

HISTOGENESIS OF HUMAN FOETAL THYMUS

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ABSTRACT

Introduction: The thymus is a primary lymphoid organ. It is a bilobed structure divided into lobules by the connective tissue septa. Each lobule consists of a cortex and medulla. Most of the studies regarding early foetal histology of this organ are animal based. The present study has been undertaken to highlight some features regarding histogenesis of human foetal thymus.

Materials and Methods: In the present study, 30 normal human stillborn/aborted fetuses were studied. The obtained fetuses were fixed in 10% formalin. After proper fixation they were subjected to dissection. The obtained specimens were processed by standard paraffin block making procedure. Sections were taken and stained with haematoxylin & eosin. The stained sections were examined under light microscopy using 10x and 40x optical magnifications and photographs taken.

Results: At 12th week, capsule was thin and cortico-medullary differentiation not much prominent. Epithelial cells and lymphocytes were present. Hassall's corpuscles were very small and immature. Distinct lobulation was seen at 18th week with well differentiated cortex and medulla. The gland became more distinct from 21st week onwards with increased number of Hassall's corpuscles of various types. 29 week onwards the thymus gland revealed an adult histological picture.

Conclusion: All structural changes viz cortico-medullary differentiation, lobulation and maturity of Hassall's corpuscles occurred within the first 18 weeks of gestation.

KEY WORDS: Thymus, Hassall's corpuscle.

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INTRODUCTION

The thymus is a primary central lymphoid organ and a key regulator of the immune system, and is responsible for cellular immunity of the body. It is a bilobed structure divided into lobules by the connective tissue septa. Each lobule consists of cortex and medulla [1].

Thymus consists of two pyramidal lobes. It is located in the mediastinum behind the sternum

and in front of the pericardium and great vessels of the heart in the adult. The primordia of thymus develop in the region of superior neck in early fetal life and reach final destination in the mediastinum by progressive descent [2].

The details of microscopic & morphometric development of the thymus are not studied to great extent in the human fetuses and most of our knowledge regarding early fetal histology of this

organ is based on the studies in different animals. Thus the findings of different workers are found to be not consistent and are contrasting in most of the cases. The present study has been undertaken to highlight some important points in histogenesis of normal human foetal thymus gland.

MATERIALS AND METHODS

Histological study of Thymus gland in human foetuses of various gestational ages was carried out in the department of Anatomy in collaboration with department of Obstetrics and Gynaecology S.R.T.R Medical college Ambajogai, Maharashtra, India.

In the present study 30 normal foetuses were obtained from the department of Obstetrics & Gynaecology S.R.T.R Medical college and hospital Ambajogai with the permission of Professor & Head of department. These fetuses included the spontaneous abortus and still born. For the above purpose the approval was also taken from the Local Ethical Research Committee. A full anatomical examination was performed in all specimens to document normal anatomical development. A standard proforma was designed and used to maintain a protocol in selecting only the normal fetuses. Twin foetuses and foetuses with gross anomalies were omitted from the study. Foetuses were collected within 3-4 hours immediately after the delivery to avoid post-mortem changes.

The obtained foetuses were fixed in 10% formalin. After proper fixation they were subjected to dissection. All the specimens were processed by standard paraffin block making procedure. The sections were taken by rotatory microtome and stained with haematoxylin & eosin. The stained sections were examined by using light microscope under 10x and 40x optical magnifications, photographs were taken.

Foetuses were arranged into three gestational age groups as follow:

Group I- 12-20 weeks,

Group II- 21-28 weeks,

Group III- 29-38 weeks.

RESULTS

Group-I (12-20 weeks): At 12th week gland was seen to be composed of delicate capsule.

Connective tissue septa (trabeculae) extend from capsule into the parenchyma. Small immature connective tissue septa arising from these trabeculae extended partially into the lobule were seen (Fig. 1). Cortico-medullary differentiation was not that much prominent, lymphocytes present at this stage. Lymphocytes can be differentiated by large dark blue staining nucleus with faint eosinophilic cytoplasm. Immature blood vessels were seen in the connective tissue of capsule & trabeculae. Epithelial cells were seen at this stage. The cells can be differentiated by the pale staining nucleus with eosinophilic cytoplasm, the cells shows cytoplasmic extensions forming network. Hassall's corpuscles were seen at this stage. These were very small & immature (Fig. 2).

At 14th week the connective tissue septa were wider & Lobulation is still continued at this stage. Corticomedullary differentiation was still continued. Epithelial cells were irregular in shape with many processes extending among the lymphocytes. Few small Hassall's corpuscles were visible in the medulla as concentrically arranged epithelial cells with central eosinophilic mass.

At 18th week Distinct lobulation was seen. The thicker connective tissue septa penetrate deeper into the substance of gland. Lobules increased in size, with increase in lobulation. Corticomedullary differentiation was complete at this stage. At the periphery of lobules numerous and densely packed lymphocytes forming darkly stained cortex were seen. At the centre lymphocytes were fewer and forming lightly stained medulla. Medulla continuous with one lobule to another (Fig. 3). Larger blood vessels were seen in the surrounding connective tissue capsule, trabeculae & parenchyma of thymus. Many Hassall's Corpuscle seen at various stages of development. Juvenile type composed of one or two hypertrophic reticuloepithelial cells. Premature type composed of small groups of hypertrophic cells showing early processes of keratinization, but without a flattened aspect, or a tendency to concentric disposition. In mature stage, the reticulo-epithelial cells appeared flattened and disposed concentrically around keratin and a mix of degenerated lymphocytes and macrophages, with or without empty space. Some Hassall's corpuscle of juvenile type, some

Fig. 1: 12 week 10x 1) Capsule, 2) Connective tissue septa, 3) Lobule, 4) Blood Vessel, 5) Immature Connective tissue Septa.

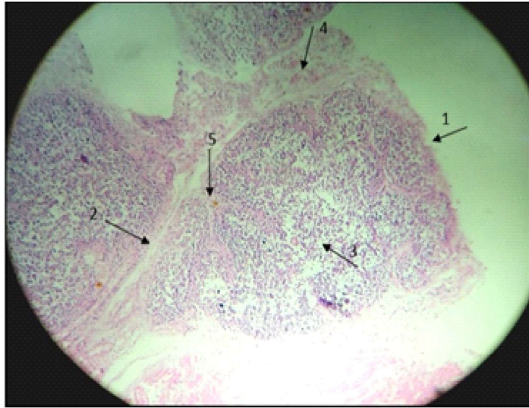


Fig. 2: 12 week 40x 1) Hassall's Corpuscle, 2) Lymphocytes, 3) Epithelial cells.



Fig. 3: 18 week 10x 1) Connective tissue septa, 2) Blood Vessel, 3) Medulla, 4) Cortex.

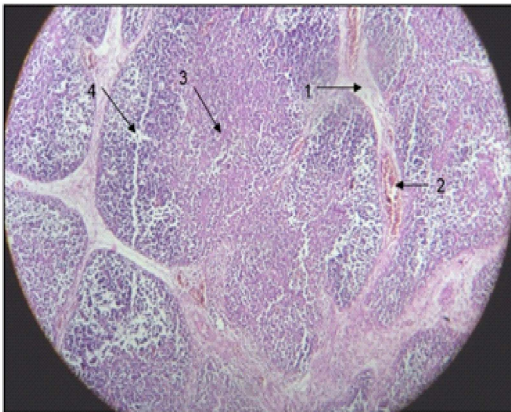


Fig. 4: 18 week 40x 1) Juvenile Hassall's Corpuscle, 2) Immat Corpuscle, 3) Mature Hassall's Corpuscle, 4) Epithelial Cell, 5) Lymphocytes, 6) Blood Vessel

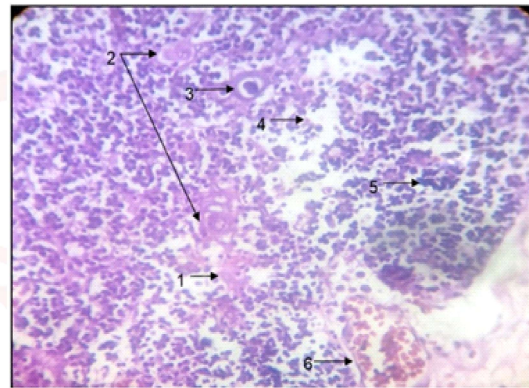


Fig. 5: 26 week 10x 1) Connective tissue septa, 2) Cortex, 3) Medulla, 4) Blood Vessel.

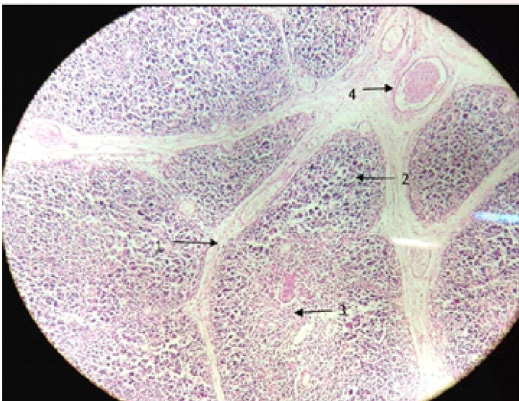


Fig. 6: 26 week 40x 1) Advanced Hassall Corpuscle, 2) Epithelial Cell, 3) Lymphocyte, 4) Blood Vessel, 5) Juvenile Hassall Corpuscle.

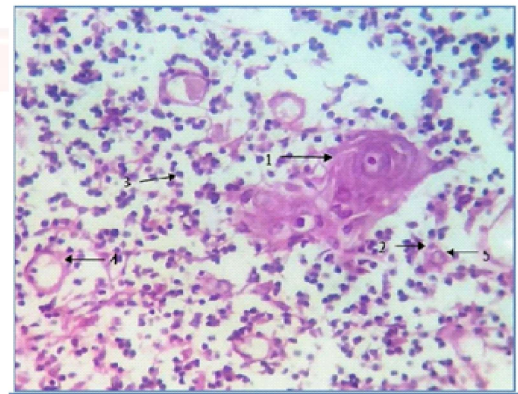


Fig. 7: 28 week 40x 1) Advanced Hassall Corpuscle, 2) Juvenile Hassall Corpuscle, 3) Immature Hassall Corpuscle, 4) Advanced Hassall Corpuscle, 5) Lymphocyte, 6) Epithelial Cell, 7) Blood Vessel.

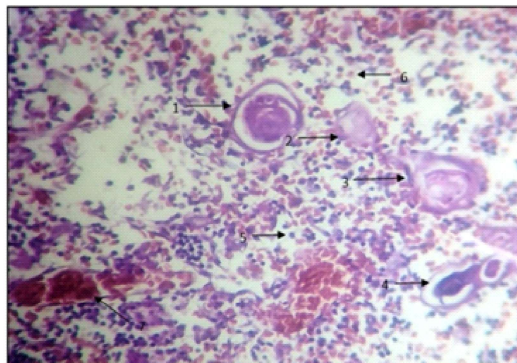


Fig. 8: 32 week 10x 1) Lobule, 2) Connective tissue septa, 3) Blood Vessel, 4) Hassall's corpuscle.

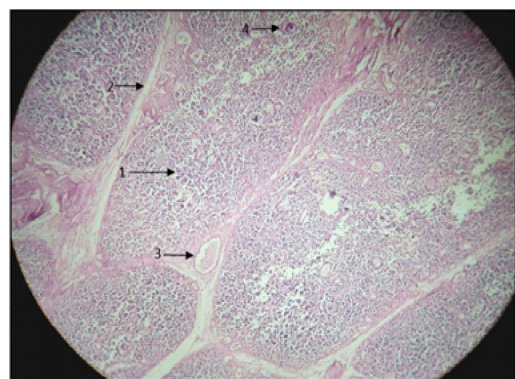


Fig. 9: 36 week 40x 1) Lymphocyte, 2) Epithelial Cell, 3) Immature Hassall Corpuscle, 4) Advanced Hassall Corpuscle.

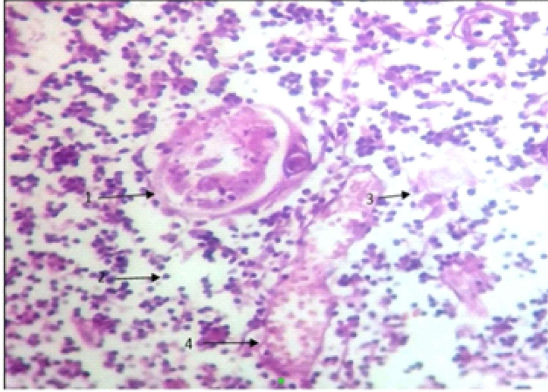


Fig. 10: 32 week 40x 1) Advanced Hassall Corpuscle, 2) Lymphocyte, 3) Epithelial Cell, 4) Blood Vessel.

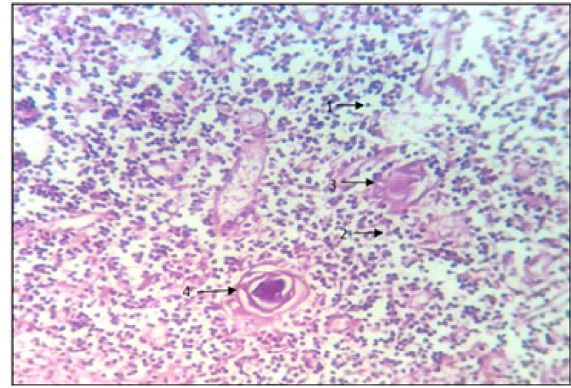


Fig. 11: 38 week 10x 1) Connective tissue septa, 2) Cortex, 3) Medulla, 4) Hassall Corpuscle, 5) Blood Vessel.

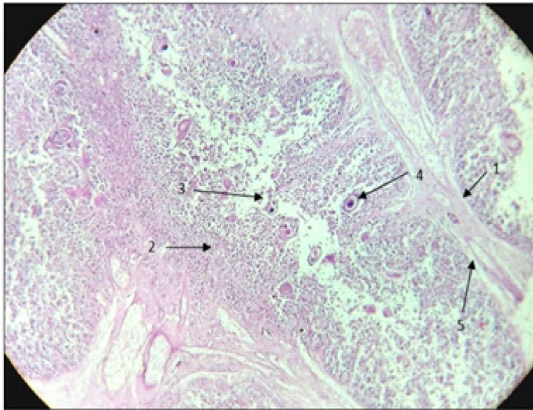
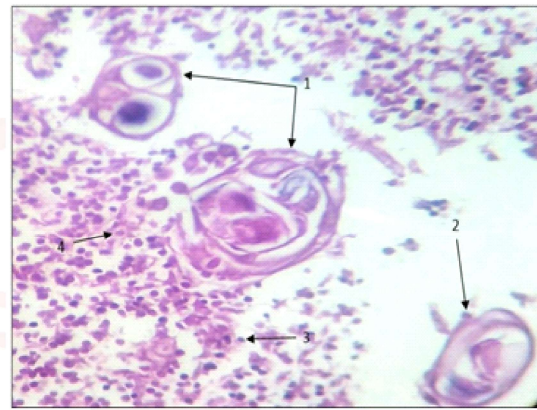


Fig. 12: 38 week 40x 1) Advanced Hassall Corpuscle, 2) Mature Hassall Corpuscle, 3) Lymphocyte, 4) Epithelial Cell.



of premature type and mature type were seen (Fig. 4).

The gland appears to be fully differentiated at this stage.

GROUP-2 (21-28 weeks): Connective tissue of capsule covering the gland became very much distinct at this stage. Septa (trabeculae) became more extensive at this stage. Connective tissue septa (trabeculae) also became thin and fine. Cortex and medulla became very much distinct at this stage. There was dense population of lymphocytes in the cortex and fewer in the medulla. Clear demarcation between cortex and medulla was seen (Fig. 5). Larger blood vessels were seen in the connective tissue septa. Also smaller blood vessels were seen at corticomedullary junction. The observed blood vessels were of larger size than that of previous group. Also observed blood vessels were more numerous & extensive. Epithelial cells were irregular in shape with many processes forming network.

Numbers of Hassall's corpuscle were more than that of previous stage. Various types of Hassall's corpuscle were seen such as Juvenile, pre-

mature, mature and Advanced. Advanced type of Hassall's corpuscle consists of varying degrees of deposition of materials at their center or periphery, whereas others HC with a distorted shape seemed to try and fuse with other nearby HC. (Raica et al) [3] (Fig. 6, 7)

GROUP-3 (29-38 weeks): The gland during this stage had an internal architecture seen in adult, with mature histological picture. Lobules of larger size were observed. The trabecular framework became more and more distinct at this stage. Corticomedullary junction was distinctly observed at this stage. Mature and larger blood vessels were seen at this stage. Blood vessels were increased in number with mature vascular framework (Fig. 8, 11). Numerous Hassall's corpuscles were present in the medulla. Various types such as Juvenile, Premature, Mature and Advanced were seen. Advanced type of Hassall's corpuscle were more numerous at this stage. They showed a graded series of increasing maturity (Fig. 9, 10, 12).

DISCUSSION

Lobulations: In the present study lobulation was present at 12th week, although lobulation still

continued at 12th week stage. Distinct lobulation present at the 18th week stage. Ghali et al [4] observed the lobulation at 10th week. Harr [5] reported the lobulation at 12th week. Ajita et al [1] found that formation of lobules started at 9th week and distinct lobules were seen at 12th week. Varga et al [6] reported noticeably wide interlobular septa at 14-16 week, Krishnamurthy JV et al [7] observed it at 16 week whereas present study observed at 14-18 week.

Cortex and Medulla: In the present study the differentiation of the cortex and the medulla was noticed during 12th week but was not much prominent and it became started to distinguish from 14th week stage onwards which was completed at 18th week.

Varga et al [6] was reported it at 13th week. At 14th week by Harr [5] and Lobach and Haynes. [8] Between 12th and 14th weeks by Von Gaudecker. [9] Ajita et al [1] reported that differentiation of cortex and medulla started at 9th week and it become more distinct at 12th to 14th week.

Blood Vessels: In the present study blood vessels were noticed at 12th week, Since the present study examined foetuses from 12th week onwards, it could not be ascertained when blood vessels starts to appear before 12th week. They became larger, mature and more numerous in second group onwards.

Ghali et al [4] reported that thymus was vascular at 11th week of gestation. Harr [5] and Hamilton and Mossman [10] reported that extrathymic blood vessels associated with connective tissue fibers and mesenchymal cells surrounding the thymus were present at 9th week. Williams et al [11] mentioned of the developing erythroblastic cell by 10th week old thymic tissue.

Epithelial Cells: As the present study carried out from 12th week onward only, the epithelial cells were seen from this week onwards. Since foetuses prior to 12th week were not examined in the present study, it could not be ascertained whether epithelial cells were present at the earlier stages.

Williams et al [11], Hamilton and Mossman [10] described the presence of epithelial cells from 8th week. Hayward [12] reported that the

epithelial component of the thymus was recognizable at 10th week.

Hassall's Corpuscles: In the present study the Hassall's corpuscle was first observed at 12th week of gestation. Hassall's Corpuscles increased in number and size during 18th to 24th week. These Hassall's corpuscles had variable sizes, ranging from very small to very large whereas smallest size was represented by early age foetuses. The shape of Hassall's corpuscles varied significantly. Various types like juvenile, immature, mature, advanced observed irrespective of gestational age, with advanced type more significantly in foetuses above 28 week of gestational age.

This polymorphic behavior of Hassall's Corpuscle observed in present study coincides with the findings of Asghar A. et al. [13].

Fawcett, et al. [14] was reported appearance of Hassall's Corpuscles as early as 8th week of gestation, From 9th week Gilhus et al [15], Ghali et al [4] was reported it at 11th week, At 12th week by Sawant [16], Ajita et al [1] reported the presence of Hassall's Corpuscles was observed from 15th week of gestation. Krishnamurthy JV et al [2] observed that Hassall's Corpuscles increased in number and size during 17th to 24th week.

Completion of Differentiation: In the present study, all significant structural changes occur in thymus within 18th week of gestation; these findings are in accordance with Sawant SP [16] who reported that differentiation was completed at 18th week. Ajita et al [1] mentioned that thymus appeared fully differentiated at 17th week.

CONCLUSION

The present study concludes that at 12th week, lobulation was incomplete. Distinct lobulation was seen from 18th week onwards. The cortico-medullary differentiation was started to distinguish from 14th and completed at 18th week. The 12th week foetus showed presence of immature, small blood vessels in the connective tissue of capsule & septa. In the IInd group onwards the blood vessels became larger, mature, and numerous. Epithelial cells were first observed at 12th week of gestation. They showed processes forming network.

The Hassall's corpuscle was first observed at 12th week of gestation. Hassall's Corpuscles increased in number and size during 18th to 24th week of gestation. Advanced types of Hassall's corpuscles were more significantly observed in fetuses from 28 week onwards. Polymorphic behavior was observed. All structural changes were occurred in thymus within 18 week of gestation.

Conflicts of Interests: None

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