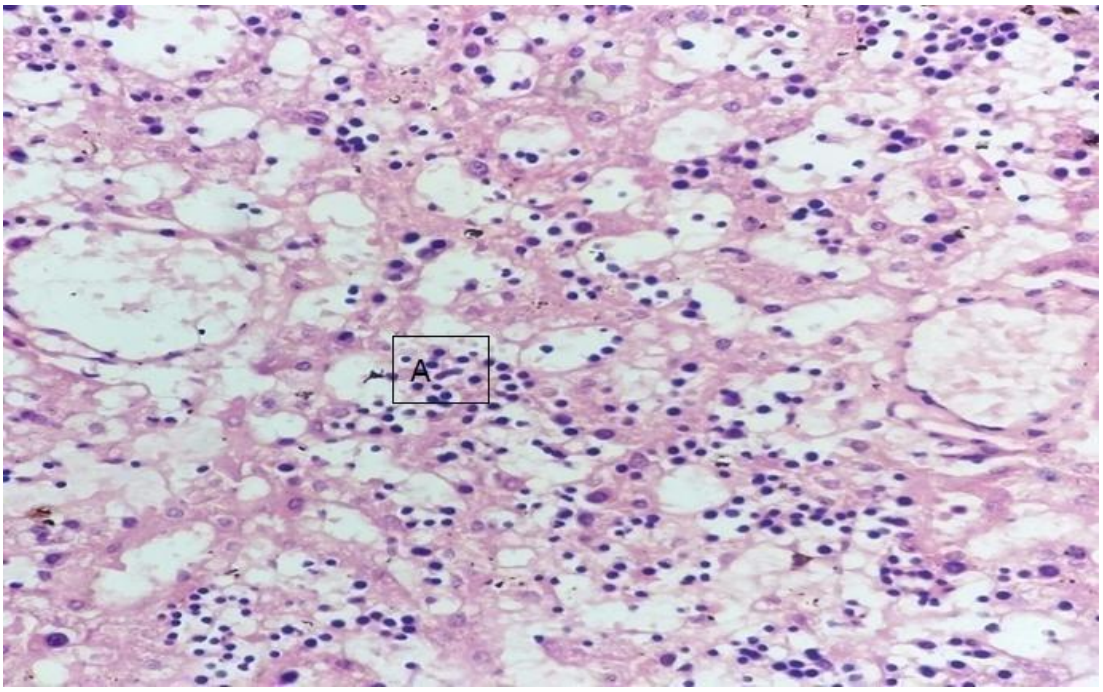


Fig 1: Photomicrograph of 20 weeks gestation, stained with H&E, x40 magnification. (see insert A-primitive brain cells, B- glial cells & astrocytes)

During 24 weeks of gestation, the process of migration is still on development. Besides the typical laminar pattern is not well developed, but the rounded granule cells with deep stained nuclei were well defined.(Fig 2)



. **Fig 2**: Photomicrograph of 24 weeks gestation, stained with H&E, x40 magnification. (see insert A- rounded deep stained granule cells)

During 30 weeks, arrangement of cells appear laminar pattern with few pyramidal cells and predominance of granule cells.(Fig 3)

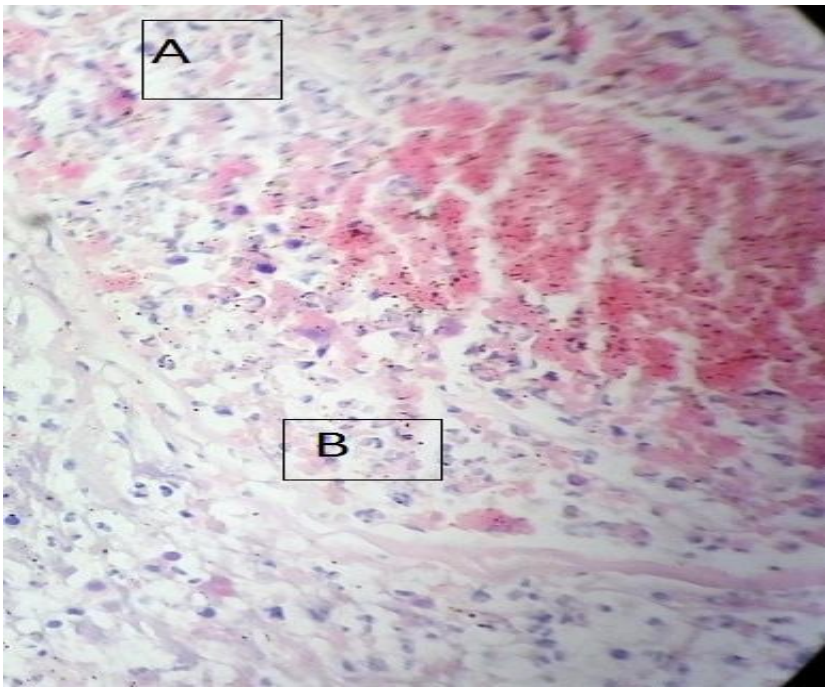


Figure 3: Photomicrograph of 30 weeks gestation, stained with H&E , x10 magnification ; (see insert A- rounded deep stained granule cells, B- few pyramidal cells)

During 40 weeks, the laminar pattern are well defined. Large pyramidal cells of betz is well defined in the frontal lobe . The 5 layered fetal laminar pattern with External marginal layer, Cortical plate ,Subcortical layer ,Intermediate zone and Ventricular zone are well defined .(Fig 4)

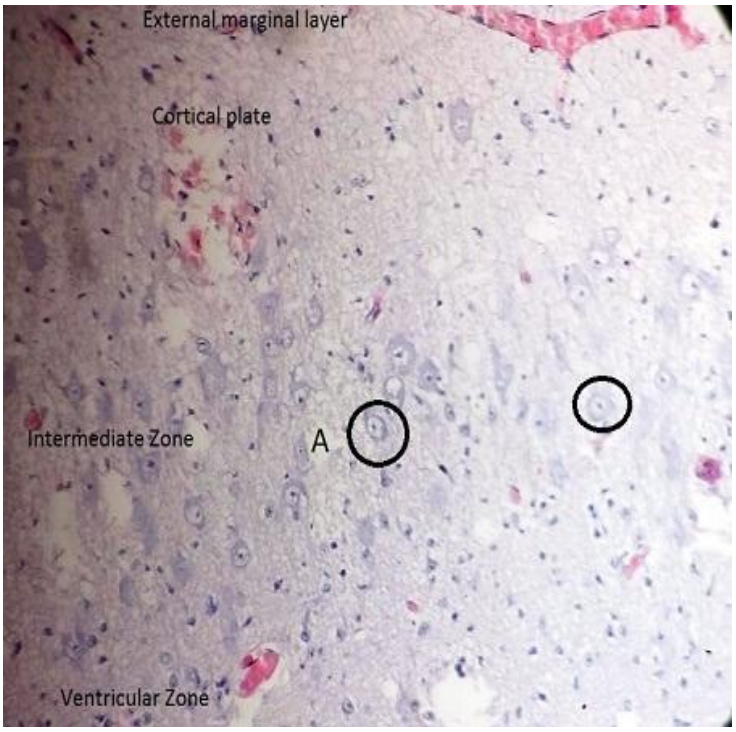


Figure 4: Photomicrograph of 40 weeks gestation, stained with H&E , x10 magnification ; (see insert A- pyramidal cells of betz)

4. DISCUSSION

As a prominent component of the fetal brain, cerebral cortex is the place where extremely complicated yet highly organized development process occur during the fetal development to form the adult cerebral cortex. The processes includes proliferation, cell differentiation, synapse formation, axon and dendritic growth, molecular specification, neural aggregation and myelination.

The fetal cerebral wall has a typical laminar organization, with few transient layers lacking their direct counterparts in the adult brain. These transient fetal laminae, namely the marginal zone, cortical plate, subplate, intermediate zone, subventricular zone and ventricular zone, have been extensively described and differ in thickness and volume during different stages of prenatal development.(5, 6, 7)

The modification into the adult neocortical pattern begins in middle weeks of 25 and 34 weeks ,as the migration and proliferation of neurons decreases. Dendrites begin to differentiate and synapses begin to develop in the deepest cortical layers, progressing to the most superficial layer.(8)

The topographic changes in pre-central, post-central, temporal, and occipital cortices do take place between 5-8 months due to differing growth and heterogeneous differentiation of cortical regions. However it's been distinguished that the young neurons are guided in their migrations by following the surfaces of radial glial cells, a bipolar cell form of astroglial lineage.(9)

In adult, differences in cortical cytoarchitecture, including abrupt changes in cell number, density, and lamination and the appearance of morphologically distinct cell types, have long been recognized. (10) Across the cortex, the density of neurons varies by as much as two-fold, primarily due to an increase in the density of upper (''supragranular'') cortical layer neurons in the caudal and medial areas .(11)

Even within a single functional area, such as primary motor cortex, the cell and neuron density may vary in a topographic manner, and these differences are thought to reflect changes in the cortical circuitry.(12)

In a study by Chong et al there was a normal appearance and the temporal pattern of neuronal migration in the human fetal brain early in the II Trimester as seen with MRI and correlated with histological sections. The presence of germinal matrix and layers of migrating neurons diminished considerably in size by 21 weeks. (13)

A study conducted by Crino on 27 weeks fetal brain tissue of focal cortical dysplasia shows a collection of abnormal cells at the junction of cortex and white matter. The abnormal cells extend, often along vessel walls, to the subpial surface. Use of a number of

cell markers shows a mixed population of cells, small oval deeply staining cells intermingled with giant cells, which themselves show heterogeneity of protein expression.(14)

Microcephaly is described as a small head. There is an major clinical differentiation between microcephaly due to damage or atrophy of the brain and microcephaly, in which the brain is small due to a genetic cause while the rest of the body is of normal size. In microcephaly the brain structure is either normal or has mild simplification of the gyral pattern. Mutations have been identified in several genes, all of which are involved in cell division and cell cycle regulation; it has been recommended that molecular evolution of these genes may have been a driving force for the increase in size of the brain during human evolution.(15)

In the present study we conclude that the five layered pattern of cortex was clearly appeared at first in the precental gyrus from 30 weeks on wards.

Conflicts of interest

The authors have no conflicts of interest to declare.

Ethics and informed consent

This work has been approved by the institutional ethical committee and informed consent was taken by all the students who participated in the present study.

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