Investigation of Human Fetal Thymus Blood Supply

M Terzic,
M Jevremovic,
B Stimec,
N Arsenovic,
V Zizic

University Clinical Center,
Clinic of Gynaecology and Obstetrics,
Belgrade, Yugoslavia

Abstract : *The fetus in utero is in a sterile environment, protected from contact with most microorganisms. The thymus plays a crucial role in the maturation of T-lymphocytes, as the generation of immunocompetent T-cells requires an intrathymic differentiation of precursor cells. Thymic pathological processes are sometimes healed only by its extirpation, so knowledge of thymus vascularisation is of great importance. The aim of this study was to investigate anatomic variations of human fetal and newborn's thymus vascularisation. The research comprised 20 newborns who died due to intracranial hemorrhage, 3-20 days after birth. Contrast (gelatin ink) injected into the abdominal aorta filled thymic arteries retrogradely. Lateral branches of the inferior thyroid artery were found to provide arterial blood to the thymus cervical part in 11 cases, while in the other nine, branches of internal thoracic arteries were found. After investigating the thoracic part of the thymus gland we found that the internal thoracic artery supplied ipsilateral lobes in 16 newborn, while in one case, the left one was found to have branches for both lobes. The thoracic part of the thymus had arterial vascularisation from pericardial vessels in two cases while in one the presence of an odd interlobal artery originating from brachiocephalic trunk was observed. Knowledge of anatomic variations of thymus arterial vascularisation is of great importance in invasive diagnostic procedures as well as in surgical intervention. (Thai J Obstet Gynaecol 1991;3: 7-11.)*

Key words: human thymus, arterial vascularisation, anatomy

At about the sixth week of gestation, the thymus is generated from the epithelium of the third and fourth pharyngeal pouches[1]. The thymus gland is the only lymphatic organ in which reticular cells are of endodermal origin. It is sited retrosternally, in the superior mediastinum. Lymphatic tissue in the thymus gland is grouped in two lateral lobes, with connective or glandular tissue between them. It is most active during fetal development and in early postnatal life. The thymus increases in size rapidly in utero, more gradually until puberty and then involutes during adult life. Previously de-

scribed as an endocrine organ, the thymus is now stated to play an important role in T-lymphocyte maturation processes. Contemporary investigations regard the thymus as part of the hypothalamus-pituitary-thymus-gonadal axis and as a participant in the regulation and modulation of neuroendocrine functions of human beings throughout their whole life[2]. Besides being phy - siological, the thymus gland can also undergo accidental involution (due to some pregnancy-associated pathological processes, malnutrition, infection or intoxication). It is also suggested that the thymus can play a certain role in the pathogenesis of autoimmune diseases. All the thymic functions and the pathological conditions mentioned are in close relation to its vascularisation, innervation and lymphatic drainage. The thymic vascular compartment is recognized for uptaking monoclonal antibodies[3]. Important variations of thymus arterial blood supply exist, caused by its mobility during development and various positions in the superior mediastinum. This includes various arterial origins of thymic arteries, their ipsi- and bilateral lobar supply as well as intrathymic vascular pattern[4]. The aim of this study was to investigate anatomic variations of thymic arterial vascularisation that are of great importance for invasive diagnostic procedures as well as for thoracic surgery.

Materials and Methods

The investigation was performed in the Clinic of Gynaecology and Obstetrics, Belgrade University Clinical Center, on 20 fetuses or newborns (11 males and 9 females). The newborns had died due to intracranial hemorrhage 3-20 days after birth. The gelatin-ink was injected through the abdominal aorta retrogradely, with subsequent filling of thymic arteries (Figure 1). The sternal and costal cartilages were carefully dissected away, preserving the internal thoracic arteries and their thymic branches. The thymus gland was freed of the capsule and its arterial vascular pattern was examined.

Fig. 1 Fetal specimen with injected internal thoracic overlying the thymus gland.

Results

Topographically the thymus is divided by the suprasternal notch into the cervical and thoracic parts. Investigating the origin of the arterial thymic vessels for the cervical part we found it to be the inferior thyroid artery in

11 cases and the internal thoracic artery in 9 cases (Figure 2), with ipsilateral arterial supply from both origins. The thoracic part of the thymus received branches mainly from the internal thoracic artery (17 cases) (Figure 3), the pericardial vessels (3 cases) and from the brachiocephalic trunk (1 case). The bilateral arterial blood supply was stated in only two cases, one coming from the left internal thoracic artery, and the other from the odd interlobal artery of brachiocephalic trunk origin.

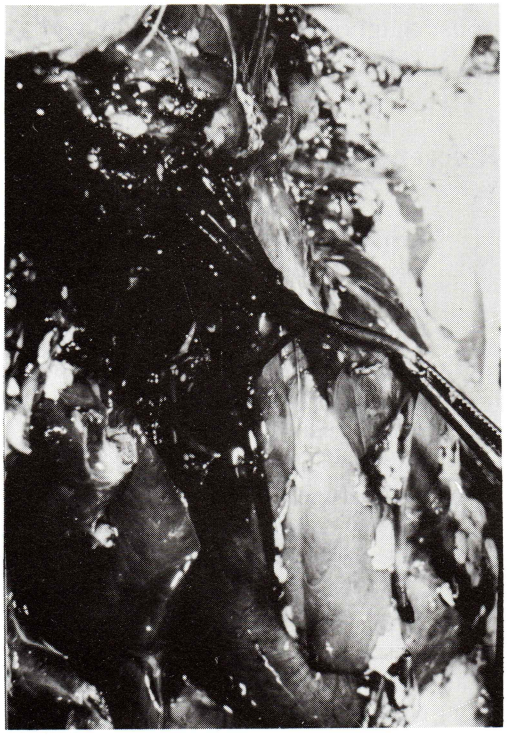

Fig. 2 Thymic artery emerging from the internal thoracic artery and entering the superior pole of thymic lobe.

Fig. 3 Odd interlobal artery giving few branches for thymic lobe.

Discussion

The study of thymic arteries vascular pattern gives reliable data of its functional capacity and physiological status. Thymic vascularisation undergoes consistent changes through development and in certain pathological conditions, such as pneumonia[5]. The vascular pattern in the involuted thymus becomes irregular and the vessels are tortuous[6]. Because of that, investigations of human fetal thymus give more precise information on their arterial blood supply in comparison to the adult thymus.

The thymic arterial circulation

has been proved to be very vulnerable and sensitive to exsanguination. It can be reduced up to 52% in status of hemorrhagic shock[7].

Thymic arteries mainly originate from the internal thoracic artery, less frequently from the inferior and rarely from the superior thyroid artery. Exceptional cases with subclavian, carotid or brachiocephalic origin have been described[1].

One among the earliest descriptions of the thymus blood supply was given by Testut[8]. In his profound studies, the atypical origin of the odd thymic artery from the brachiocephalic trunk was noted supplying both lobes, which we have also found.

Yamasaki[9] studied the thymic vessels in adult cadavers and fetuses. He described the disappearance of thymic arteries in earlier stages of deveolpment, being replaced by the superior thyroid artery. He named this branch, A. thymica suprema. No such case was found in our material. The same author found that the arterial systems of the thyroid and the thymus gland are largely dependent on the existence of the abnormalities of the constant arteries and of the anomalous arteries. These anatomical variations showed higher frequencies in fetuses than in adults. In his subsequent study, he found that the middle thymothyroid artery showed the highest frequency, compared to the superior and middle thymic artery. The supreme thymic and the thyroid ima artery arising from the internal thoracic artery were found to be extremely rare[10].

In our previous investigation we found that the thymus cervical part was supplied by the inferior thyroid artery almost three times more frequently compared to the internal thoracic artery[11]. Our reinvestigations showed a nearly equal participation of those two origins in providing arterial blood to the cervical thymus.

Kato[6] described thymic arteries in mice which branched into arterioles as they entered the thymic parenchyma. In our human material, also, no extrathymic branching was found.

In conclusion, one can say that significant variations of human fetal thymus arterial system exist and that its knowledge is necessary for thymus pathophysiological processes investigations, diagnostic procedures, as well as for surgical intervention.

References

1. Kendall MD. Anatomical and physiological factors influencing the thymic microenvironment. In: Kendall MD, Ritter MA,eds. Thymus update. The microenvironment of the human thymus. Harwood:Harwood Academic Publlishers, 1988, 27-65.
2. Jevremović M, Kartaljević G, Terzić M. Neuroendocrinological activity of human fetal thymus. In: Thymus peptide und proteine-biologische eigenschaften und klinische aspekte, Theymus Medizinischer Fachbuchverlag 1991 (in press).
3. Stet RJ, Wagenaar-Hillbers JP, Nieuwenhuis P. Thymus localization of monoclonal antibodies circumventing the blood-thymus barrier. Scan J Immunol 1987; 25:441-6.
4. Kotani M, Ohmori J, Miyakawa K, et

al. Increased vascular permeability of the automimmune New Zealand mouse. J Anat 1988; 161:83-93.

5. Shubinets MV.Restructuring of the venous bed and tissue elements of the thymus in nursing infants with pneumonia. Arkh Patol 1987;49:13-9.
6. Kato S, Schoefl GI. Microvasculature of normal and involuted mouse thymus. Light and electron microscopic study. Acta Anat 1989;135:1-11.
7. Perbeck L, Lund F, Thulin L. Intrathoracic microvascular circulation in hemorrhagically shocked rats. Studies by fluorescence tehniques. Clin Physiol 1989;9:567-79.
8. Testut-Latarjet, Traite d'anatomie humaine. G. Doin et Cie, Paris 1928.
9. Yamasaki M. On the A. thymica suprema, a provisionally named branch of the superior thyroid artery in the human. Anat Anz 1989;168:329-35.
10. Yamasaki M, Studies on the thyroid and thymic arteries of Japanese adults and fetuses. Anat Anz 1989;169:213-21.
11. Terzić M, Jevremović M, Štimec B, et al. Investigation of human fetal thymus blood supply. Verh Anat Ges (Anat Anz) Jena:Gustav Fischer Verlag, 1991: 312.

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