Variations in the Anatomical Position of the Normal and Diseased Parathyroid Glands

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Abstracts

Background: Despite the availability of expert surgeons and preoperative imaging investigations, some patients require re-operation for persistent or recurrent hyperparathyroidism. Ectopic Parathyroid Glands (PGs) are a cause for failed parathyroid exploration.

Objective: To evaluate the prevalence and location of normal parathyroid glands and diseased glands taken from subjects with End-Stage Renal Disease (ESRD).

Methods: A total of 410 parathyroid glands were recovered from 116 postmortem subjects of whom 37 were diagnosed as suffering from ESRD. In the rest, the death had resulted from disease unrelated to parathyroid disorder.

Results: 155 (69.3%) of both normal left and right superior PGs were located at cricothyroid junction; 46(29.3%) were behind the upper pole of thyroid gland; 2(2.6%) were behind pharyngoesophageal junction. 68 (47.1%) of the normal inferior PGs were found at the lateroposterior surface of the lower pole of thyroid gland; 62(43.7%) were within the thymic tongue and 14(9.7%) along the carotid artery. The normal ectopic PGs were found only in 22 cases. The superior PGs were 4(18.2%) in an extracapsular posterior position, 2(9.1%) intrathyroidal and 1(4.5%) retropharyngeal. The inferior ectopic PGs were 15(68.2%) and were found within the mediastinal thymus. 19(51-4%) of the enlarged PGs were found within the thyroid parenchma, 8(21.6%) within the thymic tongue, 6(16.2%) within the thymus, 2(5.4%) were within the carotid sheath and 1(2.7%) in the retropharyngeal or retroesophageal position.

Conclusion: The presence of ectopic PGs in secondary hyperparathyroidism is sufficiently important to justify their exhaustive search. As the preoperative image exams present low sensibility to locate them, it is necessary to develop an exploratory routine embracing the most common sites of location.

Keywords: Ectopic, parathyroid, parathyroidectomy, end-stage renal disease.

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Introduction

Parathyroid Glands (PGs) are four corpuscles localized on the posterior aspect of the thyroid gland. They are about five millimeters in diameter, situated in fibrous tissue close to Recurrent Laryngeal Nerve (RLN) and Inferior Thyroid Artery (ITA).[1]

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Superior PGs are usually dorsal to RLN whereas inferior PGs lies ventral to RLN. [2] This situation occurs in 80% of cases. [2, 3] In rest of cases, PGs vary in number, size and location. The latter varies widely as a result of different degree of migration during embryonic development.[4] Thus; strange locations of PGs are not surprising. [5,6] Wang [7] examined the anatomic distribution of normal PGs at autopsy and found the superior PGs in the juxtacricothyroidal position posteriorly in 77%, behind the upper role of the thyroid, in a subcapsular location in 22% and behind the upper oesophagus in 1% of individuals. Inferior parathyroid glands were found immediately adjacent to or on the anterior or posterolateral surfaces of the inferior pole of the thyroid gland in 57%, intrathymic in 41% and near the bifurcation of the common carotid artery in 2% of individuals.

Most patients with secondary hyperparathyroidism (HPT2) due to End-Stage Renal Disease (ESRD) do not respond to clinical treatment and after some years on dialysis, will need parathyroidectomy. [8]

Surgical failure happens in 10-30% of cases. [9] Incomplete identification of all parathyroids is the most important cause [10-12] and that is why ectopic glands are a big challenge. Preoperative imaging methods do not have high enough sensibility to detect all glands in HPT2. [8]

The purpose of this study is to define the most common sites of ectopic parathyroids in normal subjects and in subjects with HPT2 due to ESRD. We hope to help surgeons to establish a routine for cervical exploration in order to identify ectopic parathyroids glands.

Materials and Methods

A total of 410 parathyroid glands were recovered from 116 postmortem subjects of whom 37 were diagnosed as suffering from ESRD. In the rest, the death had resulted from diseases unrelated to parathyroid disorder. There were 75 males and 41 females. The age ranges from 28 to 77 years.

The parathyroid glands were obtained by dissection. A collar skin incision followed by midline incision and sternotomy was performed. Thorax was opened. Superficial neck fascia was cut in the midline, infrahyoid muscles pulled laterally, lobes of the thyroid gland were detached from the surrounding structures and pulled medially. Both RLN and ITA were cleaned. Close to the site of crossing of RLN and ITA, most of the PGS were found. Dissection continued on the dorsal surface of thyroid gland, under the capsule of thyroid gland, along the course of RLN and ITA, in the cervical and mediastinal thymic tissue and in the parapharyngeal and paraoesophageal space.

The position and number of all samples were documented and analyzed afterwards. The position of each gland was sketched on a parathyroid chart in relation to such constant anatomic landmarks as the cricothyroid junction, upper pole of the thyroid gland, thymic tongue and mediastinal thymus. All samples were weighed, then processed for examination by light microscope.

An ectopic inferior parathyroid gland was defined as a gland in a location other than or immediately adjacent to the anterior or posterolateral surface of the inferior pole of the thyroid gland or within the thymic tongue which represents cervical extension of thymus. [13] An ectopic superior parathyroid gland was defined as a gland in a location other than cricothyroidal junction posteriorly or within the capsule on the posterior surface of the upper pole of the thyroid gland. [13]

The location of an ectopic parathyroid gland was classified as: intrathyroidal, within the mediastinal thymus, retropharyngeal or retroesophageal, within the tracheo-esophageal groove or the carotid sheath. [7,13]

Results

The mean weight of the normal parathyroid gland was 35 to 45 mg and in glands taken from patients with ESRD were 520 to 1300mg.

The causes of ESRD were schistosomiasis in 20 subjects (54.1%), glomerulonephritis in 6 (16.2%) systemic arterial hypertension in 6 (16.2%).

Diabetes mellitus in 2(5.4%), renal tuberculosis in 1(2.7%), unknown cause in 2 (5.4%). We did not found more than four parathyroid glands in any individual. However, in 14 subjects only 3 glands were found.

Position of the superior PGs: Of the 157 superior PGs, 58 (71.6%) on the right side and 51 (67.1%) on the left side were found at the cricothyroid junction posteriorly (table 1, 2, Fig. 1, 2), by far the most common site of superior parathyroid. Here, the gland was dorsal to the RLN intimately related to the branches of the inferior thyroid artery.

Table (1): Normal parathyroid glands within normal (topic) and abnormal (ectopic) positions.

Parathyroid	*Topic*	*Ectopic*	*Total*
Superior- right	*81 (96.4%)*	*3 (3.6 %)*	*84*
Superior- left	*76 (95 %)*	*4 (5 %)*	*80*
Inferior- right	*73 (90.1 %)*	*8 (9.9 %)*	*81*
Inferior - left	*71 (91.1 %)*	*7 (9 %)*	*78*
Total	*301 (92.7%)*	*22 (6.9 %)*	*323*

The rest of the superior parathyroid glands lie behind the upper pole of the thyroid gland. They were of equal number (23) but differed in ratio (28.4% and 30.3%) respectively; (table 1,2). In this position, the superior parathyroid glands were invariably subcapsular lying under the pretracheal facia which forms the surgical capsule of the thyroid (Fig 2,3).

Position of the inferior parathyroid glands: These glands were distributed rather evenly between the lower pole of the thyroid and the thymus. Of the 144 inferior PGs, 35 (47.9%) of the right side and 33(46.4%) of the left side were found at the lateroposterior surface of the lower pole of thyroid gland (table 1,2) (Fig. 1,2,3).

In this position, the gland was frequently obscured by a pad of fatty tissue and blood vessels and lie ventral to the recurrent laryngeal nerve. Sixty two inferior PGs were located in the lower neck within the thymic tongue, which is a distinct structure of the thoracic inlet that extends from the lower thyroid pole to the mediastinal thymus (Tables 1,2) (Fig. 3). 30 (41%) were on the right side of the neck and 32(46.1%) were on the left side.

The rest of the inferior PGs uncovered some distance lateral to the lower thyroid pole, mostly close to the carotid artery (Table 1,2). 8(11%) were found on the right side and 6(8.5%) were found on the left side of the neck. These glands were invariably embedded in a lobule of fatty tissue.

Position of ectopic normal parathyroid glands: The superior ectopic PGs were found mostly in extracapsular position posterior to the upper pole of the thyroid gland (Table 3). Two superior glands (9.1%) were found on each side. One right superior gland (4.5%) occupied a retropharygeal position and two left glands (9.1%) were found inside the thyroid gland near its upper pole. The inferior ectopic PGs were found exclusively within the mediastinal thymus. 8(36.4%) were absent right inferior and 7(31.8%) were absent left inferior glands.

Position of enlarged parathyroid glands in ESRD: In 19(51.4%) of individuals, the enlarged PGs were found within the thyroid parenchyma, almost totally covered by thyroid tissue (Fig. 5) 6(21.6%) and 8(16.2%) were found within the thymus or its cervical extension, the thymic tongue. The rest of the enlarged PGs were found within the carotid sheath posterolateral to the thyroid in 2 cases (5.4%), retropharyngeal in one case (2.7%) and retroesophageal in another case (2.7%) (Table 4).

The normal and enlarged parathyroid gland was soft and pliable in consistency. As a result, it was easily shaped and molded by the adjacent tissue. This soft consistency was useful in differentiating a parathyroid gland from a lymph node or a thyroid nodule, both of which were firm and elastic in contrast.

Occasionally, the enlarged parathyroid gland was surrounded by a capsule which separates it from the adjacent thyroid gland (Fig. 6).

Table (2): Common locations of normal topic parathyroid gland.

Location	*No.*	*Percentage (%)*
Superior - Right		
a) Cricothyroid junction posteriorly	*58*	*71.6*
b) Behind upper pole of thyroid	*23*	*28.4*
Superior - Left		
a) Cricothyroid junction posteriorly	*51*	*67.1*
b) Behind upper pole of thyroid	*23*	*30.3*
c) Behind pharyngoesophageal junction	*02*	*02.6*
Inferior - Right		
a) Lateroposterior surface of lower pole of thyroid gland	*35*	*47.9*
b) thymic tongue	*30*	*41.0*
c) along the carotid artery	*08*	*11.0*
Inferior - Left		
a) Lateroposterior surface of lower pole of thyroid	*33*	*46.4*
b) thymic tongue	*32*	*46.1*
c) along the carotid artery	*06*	*08.5*

Table (3): Common locations of ectopic normal parathyroid glands.

Location	*No. (cases)*	*Percentage (%)*
Superior - Right		
a) Extracapsular	*2*	*9.1*
b) Retropharyngeal	*1*	*4.5*
Superior - Left		
a) Extracapsular	*2*	*9.1*
b) Intrathyroidal	*2*	*9.1*
Inferior - Right		
Mediastinal thymus	*8*	*36.4*
Inferior - Left		
Mediastinal thymus	*7*	*31.8*
Total	*22*	*100.0*

Table (4): Common locations of enlarged parathyroid glands in ESRD.

Location	*No. (cases)*	*Percentage (%)*
Thyroid	*19*	*51.4*
Perenchyma		
Thymic tongue	*08*	*21.6*
Thymus	*06*	*16.2*
Carotid sheath	*02*	*05.4*
Retroesophageal	*01*	*02.7*
Retroesophageal	*01*	*02.7*
Total	*37*	*100*

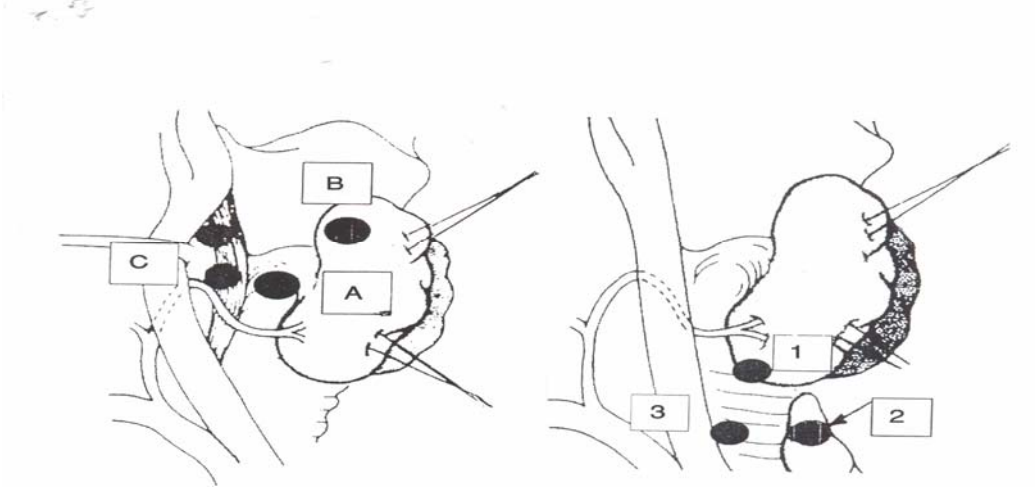

Fig. (1): Anatomic distribution of normal superior and inferior parathyroid glands. A=juxtacricothyroidal position posteriorly, B= behind the upper pole of the thyroid in a subcapsular location, C= behind the junction of the upper esophagus and lower pharynx in the midline, 1 inferior pole of the thyroid, 2= intrathymic, and 3= along the carotid artery. (Adapted from: Wang CA. The anatomic basis of parathyroid surgery. Ann Surg 1976; 183(3): 271-5).

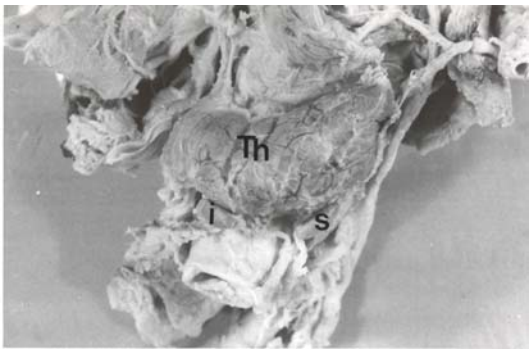

Fig. (2): Posterolateral view of the neck showing thyroid gland (Th), inferior (i) and superior (s) parathyroid glands.

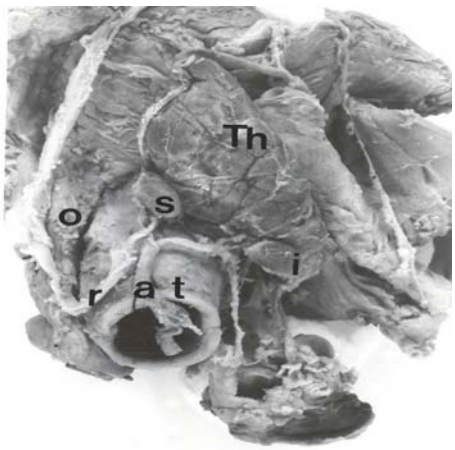

Fig. (3): Posterolateral view of the neck showing thyroid gland (Th), superior (s) and inferior (i) parathyroid glands, trachea (t) and oesophagus (o).Part of the right recurrent laryngeal nerve (r) and inferior thyroid artery (a) can be seen.

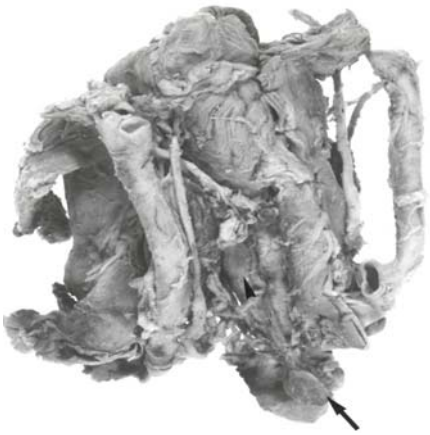

Fig. (4): Posterior view of the cervical viscera showing inferior parathyroid gland within the thymic tongue (arrow) and superior parathyroid gland at the pharyngoesophageal junction (arrow head).

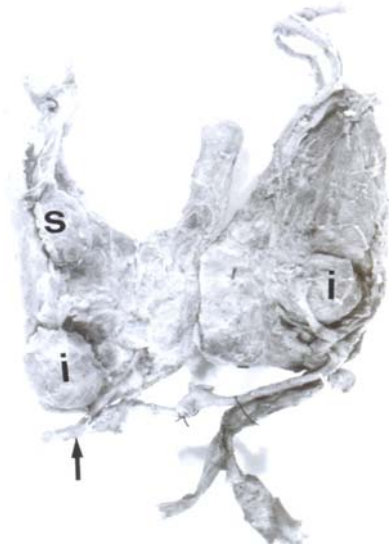

Fig. (5): Posterior view of thyroid gland taken from a subject with ESRD. One superior (s) and two inferior (i) parathyroid glands can be seen. The latter were partially embedded within the thyroid gland. Arrow points at branches of inferior thyroid artery.

Fig. (6): Part of thyroid gland (Th) and superior parathyroid gland (arrow) taken from a subject with ESRD. The latter appears enlarged and encapsulated.

Discussion

The findings of the present study are in general agreement with most of the previous similar work. [6-8,14] This study shows that despite the wide distribution, the normal parathyroid gland falls into a definite pattern, and can be uncovered in these locations in a great majority of cases. Almost 95% of the superior PGs occupied a normal (topic) position and about 5% were found in abnormal (ectopic) positions. 90.5 % of the inferior PGs were in topic positions, however 9.5% were found in ectopic positions. The higher incidence of ectopic inferior glands has been attributed to abnormal migration during embryogenesis.

Embryologically, the superior gland shares a common primordium in the fourth branchial pouch with the lateral thyroid which subsequently fuses with the lateral wing of the median thyroid. [4,5,14,15] It is not surprising, then, that superior PGs are ivariably found in close proximity to the dorsum of the superior thyroid lobe, either behind the upper pole or at the cricothyroid junction. Similarly, embryologic evidence may be seen in the distribution of the inferior parathyroid glands. It has been shown that both the inferior gland and the thymus arise from the third branchial pouch. As they descend caudally the gland separates from the thymus and in most instances is located in the anterior or lateroposterior aspect of the lower thyroid pole. In nearly half of the cases, the inferior gland remains within the thymic tongue at the thoracic inlet. A few glands may descend with the thymus into the mediastinum or may be left high in the neck as a result of early developmental arrest. This embryologic variation accounts for the wide distribution of the inferior gland and for the adoption of the terms normal (topic) and abnormal (ectopic) positions of the gland by certain authors. [8,13,14]

It is well-known that the thyroid gland is sheathed in a transparent fibrous capsule which is thick and strong in the upper and middle portions of the thyroid and thin in the lower thyroid pole. When a parathyroid gland is located within this capsule, it is designated as subcapsular; and one lying outside of the capsule is known as extracapsular. This anatomic feature is of surgical importance because, when diseased, a subcapsular parathyroid usually remains in its place and expands locally within the confines of the surgical capsule of the thyroid. An extracpsular parathyroid on the other hand, tends to be displaced into an area where it meets little or no resistance. Thus, an enlarged subcapsular parathyroid gland, located behind the upper or lower pole of the thyroid is seldom displaced to any degree and an extracapsular gland at the cricothyroid junction or within the thymus invariably falls into either the posterior or anterior mediastinum. [7] In the present study 51.4% of the enlarged PGs were subcapsular and kept in close anatomical relation to the dorsum of the thyroid gland. The PGs were almost completely embedded within the thyroid gland. The rest of the enlarged PGs were extracapsular and located within the thymus or its extension into the neck.

Ectopic PGs were the main cause of persistent hyperparathyroidism in patient with end-stage renal disease. Gomes et al. [8] found the thyroid parenchyma (33.3%) and the thymus (33%) as the most common locations of ectopic enlarged PGs. Similar results were described by Gough [16] and Phitayakorn and McHenry. [13]

Ectopic PGs continue to be a diagnostic and operative challenge in patients with hyperparathyroidism. Ectopic PGs remain a cause for failed parathyroid exploration and increased morbidity related to more extensive dissection at initial operation or because of scarring and distorsion of tissue planes encountered during reoperation.[10,12,13,17] Surgical failure happens in 10 to 30% of cases in spite of the growing surgical expertise in parathyroidectomy. [17- 20] Preoperative imaging methods do not have high enough sensitivity to detect all the glands in HPT2. [8]

In the present study, we demonstrate that the most frequent localizations of ectopic PGs were thyroid gland and thymus.

Similar findings associated with the high incidence of thyroid incidental nodules were shown in ultrasound imaging, [8] bringing up the discussion of which decision is the right one-remove or not these nodules. According to Goncalves, [21] when a parathyroid is not found in its usual location, thyroid lobes must be carefully examined looking for nodules, which should be extirpated for frozen study. Thymus removal is the next step. The same routine procedure is recommended by other authors. [17]

Conclusion

The presence of ectopic PGs in HPT2 is sufficiently important to justify their exhaustive search. As the preoperative image exams contribute very little to locate them, it is necessary to develop an exploratory routine that ivolves the most common sites of the glands. Since the most common locations were the thyroid parenchyma and thymus; we suggest a careful search of the cervical region, removal of thymus and all the incidental thyroid nodules.

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التفاوت في الموقع التشريحي للغدد جنيبة الدرقية السليمة والمصابة بتغيرات مرضية

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الملخص:

الهدف: بالرغم من توافر الجراحين ذوي الخبرة ووسائل التصوير العلمية الحديثة، فإن بعض المرضى يخضعون للتداخل الجراحي أكثر من مرة؛ نظراً لاستمرار أو عودة أعراض فرط نشاط جنيبات الدرقية، ويرجع السبب في ذلك الفشل في العثور على الغدد جنيبات الدرقية لوجودها في مواقع خارج أماكن تواجدها المعتادة. ويهدف هذا البحث الى دراسة أماكن تواجد هذه الغدد السليمة منها والمصابة بتغيرات مرضية في حالات المرحلة النهائية من مرضى الكلى.

الطرق: تمت دراسة 410 غدة جنيبة الدرقية أخذت من 116 جثة تم تشريحها بعد الوفاة، وكان سبب الوفاة في 37 حالة المرض الكلوي المتقدم، وبالنسبة لباقي الحالات فقد كان سبب الوفاة أمراضاً غير مرتبطة بالغدد جنيبات الدرقية.

النتائج: كانت مواقع الغدد جنيبات الدرقية العليا السليمة كما يأتي: 155(3ر69 %) من الجانبين الأيمن والأيسر خلف منطقة الاتصال بين الغضروفين الحلقي، 46(3ر29%) خلف القطب العلوي للغدة الدرقية، 2(6ر2%) خلف منطقة الاتصال بين البلعوم والمريء، أما بالنسبة للغدد جنيبات الدرقية السفلى فكانت كما يأتي: 68(1ر47%) خلف القطب السفلي وللناحية الوحشية من الغدة الدرقية، 62(7ر43%) كانت داخل البروز اللساني للغدة الزعترية، 14(7ر9%) قرب الشريان السباتي، وبالنسبة لمواقع الغدد جنيبات الدرقية المفارقة فقد كانت كما يأتي:

الغدد العليا 4(2ر18 %) خارج محفظة الغدة الدرقية 2(1ر9 %) وداخل الغدة الدرقية وغدة واحدة (5ر4 %) خلف البلعوم، وكان عدد الغدد السفلى 15(2ر68 %)، وكانت جميعها داخل الجزء الصدري من الغدة الزعترية.

وبالنسبة للغدد جنيبات الدرقية المتضخمة نتيجة مرض كلوي مزمن، فإن نسبة تواجدها كانت كما يأتي: 19 (4ر51 %) كانت داخل الغدة الدرقية، 8(6ر21 %) داخل الغدة الزعترية، 1(7ر2 %) خلف البلعوم، 1(7ر2 %) خلف المريء.

الاستنتاج: إن وجود غدد جنيبات الدرقية مفارقة نتيجة فرط في نشاط هذه الغدد يبرر أهمية تحديد مواقع هذه الغدد، وحيث إن وسائل تصوير هذه الغدد غير كافية لتحديد مواقعها فإن ذلك يتطلب تطوير طريقة بحث جراحية تشمل معظم الأماكن المتوقع وجود هذه الغدد فيها.

الكلمات الدالة: مفارقة، الغدد جنيبات الدرقية، استئصال الغدد جنيبات الدرقية، المرحلة النهائية في مرضى الكلى.