Research article

Stages of the evolution of thymus atrophy in children in different cities of Kyrgyzstan

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(Received: December 2022 Revised: January 2023 Accepted: February 2023)

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ABSTRACT

Introduction and Aim: Thymus atrophy occurs in response to the stress of any etiology such as cold, burn, infection, trauma, pain, and psychogenic stress. The objective of the study is to evaluate the thymus gland in children aged 7–12 years from Kyrgyzstan.

Materials and Methods: The present study assessed the anatomy of the thymus gland on 35 cadavers of children aged 7–12 years from 2015 to 2020. Anatomical methods including preparation, weighing, and measurement, and histological methods including hematoxylin-eosin staining were performed.

Results: In children aged 7–12 years, it was found that in the thickness of the cerebral layer, there is the growth of thymic corpuscles, blood capillaries, and lymphatic slits. The level of cells in the cerebral layer is diverse, there are lymphocytes in large numbers, larger light epithelial and reticular cells, as well as macrophages. In the cortical zone, the cellular composition is mainly lymphoid cells, and mitosis was found in some of them.

Conclusion: In this study, comparatively, the cortical zone prevails over the cerebral one. At this age, the thymus begins to atrophy, as well as the growth of adipose tissue.

Keywords: Thymus gland; thymus atrophy; thymic corpuscles; perivascular spaces; intralobular septa.

INTRODUCTION

The study of the morphology of the central organs of the immune system is very limited. However, information regarding the study of the age aspects of the immune system organs, as well as the study of various climatic, geographical, and environmental conditions of Kyrgyzstan is rare (1, 2). Mining and animal husbandry are intensively developing in mountainous regions, they are used as recreation areas and climatic treatment, which naturally leads to increased migration processes of the population in these climatic-geographic areas. In Kyrgyzstan, on its relatively small territory (199 thousand km) and with a population of 6 million people, 49 tailings dumps and 80 rock dumps have been located for more than 60 years, where 70 million meters of uranium production waste have been buried (2).

After entering the biosphere there is a negative effect on its individual components, including plants, animals, and humans (3, 4, 5, 6). The thymus gland not only collects lymphocytes, but also produces thymic hormones that activate the immune system, improve skin regeneration, and promote rapid cell recovery (7, 8). Children with thymus gland pathology had a high mortality rate (6, 9–11). The main functions of the thymus gland (lymphatic, immunoregulatory, and endocrine) are carried out mainly due to the secretion of hormones by epithelial cells, mainly of polypeptide nature such as thymosin, and thymopoietin. At the same time, data on the age characteristics of the structural components of the human thymus are contradictory, which is primarily due to the different gradation of age groups by researchers and the study of this organ mainly in children of the second period of childhood. Thymus atrophy occurs in response to the stress of any etiology such as cold, burn, infection, trauma, pain, and psychogenic stress (12). There are various models of stress-induced atrophy of the thymus including physiological models (childbirth, lactation), models that cause an increase in the level of endogenous glucocorticoid hormones in the blood, which include immobilization, immersion of test animals in the water, or direct administration synthetic glucocorticoid hormones, and models associated with tissue damage (irradiation, infection of animals with various bacterial, infectious, viral and parasitic pathogens) (13). Clinical data is important in medicine for accurate treatment and preventive measures in persons with varying degrees of involution and pathology of the thymus (6, 8, 14). The objective of the study is to evaluate the thymus gland in children aged 7–12 years from Kyrgyzstan.

MATERIALS AND METHODS

The present study assessed the anatomy of the thymus gland on 35 cadavers of children aged 7–12 years from 2015 to 2020. Mostly the deaths of children were due to various reasons such as traumatic brain injury, drowning, car accidents, falling from a height, frostbite, etc. The causes of death and the main diseases were determined by the conclusion of a forensic medical examination of cadavers, histological and anatomical studies. Anatomical methods including preparation, weighing, and measurement, and histological methods including hematoxylin-eosin staining were performed. The material was taken within a day after death. The inclusion criteria include the age and duration of stay in that region. The exclusion criteria include people with immunodeficiency, hemorrhagic syndrome, tumors of the blood and lymphoid systems, and any chronic diseases that lead to hematopoietic changes.

Statistical processing of the obtained data was carried out using the IBM SPSS 22.0 statistical package. The study of the relationship between the indicators was carried out using correlation analysis with the calculation of the Spearman correlation coefficient. The differences were considered significant with a probability of $p<0.05$. Clinical characteristics were analyzed using descriptive statistics presented as mean ± standard deviation. The mean values between the two groups were compared using an independent t-test, and the analysis of the relationship between various factors and functional outcomes was carried out using binary logistic regression.

Clinical characteristics were analyzed in univariate analysis, and patient characteristics for multivariate analysis were any variables with a univariate analysis value of $P <0.1$. Confidentiality was maintained concerning the data collected and this study was approved by the I.K. Akhunbaev Kyrgyz State Medical Academy Bioethics Committee (Protocol No. 1 dated March 25, 2019).

RESULTS

After the autopsy of the cadaver, the thymus in children aged 7–12 years is small, pinkish gray in color, soft consistency, and its surface is lobed. On average, they range from 10–18 g.

In children, the longitudinal dimensions of the right lobe range from 5.0 ± 8.2 cm (on average – 6.6), and the left lobe – from 5.2 ± 5.9 cm (on average – 5.55). The transverse dimensions of the right lobe range from 1.8 ± 2.7 cm (on average – 2.2), and the left – from 1.6 ± 3.6 cm (on average – 2.6). The thickness of the right lobe ranges from 0.8–1.4 cm (on average – 1.1). The thickness of the left lobe is 0.6 ± 1.4 cm (average – 1.0). The upper border of the thymus gland is at the level of the sternum handle or 1.5 ± 2.6 (average – 4.1) cm above it. The border of the right lobe is usually slightly higher than the left. The lower border of the gland extends beyond the body and the handle of the sternum: on the right by 0.6 ± 2.1 cm (on average –1.3), on the left by 1.3 ± 1.2 cm (on average – 1.2).

When examined, the thymus gland consists of numerous lobules of different sizes, separated by layers of connective tissue. The thymus has a delicate thin connective tissue capsule consisting mainly of elastic fibers, among which mainly collagen fibers are detected.

The gland tissue under the capsule consists of longitudinal layers of connective tissue fibers, mainly collagen. From the common capsule, connective tissue partitions extend deep into the gland, dividing the parenchyma of the gland into many lobules of different sizes. In children, lobules of various shapes including polygons predominate over oval-shaped lobules. In children, the lobules of the gland consist of two zones: the light zones located in the center are identical in cellular composition, but in the dark, cortical zone, the cells are very densely located, their number is much greater than in the center of the brain zone. In the thickness of the cerebral layer, there are thymic corpuscles, blood capillaries, and lymphatic slits. The cellular composition of the cerebral layer is diverse, there are lymphocytes in large numbers, larger light epithelial and reticular cells, as well as macrophages. In the cortical zone, the cellular composition is monomorphic, mainly lymphoid elements, and mitoses are found in some of them. Comparatively, the cortical zone prevails over the cerebral one and the different age of thymic corpuscles in the brain layer is noticeable.

The number of macrophages and full-blooded blood vessels is adjacent to the intra-lobular septum, and the reticular bases of the lobules are expressed clearly. Intra-lobular septa in the deceased children from cities of Kyrgyzstan were represented graphically in Fig. 1.

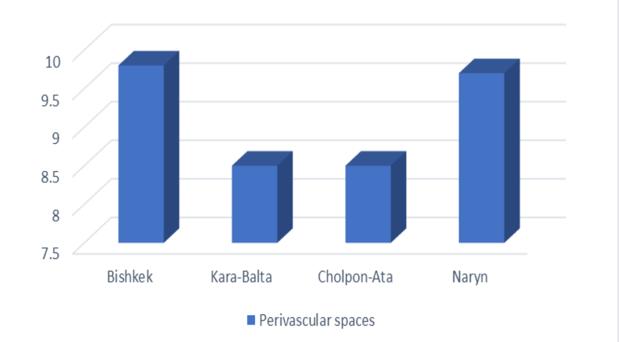

Fig. 1: Intra-lobular septa in the deceased children from cities of Kyrgyzstan.

In children aged 7-12 years, the cortical layer contains many lymphocytes located compactly. Lymphoblasts are usually found under the capsule (26%). Lymphoblasts are also found in the cerebral layer (39%), but significantly less than in the cortical layer (35%) and in the lobules there are elements of atrophy.

Levels of lymphoblasts in deceased children of Bishkek compared to the deceased children of Kara-Balty indicate 11.7% less, Cholpon-Ata by 5.7% less, and Naryn children by 10.7% more. It was established that the lymphocytes in deceased children of Bishkek compared to the Kara-Balta are 30.9% less, Cholpon-Ata is 39.4% less, and Naryn is 6.4% less. The average lymphocytes of the deceased children of Kara-Balta are 26.5% less compared to the Bishkek, the average lymphocytes in the Cholpon-Ata are 24.7% more, and in the Naryn has 29.0% lower average lymphocyte counts compared to deceased children in Bishkek.

The apoptotic bodies of Cholpon-Ata are 9.1% less in comparison with the deceased children of Bishkek, the level of apoptotic cells in Naryn are 4.0% less, and the dead children of Kara-Balta have 12.4% fewer apoptotic bodies. Levels of macrophages in the deceased children of Kara-Balty are compared to those of the Bishkek is 29.1% less, Cholpon-Ata is 2.8% less, and Naryn is 15.9% more deceased (Table 1).

According to the stereometric characteristics of the thymus in deceased children from 7–12 years, Perivascular spaces were noted that compared to the deceased children of Kara-Balta, 32.5% less compared to Bishkek, and Cholpon-Ata 23.5% less, and Naryn compared to Bishkek is 42.6% more (Table 1).

Table 1: Level of cells in a unit of the conditional area of the cortical substance of the thymus lobule in children aged 7–12 years

Cells	Bishkek	Kara-Balta	Cholpon-Ata	Naryn
	M± m			
Lymphoblasts	29.7 ± 1.8	26.2 ± 1.8	28.0 ± 1.8	32.9 ± 1.3
Medium lymphocytes	70.0 ± 1.1	514 ± 4.0	52.7 ± 2.6	49.7 ± 1.3
Small lymphocytes	299.6 ± 1.1	206.9 ± 16.4	181.5 ± 6.2	280.4 ± 8.7
Apoptotic bodies	69.3 ± 0.7	60.7 ± 2.5	62.7 ± 2.1	66.5 ± 1.2
Mitosis	31.2 ± 1.1	23.4 ± 0.7	24.6 ± 1.3	27.6 ± 1.0
Macrophages	6.9 ± 0.8	4.9 ± 0.7	6.7 ± 0.6	8.0 ± 0.6
Thymic corpuscles	9.3 ± 0.4	4.5 ± 0.7	6.7 ± 0.9	7.8 ± 0.5
Total number of cells	520.4 ± 6.7	375.8 ± 22.3	362.6 ± 12.7	472.9 ± 11.9
Stereometric characteristics of the thymus of children aged 7–12 years (M±m)				
Cortical substance	64.3 ± 5.6	57.0 ± 1.7	48.9 ± 1.0	70.6 ± 1.7
Brain matter	26.5 ± 1.9	22.4 ± 1.8	23.7 ± 2.0	27.1 ± 1.0
Perivascular spaces	8.9 ± 1.1	6.0 ± 0.9	6.8 ± 0.8	12.7 ± 0.6
Interlobular septa	9.8 ± 1.3	8.5 ± 1.3	8.5 ± 0.9	9.7 ± 0.4

The capsule and the interlobular partitions are significantly thickened, fibrous, thickened collagen fibers, mature flattened elongated fibrocytes and fibroblasts are clearly visible. Inside the lobules along the course of the vessels, there is also pronounced sclerosis, vasodilation, and thickening of their walls. The lobules consist of the cerebral and cortical layers, in many lobules the area of the cortical layer is noticeably wider than the area of the cerebral layer. The cortical layer consists of lymphoid cells due to the onset of autolytic phenomena; it was not possible to find mitoses. In the cerebral layer with the presence of lymphoid cells and lymphocytes, there is even a noticeable number of epithelioid cells, macrophages, and leukocytes. The number of thymic corpuscles is noticeably smaller, and in the thickness of the cerebral layer there are deposits of a mesh mass resembling fibrin without clear boundaries, where lobule atrophy and adipose tissue overgrowth were observed (Fig. 2).

Fig. 2: Hematoxylin and eosin staining demonstrated Lobule atrophy, adipose tissue overgrowth with epithelial and reticular cells; Single macrophages; formation of thymic corpuscles (x40).

DISCUSSION

Thus, in children aged 7–12 years old, the thymus gland consists of numerous lobules of different sizes, separated by layers of connective tissue. The thymus has a delicate thin connective tissue capsule consisting mainly of elastic fibers, mainly collagen fibers are detected among the fibers. In the cortical zone, the cells are mainly lymphoid elements, and mitosis is found in some of them. According to the level of cells, the indicators of the deceased in Bishkek – medium, small lymphocytes, apoptotic, mitosis increased, and the deceased in Kara-Balta indicators: lymphoblasts, apoptotic, mitoses, and macrophages decreased.

When characterizing the morphological changes in the thymus during atrophy, it should also be noted that thymic atrophy is accompanied by the disappearance of mitotic structures (15), a decrease in the number of double-positive thymocytes, and an increase in the number of apoptotic bodies and macrophages in the cortical part of the thymus (15–17). Macrophages phagocytize apoptotic bodies that are brightly stained with hematoxylin, which gives the histological structure of the thymus a special appearance – a starry sky pattern (16, 18). However, the elimination of apoptotic bodies and thymic epithelial cells through their scavenger receptors. In the process of atrophy, an increase in the number of neutrophils (19), mast cells, eosinophils, and plasma cells in the thymus is also observed, as well as the transmigration of lymphocytes through the vascular endothelium (20). Often there are indications of inversion of the thymus layers, in which a higher cell density is detected in the medulla rather than in the cortex (16), which may be the final stage of thymus atrophy, after which the restoration of the thymus structure begins.

CONCLUSION

In the results of the deceased in Cholpon-Ata, lymphocytes and cortical matter decreased, and in Naryn, the cells found that the levels of lymphoblasts, and macrophages increased compared to other regions. Comparatively, the cortical zone prevails over the cerebral one. At this age, the thymus begins to atrophy, as well as the growth of adipose tissue.

CONFLICT OF INTEREST

None.

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