Original Research Article

Age changes and time of appearance of oxyphil cells its relation to C cells

Indira CK[1*], Santos Joseph[2]

[1]Associate Professor of Anatomy, GMC Konni, Kerala, India
[2]Associate Professor of Anatomy, GMC Ernakulam, Kerala, India

Received: 25-08-2021 / Revised: 14-09-2021 / Accepted: 02-11-2021

Abstract

Background: Parathyroid glands play a vital role in the regulation of calcium homeostasis. Chief cells secrete PTH to regulate serum calcium level. Hypocalcaemia is associated with age related disorders such as osteoporosis. Oxyphil cells and C-cells are known to have significant age changes. Aim: Hence, it is worthwhile to focus on establishing the time of appearance of oxyphil cells, and to determine whether there is any increase or decrease of oxyphil cells as age advances. Additionally, it is imperative to analyse whether the oxyphil cell count influence the count of parafollicular cells. **Methods:** The parathyroid glands of 54 autopsied persons of various age groups (1-month to up to 80 years) were studied using haematoxylin and eosin and special stains. The sequence of changes occurring in the number, size and arrangement of parenchymal cells with respect to age were studied. The data obtained were analysed with appropriate statistical method to observe the dependence of various parameters with age. **Results:** C- cells predominated among the cell population and were present in all age groups. Number of C- cells increase until third decade with a slight decline thereafter. An earlier appearance of oxyphil cells was noted at the age of 7 years and a significant increase in number was seen after 40 years. They showed a tendency to form larger groups and nodules in old age. The number of oxyphil cells showed a strong positive correlation with age. And there was no correlation between number of parafollicular cell (C-cell) and oxyphil cell in this study. **Conclusion:** Significant age-related changes obtained in this study provide an opportunity to define the normal histological variations of C-cells and oxyphil cells with the age. This study serves as an attempt to bring some clarity regarding the function of oxyphil cell.

Keywords: Age, oxyphil cells, C cells, parathyroid

Introduction

The human thyroid is constituted by cells of varied embryologic origins [1]. Parathyroid gland was recognized by Sandstorm as an independent anatomical structure. Parathyroid glands are small, oval, endocrine glands closely associated with thyroid gland. The human parathyroid parenchymal cells are of three types namely chief cells, oxyphil cells (acidophil/eosinophil) and water clear cells (Wasserhelle). The parathyroid gland regulate serum calcium and phosphate levels via parathormone [2]. The oxyphil cell of the thyroid was first described by Askanazy in 1898. The significance of oxyphil cells in the pathophysiology of the parathyroid glands has not been elucidated completely. They are observed either singly or in small groups interspersed between C-cells. Age has been crucial factor in oxyphil cell differentiation. With age or after excessive functional stress, the C-cells begin converting to the oxyphil cells [3].Parafollicular cells (C cells) scattered throughout the thyroid gland synthesize, store, and secrete calcitonin (thyrocalcitonin). They have been called by variety of names for example- C cell, neurohormonal cell, giant-light cell, argyrophil cell, light cell and mitochondria-rich cell by various researchers. They secrete a hormone 'calcitonin' which is involved in maintaining calcium homeostasis. These cells are derived from neural crest cells that fuse with the thyroid gland. The parafollicular cells or clear (C) cells in man are part of neuroendocrine system under Amine Precursor Uptake and Decarboxylation (APUD) cells [4]. Available literature search showed a significant deficit regarding the age related studies of parathyroid gland precisely about oxyphil cells and c cells in Indian population [5]Hence, it is worthwhile to focus on the qualitative and quantitative changes in parenchymal cells with age. The main objective of this work is to establish the time of appearance of oxyphil cells, and to determine whether there is any increase or decrease of oxyphil cells as age advances. Also, we focus to analyse whether the oxyphil cell count influence the count of parafollicular cells.

Material and Methods

The present study was conducted in the Department of Obstetric and Gynecology, Govt. Medical College, Calicut. Around 54 specimens of human thyroid and parathyroid glands were collected from the autopsies done in the Forensic Department with due regards on ethical ground. Specimens were taken from autopsies done before six hours following death to avoid autolytic changes. Crush injuries of neck region, bodies with severe neck injuries, decomposed bodies, post-mortem bodies due to burns and death due to diseases of parathyroid and kidney were excluded from the study.Persons of both sexes ranging from 1-month to up to 80 years were divided into 9 age groups.

Table 1: **Age-wise distribution of study population**

Age	Group	Number of specimen	From where specimen collected
0-1month	1	9	O&G Department, GMC Calicut
1-10 yr	2	5	Forensic Department ,GMC Calicut
11-20yr	3	7	Forensic Department ,GMC Calicut
21-30yr	4	9	Forensic Department ,GMC Calicut
31-40yr	5	6	Forensic Department ,GMC Calicut
41-50yr	6	6	Forensic Department ,GMC Calicut
51-60yr	7	5	Forensic Department ,GMC Calicut
61-70yr	8	5	Forensic Department ,GMC Calicut
71-80yr	9	2	Forensic Department ,GMC Calicut

Table 1 depicted age-wise distribution of study population. From the table it is apparent that there are nine age groups beginning from neonate age group (up to 1-month), small children age group (1 year to 10 years), adolescent age group (11 years to 20 years), young children age group (21 years to 30 years), middle age group (31 years to 40 years), quadragenarian age group (41 years to 50 years), quinquagenarian age group (51 years to 60 years), sexagenarian age group (61years to 70 years) and the septuagenarian age group (71 years to 80 years). Specimen was collected along with larynx, thyroid dissected out. Thyroid tissue was taken from right upper lobe ½ cm thickness from junction between upper and middle 1/3, site for maximum parafollicular cell. Parathyroid gland was dissected from posterior border and inferior pole of thyroid gland. Parathyroid had a yellowish brown coloration and resembled split pea or bean with nodules of fat attached to it.Thyroid and parathyroid gland was fixed in Bouins fluid /formalin overnight. Sections of 5 microns were taken and stained with routine hemetoxylin and eosin stains.

*Correspondence
Dr. Indira CK
Associate Professor of Anatomy, GMC Konni, Kerala, India
E-mail: indirasudhir67@gmail.com

Erlichs hematoxylin was used known for its brilliant nuclear staining. Special stains like Luxol fast blue was used to identify oxyphil cells separately. Other special stain used was Altmann-Kull stain for identifying mitochondria.Parathyroid gland was dissected from 41 specimens. The oxyphil cells were identified by routine hematoxylin and eosin stain. The oxyphil cells varied in size from 8-12microns and were bigger than chief cells. They were polyhedral in shape with a centrally placed dense nucleus and no nucleolus. Cytoplasm was stained red with eosin showing reddish granules. Oxyphil cells were seen singly or in groups (sheets or cords).With Luxol fast blue stain, cytoplasm stained blue showing presence of phospholipid. With Altmann Kull technique cytoplasm of oxyphil cells showed red granules representing mitochondria.Parafollicular cells (C-cells or clear cells) of thyroid gland were identified by Modified Massons stain lying near basement membrane. The cells were oval in shape with clear cytoplasm and round nucleus.

Results

Table 2: Age group-wise distribution of study population with observation of oxyphil cells

Group	Age	No of cells/LPF	Finding
1.	Fetus		No change
2.(0 -10yr)	9month(M)	Nil	No change
	1 ½ yrs(M)	Nil	No change
	4 ½ yrs(F)	One	**Observed**
	7yr(F)	One	**Observed**
	9yr(F)	One	**Observed**
3.(11-19 yr)	13yr(F)	3	**Observed**
	16yr(M)	6	**Observed**
	16yr(F)	14	**Observed**
	18yr(M)	14	**Observed**
	19yr(F)	29	**Observed**
4.(20-29yr)	21yr(F)	11	**Observed**
	21yr(M)	24	**Observed**
	26yr(F)	28	**Observed**
	27yr(F)	26	**Observed**
	27yr(M)	29	**Observed**
	28yr(M)	54	**Observed**
5.(30-39yr)	30yr(F)	98	Groups of oxyphil cells in periphery
	35yr(M)	13	**Observed**
	35yr(F)	50	**Observed**
	38yr(F)	Numerous	**Observed**
	38yr(M)	11	Groups of oxyphil cells throughout field
6.(40-49yr)	40(M)	24	**Observed**
	42(M)	46	**Observed**
	45(M)	3	**Observed**
	47(F)	150	**Observed**
	47(M)	80	**Observed**
	49(F)	560	**Observed**
7.(50-59yr)	50(F)	12	Numerous fat cells
	55(F)	80	**Observed**
	59(F)	31	**Observed**
8.(60-69yr)	60(F)	100	Intermingled with fat cells
	60(M)	35	**Observed**
	60(M)	250	**Observed**
	65(F)	130	**Observed**
9.(70-79yr)	70(F)	100	**Observed**
	71(F)	28	**Observed**
	79(F)	80	**Observed**

Table 2 depicted age group-wise distribution of study population with observation of oxyphil cells. As per this table, oxyphil cells were first noted at 4 and half years specimen. An increase in number was noted with increase in age especially in females after 25years.

Table 3: Number of oxyphil cells with increasing age in over study population

Exact age	No of oxyphil cells
4 ½ yr	1
18 yr (M)	14
26yr (F)	26
30yr(F)	98
35 Yr (f)	200
42 yr (M)	160
55yr (f)	80
65yr (m)	250

Table 3 suggested the number of oxyphil cells with increasing age in over study population. Maximum number of oxyphil cells (250) was recorded in specimen of female person aged 65 years.

Table 4: Number of oxyphil cells with increasing age in females

Age	No of oxyphil cells
4 ½ yr	1
16	15
26	19
30	98
47	150
55	80
65	80

Table 4 revealed the number of oxyphil cells with increasing age in females. Maximum number of oxyphil cells (150) was recorded in specimen of female person aged 47 years.

Table 5: Time of appearance of oxyphil cells in study population

9months	nil
1 ½ yr	nil
1 ½ yr	nil
4yr	1 oxyphil cell
7yr	1 oxyphil cell
9yr	1 oxyphil cell

Table 5 calculated the time of appearance of oxyphil cells in study population. The least time of appearance of oxyphil cells in study population was recorded at 4 years.

Table 6: Descriptive statistics

Parameters	N	Mean	Std deviation	minimum	maximum
No of cells	39	60.08	99.95	0	560
Sex	39	1.5128	0.5064	1	2

Table 6 denote descriptive statistics of the available data from the current study. The number of cells identified in given study population was 39 with same of number of sex. The mean±SD of the number of cells was calculated as 60.08±99.95, and that of sex was 1.51±0.05.

Table 7: Statistics (Mann Whitney test–Result)

Statistical tests	No. of cells
Mann-Whitney U	139.500
Wilcoxon W	329.5
Z	-1.420
P value(2 tailed)	0.156

Table 7 described the contingency table of statistics. Statistical tests used in analysis included Mann-Whitney U test, Wilcoxon W and Z-test. The p-value obtained was 0.156.

Discussion

Since 1880, when Sandstrom revealed the detailed anatomy and histology of parathyroid glands [6,7] It has been clearly known that two types of epithelial cells of parenchyma are the chief cells and oxyphil cells. The time of appearance and function of oxyphil cells of the parathyroid gland and its relation to C cells of thyroid gland has been a subject of research for long.Time of appearance of oxyphil cells varied according to different investigators. In this study, oxyphil cell was first observed in a 4 and half year old child. This is definitely earlier than the time of appearance noticed by other Researchers [8-10] Erdheim (1901) first observed oxyphil cell in a 10 year old and Fischer (1911) observed in a 2 year old. Similarity in all three finding is time of first appearance of oxyphil cell happened by 10 years of age[11,12].In our study, within the younger age groups, the oxyphil cells were few in number, arranged singly or in pairs between chief cells. As age advanced, number of oxyphil cells increased. The number of oxyphil cells showed a gradual increase up to 40 years (0.1%-2.8%) and a rapid rise thereafter (6%-13.64%). Christi [13] noticed that they make up to 1.8% of the total population before 40 years and up to 9.05% after 40 years. In the present study, the number of chief cells showed a rapid increase from first to second and second to third decades. Maximum increase was observed in third decade followed by a gradual decrease until fifth decade and remained so thereafter. These finding agree well with Rother (1972) who noticed a rapid rise of chief cells in the second and third decades and decreases slowly until old age [14] These findings lead to a conclusion that they might be derived from chief cells and continuing their function to maintain the calcium homeostasis in advanced age.Many of the works were based on tumours and other diseased conditions like renal disease. Since this work is based on normal parathyroid gland, present work cannot be compared with those of Norris (1947) [15], Castleman (1935) [16], Gilmour (1947) [17]. Chief cells show slight decline in number with advancing age. This definitely leads to a possibility of decrease in serum calcium level. Old age diseases related with hypocalcaemia, such as osteoporosis are more common. This itself indicates the possibility of function of oxyphil cells in old age like chief cells to produce parathyroid hormone. Mallory and Castleman (1935) [16] has stated increase in number of oxyphil cells is related to calcium metabolism which was proven by their increase in number in renal disease.There was increase in number of oxyphil cells in females as age advanced. This is in agreement with view of Gilmour (1939) [12]. The function of the cells could not be found out as it required sophisticated equipments. According to Black and Ackerman (1950) [18], these cells possess secretory activity. But Hamperl (1950) [19] and Christie (1955) [20] were of the opinion that they are degenerate forms.Altmann and Kull stain was done for mitochondria in oxyphil cell which stained red. Presence of mitochondria indicates high energy resource. No one could extract hormone or detect any secretion from oxyphil cells. This suggests that cells are not secretory. Present work agrees with Munger and Roth that oxyphil cells contain mitochondria. From the fact oxyphil cells increase with age it can be assumed that oxyphil cells may be degenerate form of fully functioned chief cells of parathyroid gland. When the number of oxyphil cells increase the number of chief cells are also expected to increase, but that is not seen in the study, instead a decrease in the chief cell number is noted which supported the fact that oxyphil cells are degenerate forms of chief cells which cannot secrete parathormone anymore [21] An attempt has been made to study the relation of parafollicular cell with age and no link was found between the two factors which suggests there is no significant age change related to C cells.

Conclusion

The present work provides an opportunity to age changes and time of appearance of oxyphil cells its relation to C cells. C cells have been a constant in occurrence, whereas oxyphil cells appeared from the age of 4 and half years. Number of oxyphil cell showed a positive correlation with age. Our study observed no correlation between number of parafollicular cell (C-cell) and oxyphil cell. In our opinion, the oxyphil cell could be C-cell themselves which have released their hormone. This study will serve as a basic guideline for future clinical studies related with its endocrine functions.

Conflict of Interest: Nil Source of support: Nil

References

1. Salvatore D, Simonides WS, Dentice M, Zavacki AM, Larsen PR. Thyroid hormones and skeletal muscle—new insights and potential implications. Nature Reviews Endocrinology. 2014 Apr;10(4):206-14.
2. Gulve SS, Phatak SV. Parathyroid adenoma: Ultrasonography, Doppler, and elastography imaging. Journal of Datta Meghe Institute of Medical Sciences University. 2019 Jan 1;14(1):47.
3. Mete O, Asa SL. Oncocytes, oxyphils, Hürthle, and Askanazy cells: morphological and molecular features of oncocytic thyroid nodules. Endocrine pathology. 2010 Mar 1;21(1):16-24.
4. Ghosh SK. 92. Application of e-learning in anatomy–A knowledge, attitude and practice (KAP) study. journal of the anatomical society of india. 2015;64:S1-36.
5. Indira CK. Oxyphil cells of parathyroid gland–Its relation to increasing age in female. Journal of the Anatomical Society of India. 2017 Aug 1;66:S97.
6. Modarai B, Sawyer A, Ellis H. The glands of Owen. Journal of the Royal Society of Medicine. 2004 Oct;97(10):494-5.
7. Carney JA. The glandulae parathyroideae of Ivar Sandström: Contributions from two continents. The American journal of surgical pathology. 1996 Sep 1;20(9):1123-44.
8. Roth SI.The eosinophilic cells of the parathyroid (oxyphil cells), salivary (oncocytes), and thyroid (Huerthle cells) glands. Light and electron microscopic observations. Laboratory investigation; a journal of technical methods and pathology. 1962 Nov;11:933.
9. Gilmour JR. The normal histology of the parathyroid glands. The Journal of Pathology and Bacteriology. 1939 Jan;48(1):187-222.
10. Ritter CS, Brown AJ. Differential gene expression by oxyphil and chief cells of human parathyroid glands. The Journal of Clinical Endocrinology & Metabolism. 2012 Aug 1;97(8):E1499-505.
11. Christie AC. A histochemical property of the oxyphil cells of the human parathyroid glands. Journal of clinical pathology. 1955;8(4):302.
12. Gilmour JR. The normal histology of the parathyroid glands. The Journal of Pathology and Bacteriology. 1939 Jan;48(1):187-222.
13. Christie AC. The parathyroid oxyphil cells. Journal of clinical pathology. 1967 Jul 1;20(4):591-602.
14. Rother P, Scheller G, Herrschelmann B. Age-related changes in cell number, cell size and cell relations in human parathyroid glands. Endokrinologie. 1972 May;59(3):391-6.
15. Norris EH. The parathyroid adenoma; a study of 322 cases. Surgery, gynecology & obstetrics. 1947 Jan;84(1):1-41.
16. Castleman B, Mallory TB. The pathology of the parathyroid gland in hyperparathyroidism: A study of 25 cases. The American journal of pathology. 1935 Jan;11(1):1.
17. Gilmour JR. The parathyroid glands and skeleton in renal disease. The parathyroid glands and skeleton in renal disease.. 1947.
18. Black BK, Ackerman LV. Tumors of the parathyroid. A review of twenty-three cases. Cancer. 1950;3(3):415-44.
19. Hamperl H. Onkocytes and the so-called Hurthle cell tumor. Archives of Pathology. 1950 Jan 1;49(5):563-7.
20. Christie AC. A histochemical property of the oxyphil cells of the human parathyroid glands. Journal of clinical pathology. 1955 ;8(4):302.
21. Roth SI, Munger BL. The cytology of the adenomatous, atrophic, and hyperplastic parathyroid glands of man. Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin. 1962 Jul 1;335(4):389-410.