

HYPERPLASIA OF THE THYMUS AND RELATED RESPIRATORY DIFFICULTIES*

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Introduction

The thymus is an unpaired organ located in the mediastinal cavity anterior to and above the heart. It consists of two symmetrical lobes, each enclosed in a capsule, from which trabeculae extend into the gland, dividing it into many lobules. Each of the lobules consists of a cortex and a medulla. The cortex is composed of dense lymphoid tissue containing many cells (thymocytes) closely packed together. The medulla contains Hassall's corpuscles.

In newborns the thymus is fairly large, extending from the base of the heart to the upper space of the thorax. Its weight varies from 11 to 17 grams in the normal newborn, with an average of 15 grams. It grows from birth to puberty, and thereafter atrophies. Lymphocytes and reticular cells give way to fat tissue, and the Hassall's corpuscles gradually disappear.

The functions of the thymus have not yet been accurately and completely described. There is some evidence that it helps to strengthen the bones and ossify the epiphyses through hormonal action. Although its growth parallels that of the endocrine glands, its structure is different from these. The effect of the thymus on calcium and phosphorus metabolism is quite clear. Its removal causes hypercalcemia, and implantation of thymus or injection of thymus extract causes hypocalcemia.

The thymus may play an important role in the formation of immune bodies. In animals whose thymus has been removed at birth, it has been observed that their ability to form antibodies against certain antigens in serum is decreased. In rats who have had thymectomy, immunity against dead influenza viruses, sheep erythrocytes, and H antigen of *Salmonella typhi* is reduced. Inefficiency in forming

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immunity after thymusectomy is the result of dysplasia of lymphoid tissues. A male guinea pig, whose thymus had been completely excised, developed a severe sickness characterized histologically by a scarcity of general lymph tissue. In rats whose thymus had been removed at birth, there was a decrease in microlymphocytes throughout the body. In myasthenia gravis there is hyperplasia in the thymus along with auto-immune abnormalities. Removal of the excess tissue in these cases brings about an apparent improvement in the condition of the patient. This is thought to be due to a secretion from the thymus which regulates acetylcholine-cholinesterase balance. These experiments have yielded significant information on the role of the thymus in creation and maturation of lymphocytes, and its role in filling in lymphoid tissue with cells during cell migration.

In many mesenchymal diseases there is hyperplasia of the thymus. Wolf and his colleagues, in a study of one family, found primary and acquired agammaglobulinemia, accompanied by mesenchymal tissue disorders (rheumatoid arthritis, polyarticular rheumatism, idiopathic thrombopenic purpura, and regional enteritis). In the same family, synthesis of immuno-globulin was also defective. An autopsy conducted on a member of this family who died of lupus, revealed thymomas. The evidence indicates that auto-immune phenomena in mesenchymal diseases is related to thymus disorder.

Diseases peculiar to the thymus itself are rare. The thymus is known to become enlarged under certain conditions i. e. Basedow's disease, Addison's disease, early castration, myasthenia gravis, acromegaly, and in some leukemic conditions. It will contract during chronic diseases, infections, poisoning, avitaminosis, hunger, and after treatment with x-rays. Primary and secondary tumors are infrequent. Lymphosarcoma, teratoma, lymphangioma, thymoma, and more often leukemia, lymphogranulomatosis, and metastases are encountered. Lymphosarcomas and thymomas are very sensitive to x-rays.

Normally, the thymus expands until the age of puberty, and contracts thereafter. If contraction does not occur, "thymus persistence" is diagnosed. Thymus hyperplasia is characterized by an enlarged organ, two to three times normal size, and weighing as much as 60 to 70 grams.

It has been suggested that there is a close functional relationship between the thymus and the suprarenal cortex system. It is claimed that thymus hyperplasia and excessive growth of lymph tissue are both

caused by hypofunction of the suprarenals. Rapid contraction of the enlarged thymus following eight to ten days of ACTH or suprarenal cortex steroid therapy supports this view. The thymus may enlarge again after drug therapy is terminated. The flow of glycocorticoids increases during periods of stress, and causes contraction of the thymus and the lymphatic tissues. In *status thymicus*, the thymus malfunction is thought to be caused by suprarenal insufficiency.

Case Reports

The two patients whose cases are reported here were seen at Zeynep Kamil during the past year.

Case 1. This 25 day old boy was admitted to the hospital with complaints of fever, cyanosis, apneic crises, and intense dyspnea for three days prior to admission. Examination verified these initial complaints and also revealed contraction in the jugulum, epigastrium, and the intercostal area. Stridor was apparent. Hyperplasia of the thymus could be seen in the x-ray (Figure 1).

After oxygen therapy and administration of antibiotics and cortisone for ten days, dyspnea and cyanosis disappeared. Contraction in the intercostal areas and in the epigastrium decreased, and stridor was heard only when the child cried or took food. An x-ray at this time showed that the shadow of the thymus had decreased in size (Figure 2). Clinical and radiologic examinations, two and three months later, showed no signs of hyperplasia and only slight stridor.

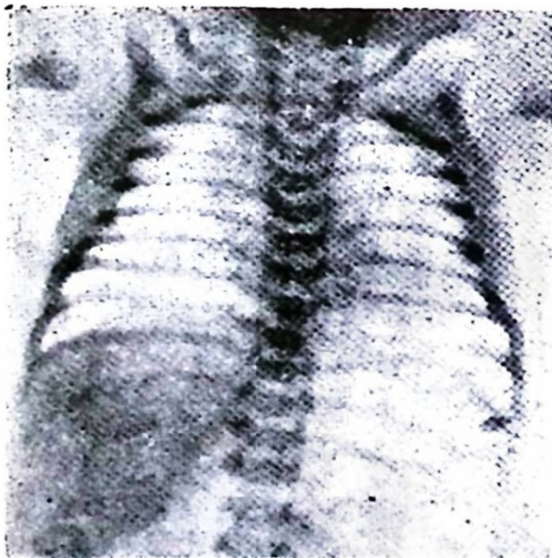


Figure 1.

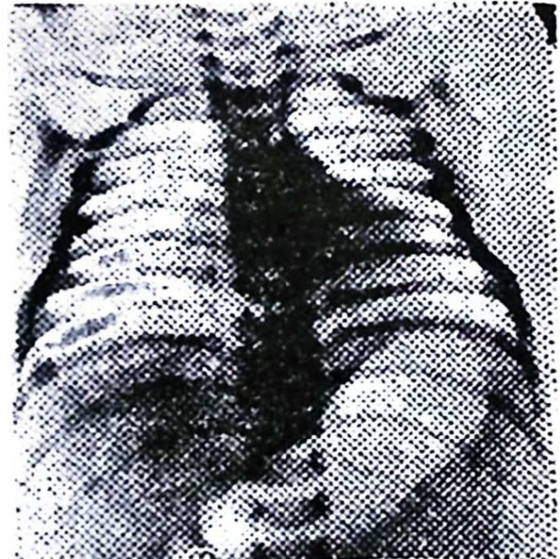


Figure 2.

Case 2. This five month old boy was admitted to the hospital with complaints of fever, coughing, and rales. Physical examination also revealed slight contraction in the jugulum, stridor, and rales in the lungs. Hyperplasia of the thymus could be seen in x-rays (Figure 3). Coughing and stridor disappeared after administration of cortisone and antibiotics for ten days. In the control x-ray, the shadow of the thymus was smaller (Figure 4).

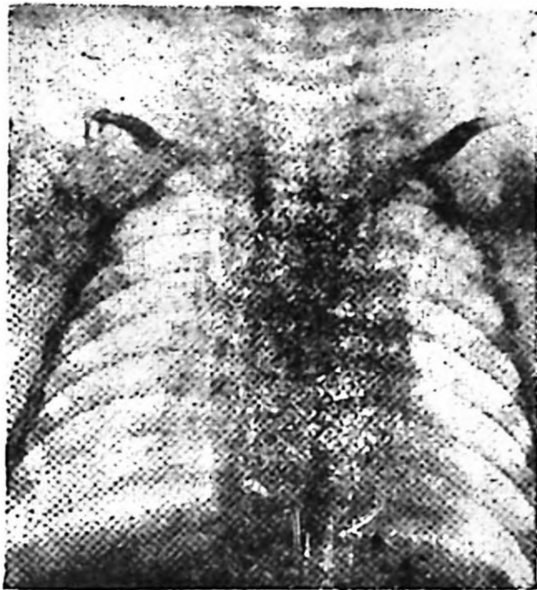


Figure 3.

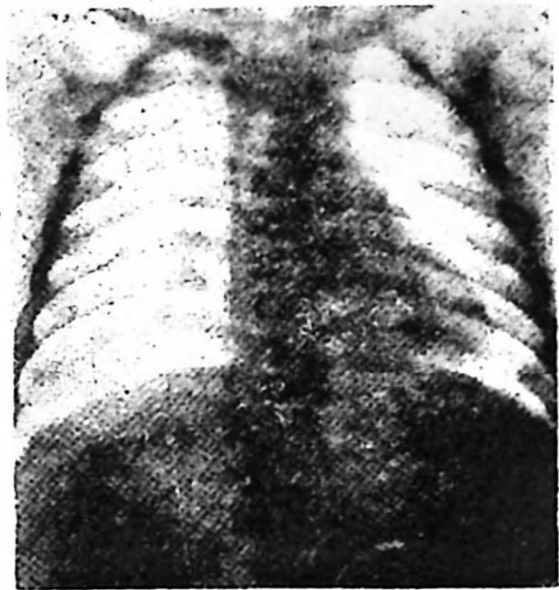


Figure 4.

Discussion

Immediately following birth and during the first year of life, hyperplastic thymus is frequently seen in radiologic examination, and does not necessarily indicate a pathologic condition. One or both lobes of the organ may be enlarged and resting on the heart, and can be clearly seen in lateral x-rays. Other conditions, such as venous stasis, enlarged paratracheal ganglions, struma protruding into the thorax, or mediastinal pleuritis, can also produce similar shadows in x-rays, and it is necessary to consider the patient's general condition, clinical test results, blood tests and detailed studies of the x-rays, before a definite diagnosis of pathological thymus hyperplasia can be made.

Thymus hyperplasia in children often causes serious respiratory difficulties, the most common of which is stridor. We saw this in both of our patients. Pfaundler, Husler and Flanzmann, among others, held that stridor was the result of pressure by the enlarged thymus on the trachea. Finkelstein, however, argues that thymus tissue, being softer than tracheal tissue, could not possibly cause constriction of the trachea. Fanconi reports cases in which the enlarged thymus contracted following treatment, without alleviation of stridor. Other authors suggest that hyperplasia of the thymus aggravates the conditions which cause stridor, thereby intensifying the respiratory difficulty. In our patients stridor decreased or disappeared following treatment of the enlarged thymus. Hövels has also reported a case of hyperplasia of the thymus accompanied by expiratory stridor, cyanosis, and

apneic crises in which all symptoms disappeared after ACTH therapy. He concluded therefore that an enlarged thymus could exert pressure on the trachea.

Conclusion

There seems to be no need for special treatment in cases of simple thymus hyperplasia diagnosed by x-ray. However, if the enlarged thymus is causing other difficulties (stridor, cyanosis, etc.) ACTH or cortisone should be given to alleviate these symptoms and to bring about contraction of the thymus. These clinical symptoms are often in evidence after the thymus itself has returned to normal size.

Summary

The author presents a review of current investigations related to the thymus and its functions. Two cases of thymus hyperplasia with respiratory difficulties are presented, and diagnosis and treatment are discussed.

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