Hyperfunctioning intrathyroid parathyroid gland: a potential cause of failure in parathyroid surgery

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Summary: Four patients with hyperfunctioning intrathyroid parathyroid are reported. In each case the intrathyroid parathyroid was embedded within the thyroid parenchyma and appeared as a solitary 'cold' thyroid nodule by radioactive iodine scanning. It is believed that the intrathyroid parathyroid evolves as the lateral lobe of the thyroid fuses with the isthmus in the early development of the thyroid. Embryologically, an intrathyroid parathyroid is thus likely to be the superior gland. When the superior parathyroid gland is missing at the time of exploration, a nodule within the ipsilateral lobe of the thyroid may well be an intrathyroid parathyroid. Under these conditions, lobectomy for the exclusion of such a gland is mandatory.

Introduction
Hyperfunctioning intrathyroid parathyroid is rarely encountered. If it is present and remains undetected, it can be the cause of failure in parathyroid exploration. We have cared for 4 such cases at the Massachusetts General Hospital since 1960. The clinical and pathological data for these cases are summarized in Table 1.

Case reports
Case 1: A 47-year-old woman was admitted to the Massachusetts General Hospital with recurrent renal stones associated with an intermittent urinary tract infection of approximately one year's duration. The patient had had hypercalcaemia ranging between 12 and 13 mg/100 ml for nearly three years. A presumptive diagnosis of primary hyperparathyroidism was made, and exploration of the neck was undertaken.

The left side of the neck was explored first because it was fuller than the right. A normal parathyroid gland was uncovered at the posterior lateral aspect of the lower pole of the thyroid. It was characteristic of an inferior parathyroid gland. The second gland was not found despite a long search. The opposite side of the neck was then explored, and two normal-sized glands were indentified. As the left superior gland was missing, the left side was again explored. After a short while, a lump was noted in the upper pole of the thyroid. The probability of an intrathyroid parathyroid was raised. The upper pole of the thyroid was resected; a large mass (2 x 1 x 1 cm) was uncovered, ovate in shape and completely encased within the thyroid. A diagnosis of intrathyroid parathyroid adenoma of the left upper gland was made and confirmed by frozen section (Figure 1).

The postoperative course was uneventful. The serum calcium level fell to 7.2 mg/100 ml. After a brief course of calcium citrate, it slowly reverted to a normal level.

Case 2: A 60-year-old man was admitted to the Massachusetts General Hospital because of intractable duodenal ulcer associated with frequent bouts of haemorrhage over a period of 40 years. A subtotal gastrectomy had been performed elsewhere 26 years earlier. Ten years prior

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Table 1. Clinical and pathological data of 4 patients with intrathyroidal hyperfunctioning parathyroids

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Clinical manifestation</th>
<th>Physical examination</th>
<th>Serum calcium (mg/100 ml)</th>
<th>Plasma PTH (pmol/ml)</th>
<th>Pathological findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>47</td>
<td>Renal stone</td>
<td>Neck mass (L)</td>
<td>12-13</td>
<td>7.2</td>
<td>—</td>
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<tr>
<td>2</td>
<td>M</td>
<td>60</td>
<td>Duodenal ulcer</td>
<td>Neck mass (R)</td>
<td>15.7</td>
<td>7.8–8.3</td>
<td>—</td>
</tr>
<tr>
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<td>M</td>
<td>64</td>
<td>Renal stone</td>
<td>Neck mass (R)</td>
<td>11–12</td>
<td>8.0</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>48</td>
<td>Nausea, vomiting</td>
<td>Neck mass (R)</td>
<td>15</td>
<td>8.0–9.0</td>
<td>41</td>
</tr>
</tbody>
</table>

L = left, R = right, U = upper

Figure 1. Photomicrograph of intrathyroid parathyroid (A) completely surrounded by thyroid parenchyma (B), Case 1. (×14)

to the present admission, the patient noted a firm but asymptomatic nodule in the right side of his neck. During the past year, the patient had lost about 25 lb (11.25 kg).

On examination, the patient appeared chronically ill. A 3 cm nodule could readily be seen in the right side of the lower neck. It appeared firm and smooth by palpation and was not tender. There was no associated lymphadenopathy. Radioactive iodine (^131I) scanning showed a nonfunctioning area which was interpreted as a solitary cold nodule of the thyroid.

On admission, the serum calcium level was 15.7 mg/100 ml. The serum phosphorus was 1.9 mg/100 ml with an alkaline phosphatase of 7.1 Bodansky units. A 24-hour urinary excretion was 366 mg. A presumptive diagnosis of primary hyperparathyroidism with a coexisting nonfunctioning thyroid nodule was made, and for this his neck was explored. At operation, three normal parathyroid glands were identified – two in the left and one in the lower right side of the neck. The right superior parathyroid gland was missing. Palpation of the right lobe of the thyroid revealed a firm nodule within the upper pole. An intrathyroid parathyroid was suspected and a right lobectomy was performed. On sectioning the specimen, a 3.1 × 3.0 × 2.5 cm parathyroid mass was uncovered. It was soft and yellowish-tan in colour completely enveloped by the thyroid. Frozen section examination confirmed the diagnosis of an intrathyroidal parathyroid adenoma of the right superior gland.

The postoperative course was smooth. By the fifth day, the serum calcium had fallen to 7.8 mg/100 ml. The patient received supplementary calcium. When he was discharged on the seventh day, his serum calcium was 8.3 mg/100 ml.

Case 3: A 64-year-old man was admitted to the Massachusetts General Hospital with recurrent renal stone of two year's duration. Two years prior to the present admission, the
patient had been treated for a transitional cell urinary bladder carcinoma, Grade II. About a year later, he was found to have an elevated serum calcium level of 11–12 mg/100 ml and plasma parathyroid hormone (PTH) of 20 μmol/ml (normal 10). The 24-hour urinary calcium excretion was 622 mg.

Hyperparathyroidism was suspected, and exploration of the right side of the neck was undertaken first. At surgery, a flat yellowish-brown inferior parathyroid gland of normal size was uncovered in the lateral posterior of the lower pole of the thyroid. The right superior gland was not found. The left side of the neck was explored and two normal parathyroid glands were uncovered. As the right upper gland was missing, the right side was again explored and a palpable nodule noted within the thyroid lobe was excised by a lobectomy. The nodule proved to be an intrathyroid parathyroid adenoma, 3 × 3 × 0.5 cm in size, yellowish-tan in colour, and finely granular in texture. It was completely enveloped by the thyroid. The diagnosis of an intrathyroid parathyroid adenoma was confirmed by frozen section examination. The patient had a smooth postoperative course, and both serum calcium and PTH reverted to normal levels.

Case 4: This 48-year-old woman entered the Massachusetts General Hospital because of nausea, vomiting, and a progressive loss of weight over a period of six months. Levels of 15 mg/100 ml serum calcium and 1.6 mg/100 ml phosphorus were noted, and the PTH level was 41 μmol/ml. A diagnosis of acute hyperparathyroidism was made. At operation three normal parathyroid glands were identified, two in the left and one in the lower right side of the neck. Despite a long search, the right superior gland could not be located. Palpation of the thyroid revealed a mass in the upper pole of the right thyroid which suggested the presence of an intrathyroid parathyroid. A right lobectomy was therefore performed. An intrathyroid parathyroid completely surrounded by the thyroid was uncovered (Figure 2). A diagnosis of an intrathyroid parathyroid adenoma of the right superior gland was confirmed (Figure 3).

The patient had a smooth postoperative course. She was discharged on the fourth postoperative day when her serum calcium and PTH had fallen to normal levels.

Figure 2. Intrathyroid parathyroid adenoma (A) embedded within the thyroid and adjacent to thyroid follicular adenoma (B), Case 4

Figure 3. Photomicrograph of intrathyroid parathyroid adenoma (A) surrounded by thyroid parenchyma, Case 4. (× 17)
Discussion
The incidence of hyperfunctioning intrathyroid parathyroid has been variously reported between 1% and 3% (Black & Zimmer 1956, Hellstrom & Ivemark 1962, Pyrah et al. 1966). Sporadic accounts of this type of hyperparathyroidism have appeared in the literature (Coffey et al. 1965, Goodman & Egdahl 1969, Lahey & Haggart 1935, Tolstedt et al. 1960). Prior to 1960, no patients with intrathyroid parathyroid gland had been encountered at the Massachusetts General Hospital (Cope 1960). Since that time, there have been only 4 cases of hyperfunctioning intrathyroid parathyroid gland (0.5% of 714 patients treated for hyperparathyroidism).

An intrathyroid parathyroid is completely surrounded by the thyroid. It is seldom visible to the naked eye but may be detected only by palpation as a discrete nodule within the substance of the thyroid, as it was in the 4 patients reported here. In contrast, a parathyroid gland located in the crevices of the thyroid may be partially covered by the thyroid but not completely submerged within it. Strictly speaking, such a gland is not truly intrathyroid parathyroid; rather it is a subcapsular gland. Many subcapsular parathyroids have been mistaken for intrathyroid parathyroids. This error undoubtedly accounts for discrepancies in the literature reporting the incidence of this disease entity.

Just how a parathyroid becomes embedded within the thyroid gland is not known. It is conceivable that in early embryonic life the parathyroid is trapped within the thyroid as the lateral lobe of the thyroid fuses with the median lobe. If this interpretation is correct, the intrathyroid parathyroid will be the adult superior parathyroid, since the adult superior gland takes origin with the lateral lobe at the fourth branchial pouch. Our findings support this hypothesis as all four intrathyroid parathyroid glands in our series were superior glands.

In none of the four intrathyroid parathyroid glands was there a distinct cleavage plane between the gland and the thyroid as there is between an extrathyroid parathyroid gland and the thyroid. It is virtually impossible to dissect an intrathyroid parathyroid gland from the thyroid without resecting a portion of the thyroid. Moreover, there are seldom large blood vessels between the thyroid and the intrathyroid parathyroid. The absence of large blood vessels and a distinct cleavage plane are characteristic of intrathyroid parathyroid and thus favour this diagnosis.

A hyperfunctioning parathyroid often appears 'cold' by scan with $^{131}$I and, on the basis of scanning alone, is indistinguishable from a solitary nonfunctioning thyroid nodule. At the time of exploration any nodule within the thyroid must be considered to be an intrathyroid parathyroid until proven otherwise. If it is the superior gland that is missing, the probability that the nodule is an intrathyroid parathyroid is even more pronounced and requires a thyroid lobectomy to exclude it. If the missing gland proves to be the inferior gland, clearly a thymectomy would be the procedure of choice.

References
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