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Study on Morphogenesisis And Histogenesis of The Human Fetal Thymus in The First Trimester.

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ABSTRACT

The thymus is a remarkable organ with respect to its development and functional differentiation. It is a pinkish grey mass and is a primary lymphoid organ. Thymus develops from third branchial pouch along with inferior parathyroid gland. It increases in mass up to puberty. Afterwards it regresses and remains as a fibrous mass thereafter. The present study is based on the findings carried out on 10 human fetuses during the first trimester. The fetuses were obtained from various labor rooms, operation theatres and obstetric wards of Government Medical College Jammu. Products of still births and abortions, which were either induced or natural or from hysterotomy procedures were included in the study. On morphological and histological study we observed that the rudiment of the organ was covered by a capsule at stage corresponding to CR length 58 mm. Corticomedullary differentiation occurred at 11 weeks of gestation. From our study we concluded that the developments taking place in human fetal thymus during the first trimester are; capsule formation, lobulation of the organ, differentiation of thymocytes and corticomedullary differentiation.

KEYWORDS :

INTRODUCTION

Thymus is a primary lymphoid organ and a key regulator of the immune system. It is unique to the class mammalia. Grossly, it is a pinkish grey mass and lies in the superior mediastinum immediately behind the sternum. It is composed of 2 lobes which are further divided into lobules with an outer cortex and an inner medulla. The cortex is studded with extensive population of T lymphocytes, dispersed reticular epithelial cells, and a few macrophages. The medulla contains Hassall's corpuscles which are concentrically arranged flattened epithelial reticular cells that become filled with keratin filaments. Thymus undergoes changes in size, structure, composition, and activity during life than any other organ. These changes start from fetal life and continue throughout life. Thymus is more prominent during early fetal life (**Galen, 130 AD-200**) and reaches its highest relative weight at the time of birth but its absolute weight continues to increase until the onset of puberty. Thereafter, it involutes progressively throughout life (**Bratton A. B, 1925**). It develops from the endoderm of the 3rd pair of pharyngeal pouches and from the adjoining mesenchyme into which epithelial tubes grow. The tubes soon become solid cords that proliferate and give rise to side branches. Each side branch becomes the core of the lobule of the thymus. Epithelial cords become arranged around a central point forming small groups of cells -The Thymic corpuscles or Hassall's corpuscles. Incomplete septa are formed between the epithelial cords dividing the lobes into lobules. The interstices between the epithelial cells are filled by lymphocytes (**Keth.L.Moore, T.V.N Persaud**). The basis for the development of the thymus is a primordium surrounded by a thin layer of mesenchyme. Neural crest cells are also thought to play an important role in the organogenesis of the thymus. It cannot be differentiated prior to the differentiation of inferior parathyroid gland at stage 16 but thereafter it is represented by 2 elongated diverticula which soon become solid cellular masses and grow caudally into the surrounding neural crest mesenchyme (**Grays Anatomy 40thedition**). Ventral to the aortic sac, the two thymic rudiments meet but do not fuse and they are subsequently united by connective tissue only. After the neck is fully developed and the heart has descended, the thymus comes to lie in its final location. The connection with the 3rd pouch is subsequently lost but the stalk may persist for some time as a solid cellular cord. As the thymus proliferates and descends, the local cardiac neural mesenchyme controls the pattern and development of the gland. Crest mesenchyme forms the connective tissue septa which produce the lobulated structure of the gland.

MATERIAL AND METHODS

The present study was conducted in the department of Anatomy Government Medical College Jammu after approval from the college ethical committee. 10 human fetuses were collected from operation theatres, labor rooms and obstetric wards of department of Gynecology and obstetrics, Government Medical College Jammu, Government hospital Gandhi Nagar, Jammu and various nursing homes operating in and around the Jammu city. The fetuses were obtained as products of still births and abortions which were either induced or natural. The specimens were divided into 2 groups of 5 specimens each. Group 1 contained fetuses of CR length 58mm (gestational age:-10-11 weeks),

group 2 contained fetuses of CR length 65-84 mm (11-12 weeks). Specimens having any congenital malformations were excluded from the study. The specimens were put in jars containing 10 percent formalin. Crown rump length was measured with the help of vernier calipers. Age assessment of the fetuses was done according to the rule as described by **Hamilton, Boyd and Mossman (1976).** Thymus was removed by an incision which extended from lower part of the neck to the entire thoracic cavity. The thymus was dissected out, and grossly examined for length, breadth, weight, color, texture, and location. The dissected tissues were processed by using standard histolological techniques. 5-7 micrometer thick sections of the tissues were made. These sections were then stained with H&E and Masson's trichrome stain. The slides were mounted and observed under compound light microscope and the observations were recorded.

OBSERVATIONS

In our present study, at 58 mm CR length the gland is located in the superior mediastinum and exhibited a cellular network with a delicate connective tissue capsule (fig. 1).The capsule is made up of loosely arranged array of collagen fibrils with a scanty cellular component composed predominantly of fibroblasts. Some spindle shaped cells with densely staining nuclei and scanty eosinophilic cytoplasm were seen interspersed among the fibroblasts. These spindle shaped cells probably represent the migrating thymocytes invading and populating the thymic parenchyma. As shown in fig. 2 fine and delicate extensions are seen arising from the inner aspects of the capsule which are connective tissue trabeculae. At 65 mm CRL, the gland is a bilobed structure enclosed by a more compact connective tissue capsule. The trabeculae are more appreciable and are seen to invade and divide the gland into small almond sized lobules (fig. 3). Corticomedullary differentiation is recognized at this stage of development as shown in the fig. 3. The thymic parenchyma beneath the thymic capsule reveals 2 faintly distinguishable regions-an outer dark area, the cortex and a pale inner area, the medulla. At 76-84 mm CRL, we observed that the cells making up the thymic parenchyma became more recognizable. These cells represent the thymic lymphocytes. In addition to this, thymic reticular cells were represented by small round cells with abundant cytoplasm and a large central nucleus. At this stage, we also observed vascular invasion of the connective tissue capsule.

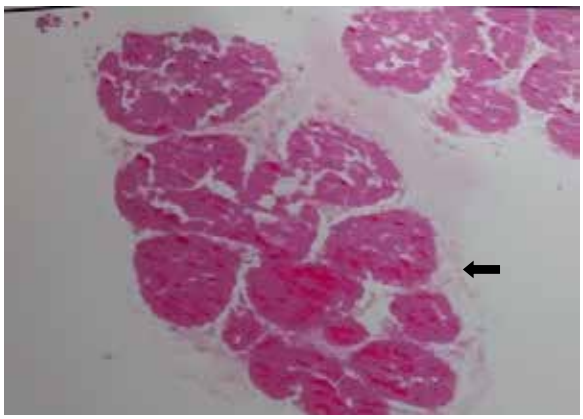

Fig 1: showing thymus gland of fetus of 58 mm CR length surrounded by a delicate connective tissue capsule as shown by arrow in the figure.

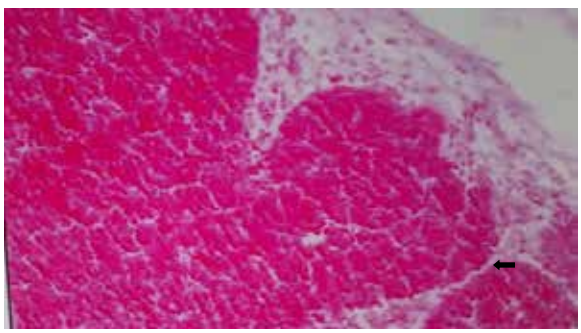

Fig 2: Photomicrograph of thymus of human fetus at 58 mm of CR length showing fine and delicate extensions arising from the capsule as shown by arrow

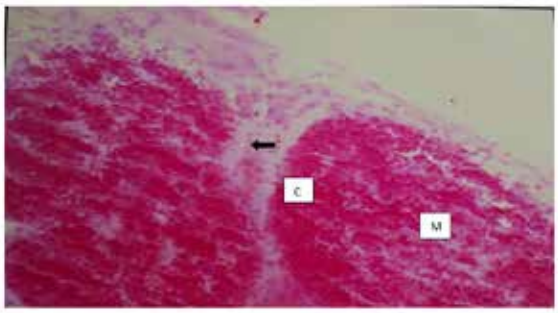

Fig 3: photomicrograph of human fetal thymus at 65 mm CR length showing well defined trabeculae arising from the capsule and dividing the thymus into almond shapes lobules with differentiation of cortex (C) and medulla (M).

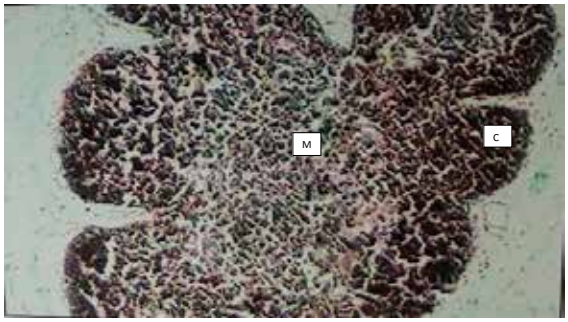

Fig 4: photomicrograph of fetal thymus at 84 mm CR length showing well defined cortex (C) and medulla (M).

DISCUSSION

The process of thymic development entails a process of growth, differentiation and regression. Thymus develops from the third pharyngeal pouch which initially expands and develops as a solid dorsal bulbar part and a hollow elongated ventral part. Thymus develops from the ventral part of the pouch. Proliferation of the epithelium of the elongated ventral part takes place at 6 weeks (**Keth.L.Moore**). The present study also reveals the changes in microscopic structure of fetal thymus from 58 mm CRL (corresponding to 75 days). In the present study, it was observed that the capsule is in the form of delicate connective tissue network at 58 mm CRL. At this stage, we also observed spindle shaped cells which represent migrating thymocytes. Delicate extensions of collagen fibers pass towards the thymic parenchyma which represents the connective tissue trabeculae. At this stage, there is no differentiation between the cortex and the medulla. These observations differ from the time scale mentioned by other authors (**Von Gaudecker and Mullerhermelink, 1980**) who reported presence of the capsule as early as 8th week of intrauterine life, whereas **Haar, 1974** has reported its presence by 9 weeks of intrauterine life. In our present study, we observed that the gland is enclosed by a more compact connective tissue capsule at 65 mm CRL, corresponding to 11 weeks of gestation. In our present study, we also observed that the small gland is divided into inconspicuous lobules by fine connective tissue trabeculae at 10 weeks of gestation. Similar findings are reported by **Ghali et al, 1980.** However, our findings differ from **Haar et al, 1974** who reported that lobular formation begins by 9 weeks of gestation. In our present study, we observed that the differentiation of thymic cortex and medulla is first noted at 11 weeks of gestation as 2 areas with different cellular densities. This finding in our present study is similar to that of **Ghali et al, 1980.** However, **Hamilton and Mossman, 1976** have reported differentiation of cortex and medulla at 40 mm CRL corresponding to 9 weeks of gestational age, whereas **Hayward, 1970 and Muller Hermelink, 1996** observed corticomedullary differentiation at 12 weeks of intrauterine life. **Haar, 1974 and Lobach and Haynes, 1987** reported that corticomedullary differentiation occurs at 14 weeks of intrauterine life. In our present study, we also observed the evidence

of thymic vascularity at 11 weeks of gestation, as delicate vascular spaces invading the capsule. This is in accordance with **Ghali et al, 1980** who reported that thymus becomes vascular at 11 weeks of intrauterine life. However, **Haar, 1974 and Hamilton and Mossman, 1976** have reported that extrathymic blood vessels associated with connective tissue fibers and mesenchymal cells surround the thymus at 9th week of intrauterine life. The findings of thymic vascularity in our present study also differ from the studies of **Williams et al, 1995** who reported that erythroblastic cells occur in thymus at 10 weeks of gestation.

SUMMARY AND CONCLUSION

From the present study, we observed that the thymus is located in the superior mediastinum in the stage CRL 58 mm and is in the form of a cellular network surrounded by a capsule. At 65 mm CRL corresponding to 11 weeks gestation, the thymus is a bilobed structure surrounded by a compact capsule. Towards the end of the first trimester, the thymic lobules increase in size, corticomedullary differentiation becomes more obvious and vascular invasion of the connective tissue capsule has taken place. Thus it is concluded that the developmental stage of thymus is important to know the gestational age of the fetus. Furthermore, it opens up a new door for research work in the field of embryology and immunology.

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