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Mini Review

Location of Anterior Pituitary Gland Tissue is interrelated with Sella Turcica Morphology in Human Fetuses - Review and Perspective -

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ABSTRACT

This mini review is based on immunohistochemical studies on the human pituitary gland during the last 25 years. The normal development of the pituitary gland and its supporting sella turcica is presented. Furthermore focus is on pathological development, demonstrating ectopic adeno-pituitary gland tissue and abnormal sella turcica morphology. It is highlighted how the sella turcica morphology can predict abnormal formation and ectopic locations of the anterior pituitary gland tissue.

INTRODUCTION

Normal and pathological development of pituitary gland tissue and sella turcica morphology in human fetuses have received sporadic attention in the literature. The pituitary gland (or hypophysis) is composed of two main lobes, the adenohypophysis (anterior lobe) and the neurohypophysis (posterior lobe). It is well known from human and animal studies that the anterior lobe of the human pituitary gland originates from the surface - ectodermally derived pharyngeal epithelium immediately anterior to the buccopharyngeal membrane, while the posterior lobe of the pituitary gland has a neuro-ectodermal origin. The neurohypophysis is connected through the infundibulum cerebri (neural stalk) to the hypothalamus. [1-4]. Accordingly, the different components of the pituitary gland have different embryological origins.

Development of the pituitary gland starts at the age of 3 weeks of gestation (GA). After the gland has developed, and the invaginated adenohypophysis has lost its connection through Rathke's pouch with the pharyngeal tissue, the gland-supporting cartilaginous cranial base appears [5-7]. Earlier studies state that a small portion of the adenohypophysis normally persists in the wall of the pharynx as a pharyngeal hypophysis [8-11].

The pituitary gland often evades examination in routine fetal autopsies. The reason for this may be that the gland is difficult to access and that a throughout examination should include the adjacent cranial base.

Since 1995, systematic studies on mid-axial tissue blocks from human fetuses, focusing on pituitary gland tissue and sella turcica in human normal and pathological fetuses, have been published by Inger Kjær and co-workers. In this short overview of the publications by Kjær et al, the development of the normal pituitary gland and the development of the sella turcica, will be introduced. Thereafter several pathological conditions in the development of this key region in the early brain and cranial base development will be highlighted.

NORMAL DEVELOPMENT

Pituitary gland

At the initial stage of pituitary gland formation, there is a pituitary gland placode in the pharyngeal region, consisting of an adhesion between the infundibulum cerebri (offshoot from the brain) and the pharyngeal ectoderm [12-16]. Due to migration of the neural crest cells in connection with craniofacial development, this early placodal region is drawn cranially, resulting in appearance of a pocket, named Rathke's pouch (Figure 1, 2) [14,16]. Immunohistochemical NGFR (Nerve Growth Factor Receptor) reaction has been observed in the neuro-pituitary lobe at the border-line against the anterior lobe of the gland (pars intermedia) from the age of 16 weeks GA.

Sella Turcica

The gland develops before the formation of the sella turcica.

This timing in normal development is important to consider in pathological cases. The sella turcica appears in the initial stages in cartilage and later as a bony structure, supporting the mature gland. Sella turcica has an anterior wall and a posterior wall, connected by the floor in the sella. The posterior wall is the first structure to develop in the sella. This posterior wall develops from the paranotocordal mesoderm [16-18]. The anterior wall and the floor of the sella develop shortly after from the neural crest cells, ectomesenchymally derived.

PATHOLOGICAL DEVELOPMENT

Abnormal development of the tissues in the pituitary gland placode and/or abnormal development in the surrounding tissues (neural crest cells or the mesenchyme in the cranial part of the notochord), could cause pathological development in the region. The abnormal gland development might result in absence of the sella or in sella malformations, such as abnormal posterior wall formation or malformation in the floor or in the anterior wall [19].



Figure 1: Histological section seen in the sagittal view of the cartilaginous cranial base (purple) of a human fetus, GA 14-15 weeks [12,16]. Anterior to the left. Note the pituitary gland in the sella turcica (arrow). The anterior lobe of the pituitary gland is dark blue and the posterior lobe of the pituitary gland is light blue. Toluidine blue staining.

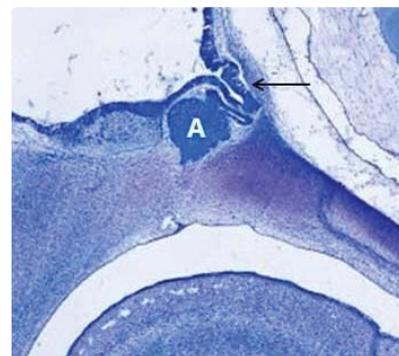


Figure 2: Histological sagittal section of the central part of the cranial base in a human fetus, GA 7 weeks [12,16]. Anterior to the left. At this stage of development, the anterior lobe of the pituitary gland (A) is attached to the posterior lobe of the gland. The infundibulum cerebri, which connects the posterior pituitary lobe to the hypothalamus, is marked by an arrow. The sella turcica has not formed yet. Toluidine blue staining.

Absence of sella Turcica

In certain craniofacial malformations it has been observed that the entire anterior pituitary gland tissue persist in the pharyngeal epithelium (Figure 3) [20].

Posterior wall deficiency in sella Turcica

In anencephaly there seems to be a malformation in the infundibulum cerebri in the pituitary gland placode, resulting in absence of the neuropituitary gland tissue and ectopic posteriorly located adeno-pituitary gland tissue in a malformed (not concave) sella turcica [21]. Also in trisomy 18 and in Meckel Syndrome malformation of the posterior wall, extending to the floor are associated with posteriorly located ectopic adeno-pituitary gland tissue (Figure 4) [22,23].

Anterior wall deficiency in sella turcica

In holoprosencephaly and other craniofacial abnormalities caused by abnormal neural crest cells, the anterior wall is malformed, often combined with a canal in the floor [16,19]. In this case, most parts of the gland tissue are located subpharyngially (Figure 5). In Down syndrome and in combined cleft Lip and palate conditions [24] malformations in the floor of the sella turcica is often combined with anterior wall deficiency.

Absence or malformed floor in sella Turcica

In different types of encephaloceles, the floor can be missing partly and the adeno-pituitary gland tissue located subpharyngeally (Figure 6) [25,26]. The subpharyngeal gland tissue reacts positively

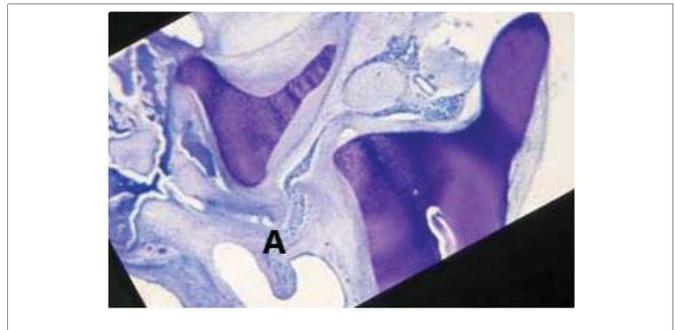


Figure 5: Histological sagittal section of the central part of the cranial base in a human holoprosencephalic fetus, GA 17 weeks [16,21]. Anterior to the left. The figure demonstrates a severely malformed pituitary gland region with malformed anterior sella wall and absence of sella turcica floor. Ectopic location of adeno-pituitary gland tissues (A) subpharyngially. Toluidine blue staining.

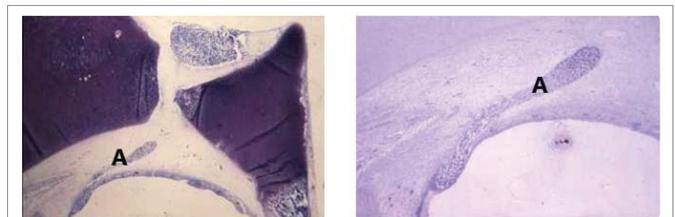


Figure 6: Histological sagittal sections of the central part from the same cranial base in a fetus with lumbosacral myelomeningocele, GA 18 weeks [16,25,26]. Anterior to the left. The figure to the left demonstrates a severely malformed pituitary gland region with absence of sella turcica floor and ectopic location of adeno-pituitary gland tissues (A) subpharyngially. The subpharyngially adeno-pituitary gland tissue is magnified in the figure to the right. Toluidine blue staining.

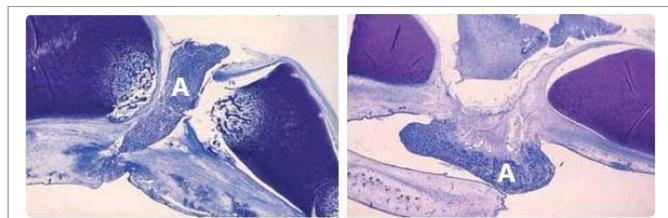


Figure 3: Histological sagittal sections of the central part of the cranial base in two human fetuses, GA 14-21 weeks, with severe craniofacial malformations [16,20]. Anterior to the left. The figures show malformed pituitary gland regions with absence of sella turcica floor and ectopic location of adeno-pituitary gland tissues (A). Left figure demonstrates partially pharyngially located gland tissue and right figure demonstrates totally pharyngially located gland tissue. Toluidine blue staining.

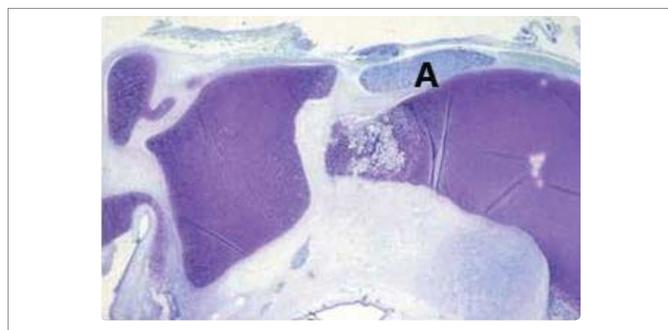


Figure 4: Histological sagittal section of the central part of the cranial base in a human fetus with anencephaly, GA 19 weeks [16,21]. Anterior to the left. The figure shows a severely malformed pituitary gland region with absence of sella turcica floor and ectopic location of adeno-pituitary gland tissues (A) in the region corresponding to the posterior wall of sella turcica (not developed). Toluidine blue staining.

on TSH (Thyroid Stimulating Hormone) immunohistochemically staining.

CONCLUSION AND PERSPECTIVES

This short review demonstrates how sella turcica can predict abnormal formation and ectopic locations of the anterior pituitary gland tissue. Former studies also demonstrate that immunochemical analyzes can reveal early functions of the gland. Pituitary gland tissue and sella turcica have been investigated in the few cases of more rare conditions, such as human Triploidy [27], Fragile X Syndrome [28] and Fetal Hypohydrotic Ectodermal Hypoplasia [29].

PERSPECTIVES

The observations of the early prenatal interrelationship between the formation of the anterior lobe of the pituitary gland and the morphology of the supporting sella might be important for postnatal clinical diagnostics. The shape of the sella turcica has been described radiographically in postnatal Encephaloceles [30], Down Syndrome [31], and postnatal Combined Cleft Lip and Palate [32]. In all cases, the postnatal morphology of the sella was identical to prenatal morphologies, but associated postnatal analyzes of the pituitary gland in these cases are still lacking. In newer studies radiographic investigations on sella turcica morphology are combined with neuro-radiographic imaging of the brain [33,34]. Studies on sella turcica and the pituitary gland are important, not only for analyzes in endocrinology, but also for analyzes in other medical disciplines, such as craniofacial surgery [34] and orthodontics [35].

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