Ageing and its Effect on the Functional Capacity of the Thymus

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Background: Thymus gland is the only primary lymphoid organ in mammals, the first organ to become lymphoid and influences the development of other lymphoid organs in the body. It develops from the 3rd pharyngeal pouch in 5th week of intra uterine life and is located in the anterior and superior mediastinum of the thorax. Survival of an organism is influenced by an adequate immune system, and the thymus is a dependable lymphoid organ responsible for cell mediated immunity via T-cell training and maturation. It also produces hormones that play a role in immune mediation. However, the gland is said to increase in size from birth onwards but undergo involution after puberty and may disappear by middle age as reported in other parts of the world. Hence the need to establish what happens in Ugandans, with an aim to determine the functional capacity of the gland as one grows or if T-cell production does continue. The objective of this study was to determine the structural changes and functional ability of the thymus gland with age among Ugandans.

Methods: This was a descriptive cross-sectional study. The study was carried out at Makerere University and the associated Mulago teaching hospital. Autopsy cases at Mulago hospital and Kampala city mortuaries were used for the study.

Results: A total of 41 cases were dissected comprising of 71% male and 29% female specimens. Of them, 34% were pre-puberty and 66% were post- pubertal individuals. The age range was six months to seventy years with a mean age of 22.3, median 34.75 and mode 25. Seventy five percent of all cases were 30years and below, only 5% were more than 45years. It should be noted that only The thymus tissue was found in 39 cases and absent in two aged 40 and 43 years respectively.

Conclusions/Recommendation: The relative size of the cortex and proportion of lymphoblasts decreased with age while the medulla and lymphocytes increased. The fat content of the gland increased with age. The study showed a positive correlation of weight of the glands with age from birth to puberty, later the correlation becomes negative. There is a decrease in the activity of the gland as shown by the reduced ratio of lymphoblasts to lymphocytes.

Introduction

Thymus gland is the only primary lymphoid organ in mammals, 1st organ to become lymphoid and influences the development of other lymphoid organs in the body. It develops from the 3rd pharyngeal pouch in 5th week of intra uterine life and is located in the anterior and superior mediastinum of the thorax[1-5]. Survival of an organism is influenced by an adequate immune system, and the thymus is a dependable lymphoid organ responsible for cell mediated immunity via T-cell training and maturation[5-8]. It also produces hormones that play a role in immune mediation[2,9]. However, the gland is said to increase in size from birth onwards but undergo involution after puberty and may disappear by middle age as reported in other parts of the world[10-16]. Hence the need to establish what happens in Ugandans, with an aim to determine the functional capacity of the gland as one grows or if T-cell production does continue. The aim of this study was to determine the structural changes and functional ability of the thymus gland with age among Ugandans.

Methods

This was a descriptive cross-sectional study. The study was carried out at Makerere

University and the associated Mulago teaching hospital. The autopsy cases at Mulago hospital and Kampala city mortuaries were studied. Forty one autopsy cases aged six months to seventy years who had died of acute illnesses or accidental causes. All autopsies were done within 48 hours of death to minimize the effect of death related tissue changes. The glands where dissected, weighed and dimensions measured and then fixed in 10% formalin. The fixed specimens were later sectioned and prepared for microscopic examination; H&E and immunostaining which contain antibodies to T and B lymphocytes were employed.

Ethical review and approval of the study was sought from the faculty of medicine research and ethics committee which conducts reviews on behalf of the Uganda National Council for Science and technology. Consent to dissect the gland was granted by the next of kin of the deceased persons after adequate information on the objective.

Results

A total of forty one cases were dissected comprising 71% males and 29% females. There were 34% pre-puberty individuals as puberty was standardized to 15years while 66% were above 15 years. The age range was six months to seventy years with a mean age of 22.3, median 34.75 and mode 25.The majority (75%) of all cases were 30years and below, only 5% were more than 45years. The thymus was identified in 39 cases (95%), The remaining two cases aged 40 and 43 respectively had no demonstrable thymus tissue.

Table 1. Age distribution

Age range	Number	%
0-15	14	34
16-30	17	41
31-45	8	20
46 and above	2	5
Total	**41**	**100**

Table 2. Association of Age with Median Weight

Age range	Number	Median Wt (Gms)	P-value
0-15	14	19.6	
16-30	17	15.2	0.017
31-45	6	9.7	
46 +	2	2.8	
Total	39		

Table 3. Association of Age with Weight with Median age.

Weight	Number	Median age
0.4-10	11	35.0
11-20	16	20.0
21-30	8	16.0
>30	4	8.5
Total	**39**	

Table 4. Relationship between age and histology

Histology	No	Median age	P-value
Cortex larger	13	5.0	
Cortex=medulla	9	20.2	0.003
Medulla larger	17	28.0	
Total	39		
No fat	4	3.0	
Small areas of fat	20	13.5	0.001
Large areas of fat	2	34.0	
Mainly fat	13	30.0	
Total	**39**		

The weight of the gland increased with age up about 15 years of age but later diseased as one aged. Ninety three percent (93%) of the glands in children weighed 14.8gms and above with a mean weight of 22.593gms (Tables 1,2). The mean weight of the post-puberty groups was 14.943gms.

Table 4 shows the histological features of the thymus.

Discussion

The findings showed an increase in weight of the thymus glands from birth to about puberty and a progressive decrease in weight of the glands afterwards. However, even at an advanced age (70 years), there was recognizable thymus tissue capable of continuing the functions of the gland. This is an indicator that even in advanced age, the gland persists although it was very small in size and showed minimal activity as far as lymphocyte training is concerned. On the relative weight of the glands with age, it was noted that glands of young cases were mainly covered by the cortex which was a densely compacted concentration of immature lymphocytes or lymphoblasts whereas those of older cases were mainly composed of the medulla which had a loose concentration of lymphocytes. As the individual grew the percentage of the cortex reduced and this was probably responsible for the weight reduction of the gland with age. The result of histology of the glands also revealed that glands with a cortex larger than medulla had a median weight of 20.0gms, while glands where medulla was larger than cortex had a median weight of 11.0gms.

With age, the fat content of the glands increased although fat infiltration of the thymus started early before puberty with a median age for glands without fat being 3 years while the median age for glands with small areas of fat was 13.5 years. The available literature does not usually report this occurrence. The higher the fat content, the lighter the gland because fat is less dense than gland tissue.

The largest gland as per weight was recorded at an average age of 8.5 years, where the average weight of the gland was about 33 grammes while at 16 years, the average weight was 25 grammes. At 20 years the weight was 15 grammes while at 35 years, the weight was about 10 grammes and at 50 years, the average weight of the thymus was 5 grammes. Since the cortex contains mainly immature T-cells (lymphoblasts), which mature to become T-lymphocytes (thymocytes) that migrate to the medulla, this implies that glands of older people which have more medulla than cortex are less active in training but have more immunocompetent T-lymphocytes. Hence fewer lymphoblasts in the remaining cortex available for training but there are more mature lymphocytes available for immunological activity. This also means that adult thymuses have already trained T-lymphocytes in their pools and thus may remain relatively dormant. This was supported by the fact that even the gland of a seventy year old showed active lymphocytes as evidenced by Haematoxin and Eosin (H&E) and the Immunostaining histological techniques.

The histological staining of thymic tissue using H & E showed that the cortex was densely stained whereas the medulla was less densely stained. This was due to a high concentration of lymphoblasts in the cortex. Hence the adult thymus glands had a smaller concentration of lymphoblasts and more T-lymphocytes may have less training activity but more immunological competence. The initial increase in fat content from no fat to small areas of fat was accompanied by an increase in the weight of the gland. This was due to the fact that absolute gain in weight of the gland occurred as one grew from birth up to puberty caused by increased size and activity of the cortex for training of lymphocytes. However, after puberty, as the amount of fat increases in a gland that is less active and hence formed mainly of medulla, the glandular weight decreases.

Most (89.7%) of the glands including that of a one year old had recognizable fat tissue which implies that fat infiltration starts way long before puberty, something not usually highlighted in the literature. The fat cells seemed to replace the thymocytes in the medulla, but since the relative density of fat is lower than that of other cells, the weight of the gland would decrease following fat infiltration especially in a relatively dormant gland. It should be noted that at the age of

30 years, the gland was mainly filled with fat cells a trend similar to what is reported elsewhere. The glands were relatively grey in the young, as one grew, the colour became brownish grey before turning brown. However, with advancing age, the gland turned yellow as the amount of fat increased. The grey colour signified the predominantly lymphoblast filled cortex. Out of the 41 cases studied, two cases (4.9%) had no thymus glands at autopsy and their ages were 40 and 43 years. Their mediastina was filled with fat just like it occurs in any body. Failure to get the thymus gland could have been due to fat infiltration, congenital absence of the gland or an anatomical variation with gland tissue being located in an ectopic site. (2,3)It should be noted that these cases had no signs of immune suppression or opportunistic infections as would be expected in individuals with congenital absence of the gland.

Conclusions/Recommendations

The study showed a positive correlation of weight of the glands with age from birth to puberty, later the correlation becomes negative. There is a decrease in the activity of the gland as shown by the reduced ratio of lymphoblasts to lymphocytes.Thymus gland was present in all age groups although weight increased during childhood but later decreased with age post puberty. The concentration of lymphocytes decreased with age but even at 70 years, there is still some activity in the gland as evidenced by the histological examinations. 89.7% of the glands including that of a one year old had recognizable fat tissue which implies that fat infiltration starts way long before puberty.

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