FETAL THYMUS - REVIEW

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Abstract

This is review of the literature regarding fetal thymus development, its role in immune system, research regarding prenatal thymus evaluation in fetal congenital heart defects, abnormal karyotypes, intrauterine growth restriction. The methods of fetal type measurements both in singelton and multiple pregnancies are discussed and presented.

Key words: *role of the thymus, thymus measurements*

INTRODUCTION

The thymus (latin:. glandula thymus) is a specialized organ of the immune system located in the anterior mediastinum, behind the sternum which is the primary and central lymphatic organ that controls the development of peripheral (secondary) lymphoid tissues in the prenatal and postnatal period. Within the thymus, T-cells, critical to the adaptive immune system, mature.

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Each T cell attacks a foreign substance which it identifies with its T cell receptor. T cells have receptors which are generated by randomly shuffling gene segments. Each T cell attacks a different antigen. T cells that attack the body's own proteins are eliminated in the thymus. Thymic epithelial cells express major proteins from elsewhere in the body. First, T cells undergo "Positive Selection" whereby the cell comes in contact with the Major histocompatibility complex self-MHC expressed by thymic epithelial cells; those with no interaction are destroyed. Secondly, the T cell undergoes "Negative Selection" by interacting with thymic dendritic cells whereby T cells with high affinity interaction are eliminated through apoptosis (to avoid autoimmunity), and those with intermediate affinity survive.

The thymus is composed of two identical lobes and is located anatomically in the anterior superior "Mediastinum"

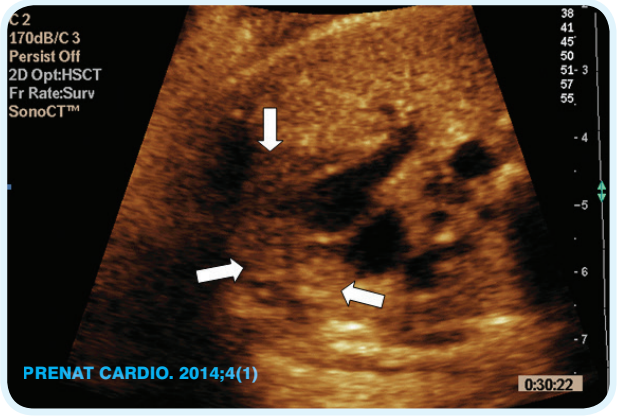

Photo 1. Normal 3 vessels view in fetal mediastinum and thymus

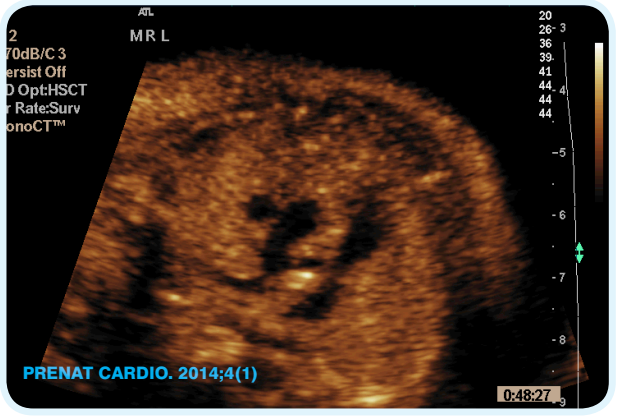

Photo 2. Right aortic arch and normal thymus

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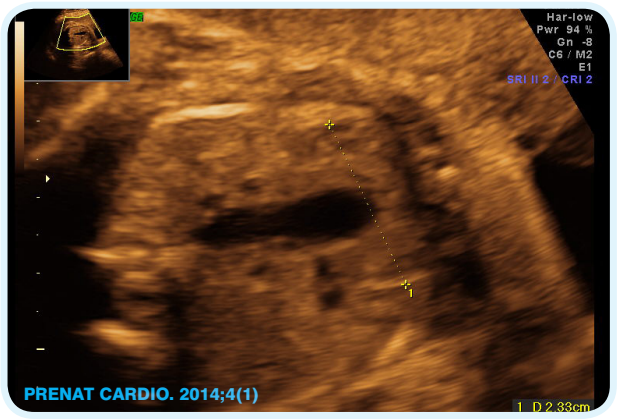

Photo 3. Abnormal mediastinum due to congenital heart defect and thymus measurement

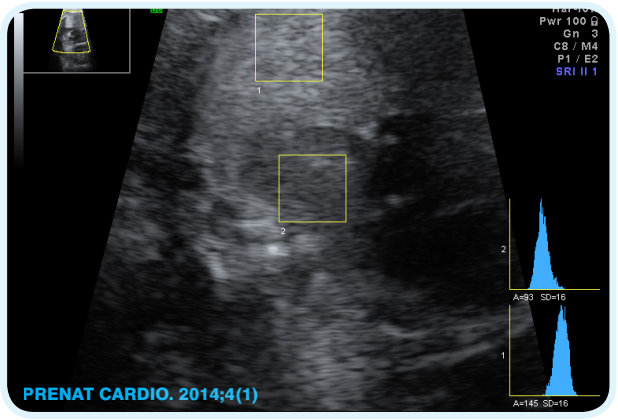

Photo 4. Comparison of thymus echogenicity and lung echogenicity by histogram

in front of the heart and behind the "Sternum".

Histologically, each lobe of the thymus can be divided into a central and peripheral cortex which is surrounded by an outer capsule. The cortex and medulla play different roles in the development of T-cells. Cells in the thymus can be divided into thymic stromal cells and cells of hematopoietic origin (derived from bone marrow resident). Developing T-cells are referred to as thymocytes and are of hematopoietic origin. Stromal cells include thymic cortical epithelial cells, thymic medullary epithelial cells, and dendritic cells.

The thymus provides an inductive environment for the development of T-lymphocytes from hematopoietic progenitor cells. In addition, thymic stromal cells allow for the selection of a functional and self-tolerant T-cell repertoire. Therefore, one of the most important roles of the thymus is the induction of central tolerance.

The thymus is largest and most active during the neonatal and pre-adolescent periods. By the early teens, the thymus begins to atrophy and thymic stroma is mostly replaced by adipose (fat) tissue. Nevertheless, residual T lymphopoiesis continues throughout adult life.

WHY IT IS IMPORTANT TO EVALUATE THE FETAL THYMUS

One of the first publications on the identification of the thymus in newborns with heart defects was released in 1995 by Yeager & Sanders [1].

Visualization of the fetal thymus by ultrasound was reported for the first time about 25 years ago [2], but significant interest in the fetal thymus increased after the year 2000 with the advent of high-resolution ultrasound, which enabled more precise demarcation of the shape and border of the thymus [3, 4, 5, 6].

The thymus is an essential part of the adaptive immune system both prenatally and postnatally. It develops from the third pharyngeal pouch, which gives rise to endodermal-derived thymus cortical epithelium and the third pharyngeal cleft that is thought to give rise to ectodermal-derived medullary thymus epithelium. The fetal thymus grows rapidly in utero reaching its greatest relative size at the time of birth.

During the past decade there has been a growing interest in assessing fetal thymic size using high-resolution ultrasound in examining fetuses with impaired thymic growth. A hypoplastic fetal thymus is typically found in association with 22q11 deletion (del.22q11), [4, 5, 6 7, 8,9] in fetuses with intrauterine growth restriction (IUGR), [10,11] or prematurity, as well as trisomies 21, 18 and 13 [12, 13].

When fetal CHDs are present, especially conotruncal anomalies, assessment of fetal TV may be helpful. Fetal TV may become helpful in deciding when to test for the 22q11 microdeletion, in addition to a standard fetal karyotype [14].

Fetal thymus was evaluated both in singelton and in twin fetuses [15]. Their ndings also suggest that the perimeter and transverse diameters of the fetal thymus in uncomplicated singleton and twin pregnancies are similar and are not affected by twin order or chorionicity.

The fetal thymus size does not affect the sex of the fetus [16]

Decreased thymus size was noticed in full-term newborn infants of smoking mothers [17].

Recent research suggests that many adult chronic, degenerative diseases are at least in part the result of

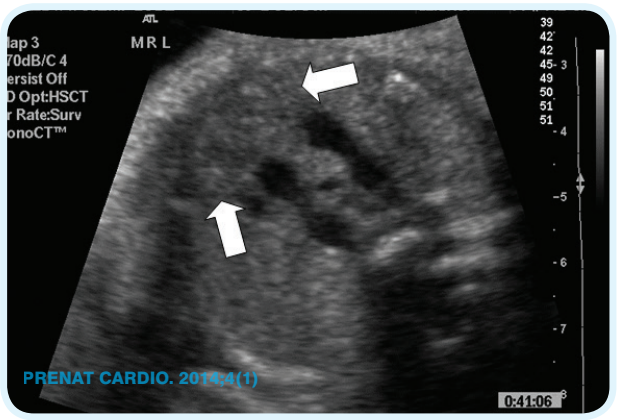

Photo 5. Right aortic arch and abnormal thymus

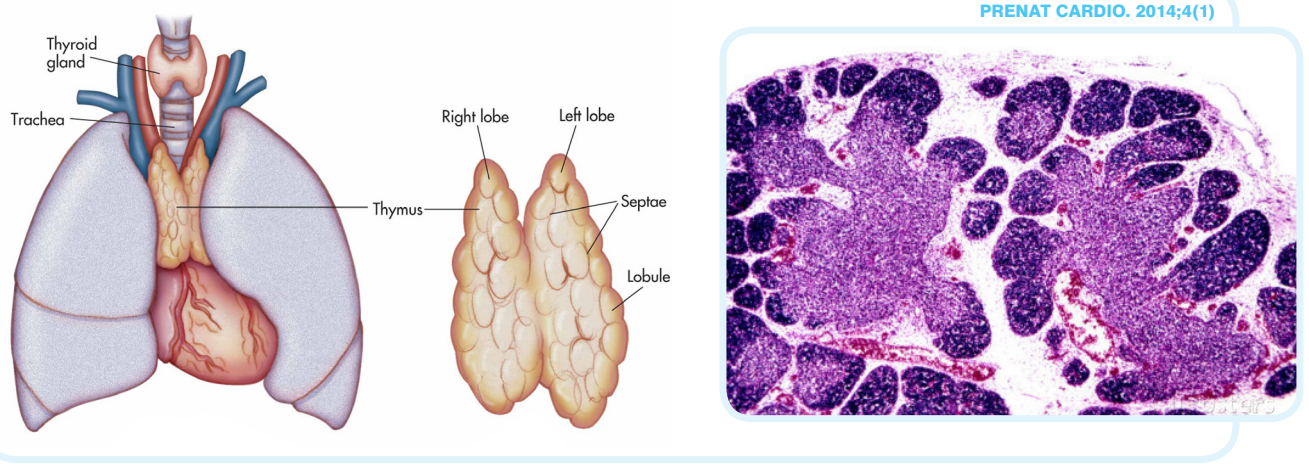

Figure 1. Thymus

fetal and early infant programming of cardiovascular and endocrine systems, and evidence is mounting for an association between low birthweight and adult hypertension, coronary heart disease and diabetes. However, the implications of early enviroments for the development and function of the immune system in adulthood are unknown.

It was found recently that prenatal undernutrition is associated with reduced antibody response to typhoid vaccination in adolescents from the Philippines, whereas postnatal diarrheal morbidity and rapid weight gain are positively associated with immunocompetence [18] .

MEASUREMENTS OF THE THYMUS:

The thymus is identi ed in the three vessels and trachea view, between the great vessels posteriorly and the posterior chest wall anteriorly. The intrathoracic mediastinal diameter is measured, along a line traced between the anterior edge of the thoracic vertebral body posteriorly and the internal edge of the sternum anteriorly. Along this line the anteroposterior diameter of the thymus is measured, between the border of the transverse aortic arch posteriorly and the posterior chest wall anteriorly.

Several studies have reported the reference ranges of different parameters representing thymic size, such as the perimeter, transverse diameter, three-dimensional thymic volume and TT-ratio or volume contrast imaging

In normal fetuses, the TT-ratio did not vary with gestational age between 15 weeks and term, having a mean ± SD value of 0.4417±0.043 (95% CI, 0.357–0.526).

At 19 weeks of gestation, the average transverse diameter was 12 mm, at 33 weeks the diameter in mm was equal to the number of gestational weeks (i.e. 33 mm) and at term it was slightly greater than the number of gestational weeks. This growth pattern is similar to those of other fetal organs, such as liver, kidney, thyroid colon and rectum. The average transverse thymic diameter in mm was similar to the AC in cm, especially in the second trimester, which may be very useful information in day-to-day fetal sonography and echocardiography [19] . Results from analysis of Gamez [15] suggest that fetal thymic measurements between 19 and 38 weeks' of gestation can be obtained in almost 96% of pregnancies. The failure rate to obtain thymic measurements was 12.5% in twins and 2.8% in singleton pregnancies, with failure more likely to occur towards the end of pregnancy.

According to Achiron the thymus could not be visualized in only a few cases, due to maternal obesity or fetal position, so an accurate sonographic evaluation was obtained in over 99% of cases, interobserver variability was 3.1% and reproducibility of 98%[3] .

There are also publications about new methods of thymus assessment: by MRI [20] and using four-dimensional spatiotemporal image correlation volumes [21] , or by 3 dimensional ultrasound [22]. However simple methods from 2D are still used [23,24].

It might be important to evaluate thymus both in singleton as well as in twin pregnancies. According to Copel [14] and Gomez[15] transverse diameter of thymus was similar in normal singleton and twin fetuses throughout the pregnancy. Therefore, when assessing the size of the fetal thymus in twins, the normative data from normal singleton fetuses can be used reliably.

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