

## PARATHYROID CARCINOMA: A REPORT OF TWO CASES

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Since parathyroid carcinoma is a rare cause of hyperparathyroidism, few clinicians have had experience in managing such cases. Physicians and surgeons managing parathyroid disease must have a high index of suspicion to diagnose parathyroid carcinoma. Diagnosis can be difficult histologically, but clinical features with biochemical studies and microscopic study can help. The purpose of this study is to present the experience of King Faisal Specialist Hospital and Research Centre (KFSH&RC) in Saudi Arabia.

### Case Reports

#### Case 1

A 51-year-old Saudi male from the Western Province was diagnosed with hyperparathyroidism at his local hospital. He had a history of general weakness, lethargy, general bone aches and multiple joints pain. He had left lower parathyroidectomy and left hemithyroidectomy at the same hospital, and had an uneventful postoperative course. However, he continued to have hyperparathyroidism with hypercalcemia, with his parathyroid hormone (PTH) at 1064 ng/L (10-65), calcium (Ca<sup>++</sup>) at 3.88 mmol/L (2.10-2.55), alkaline phosphatase at 181 U/L (40-115), phosphate (PO<sub>4</sub>) at 0.66 mmol/L (0.70-1.45), but with normal albumin. The patient also had renal function impairment, with creatinine at 169 μmol/L (60-115). He was referred to KFSH&RC for further management.

The patient was treated intravenously with normal saline and diuretics. Sestamibi scan showed uptake in the left neck at the site of the left thyroid and also uptake laterally (Figure 1). The patient had exploration of his neck, where a recurrent tumor at the site of previous surgery, measuring about 2.5x2x1.5 cm in maximum diameters, was resected.

Left neck dissection demonstrated a metastatic left internal jugular lymph node measuring about 2x1.5x1.5 cm in maximum diameters. Both tumors were easy to dissect from the surrounding tissues. There was no gross

residual tumor left. We used meticulous dissection to avoid capsule rupture that could have led to tumor cell seeding. After the operation, the patient regained normal calcium levels. Six months later, the patient had normal calcium and normal parathyroid hormone, and his renal function had improved. Ultrasound scan of his kidneys demonstrated bilateral normal size without any evidence of stones. Sestamibi scan showed no uptake at the previous site of the parathyroid carcinoma.

#### Case 2

A 67-year-old Saudi female from Riyadh noticed a voice change of two months' duration. Examination confirmed right vocal paralysis. Preoperatively, she had high calcium of 2.62 mg/dL (normal 2.2-2.55). CT scan showed a 2-cm mass in the paratracheal area of the right neck. Exploration of the right neck demonstrated large inferior parathyroid glands (2.5 cm in diameter) adherent to the adjacent structures, including recurrent laryngeal nerve, trachea and the esophagus. We performed excision of the tumor and right hemithyroidectomy. Postoperatively, the patient regained normal calcium and PTH levels. Six months later, the patient's calcium and PTH levels were still normal.

#### Pathological Findings

One of the specimens measured 2.4x1.8x1.4 cm in maximum dimension. It was surrounded by an intact capsule. Microscopically, there were pleomorphic nuclei, prominent nucleoli and mitosis (Figure 2). The lymph

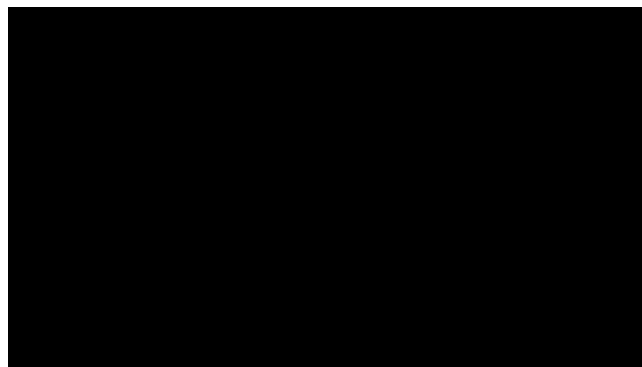


FIGURE 1. Sestamibi scan. Delay phase demonstrates uptake in the left neck.

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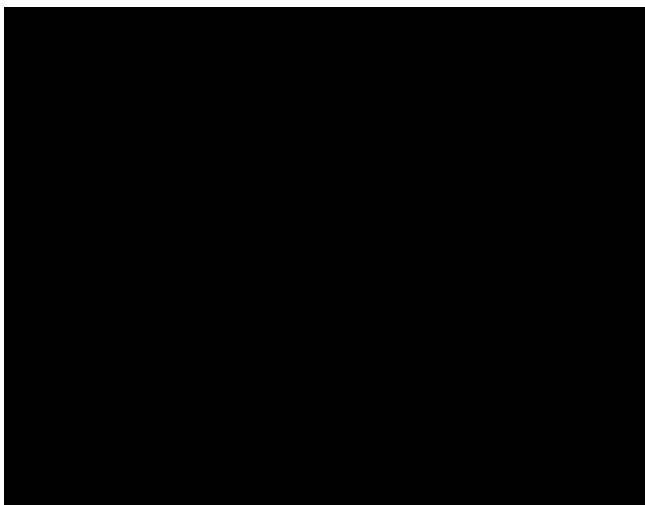


FIGURE 2. Photomicrograph showing parathyroid carcinoma with pleomorphic nuclei, prominent nucleoli and single mitosis (300x).

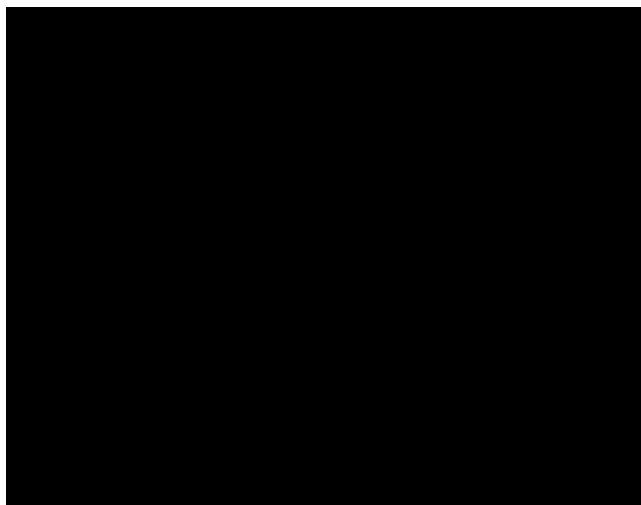


FIGURE 3. Photomicrograph showing metastatic parathyroid carcinoma to the lymph node (300x).

nodes from the lateral area to the left internal jugular vein demonstrated metastatic parathyroid carcinoma (Figure 3).

### Discussion

Parathyroid carcinoma is a rare cause of hyperparathyroidism.<sup>1-4</sup> Review articles show incidence figures ranging from 0.5% to 3%, and 5% in the Japanese population. To perform adequate surgery for the patient, it is important to recognize the disease in the initial stages. Surgeons who deal with parathyroid gland diseases should be aware of these and expect parathyroid carcinoma if the parathyroid gland is suspicious. Parathyroid gland with large size adherent to adjacent structures, palpable neck mass, lymph node enlargement and distant metastases should attract the surgeon's attention for the possibility of parathyroid carcinoma.

The two cases presented and other cases in the literature<sup>4-6</sup> have common features. In our first case, we discussed the patient who presented with high calcium and during whose surgery the surgeon noticed the tumor to be adherent to the adjacent structures. The second case presented with recurrent laryngeal nerve paralysis.

Data on parathyroid carcinoma have been reviewed by Woolner et al.,<sup>7</sup> Holmes et al.,<sup>8</sup> and Shane and Bilezikian.<sup>9</sup> They reported different patterns of the natural history of the parathyroid carcinoma. They categorized parathyroid carcinoma into four types: 1) noninvasive tumor incompletely removed at operation with subsequent growth of tumors in which there was a favorable response after complete tumor removal; 2) invasive tumors of the parathyroid with no recurrence or metastasis; 3) invasive tumors in which surgical removal of the parathyroid produced temporary remission of symptoms but hypercalcemia recurred without known metastasis; and 4) tumors inadvertently or intentionally grafted into neck

muscles to prevent tetanus, in which there are multiple recurrences.

Black and Ackerman<sup>10</sup> presented 20 patients with parathyroid carcinoma in 10 cases in which the diagnosis was made on gross specimen. They stressed that the microscopic appearance of parathyroid cancer might be confused with the appearance of adenomas, because an adenoma may have pleomorphic cells and giant cells with large nuclei, as well as small nests of tumor cells lying free within the blood vessels. Schantz and Castleman<sup>11</sup> reviewed 70 cases with parathyroid carcinoma and noted that the most important features were: 1) local invasion of adjacent structures; 2) capsular or vascular invasion, fibrous trabeculae or mitosis; and 3) nodal or distant metastases.

Diagnosis of parathyroid carcinoma can be difficult, so a high suspicion index is needed to diagnose these cases initially. If the surgeon suspects a parathyroid carcinoma, he should keep the capsule intact as much as he can. Gentle dissection should be maintained at all times. Ipsilateral thyroid lobectomy should be performed if the tumor is adherent or adjacent to the gland. The muscles involved should be excised. Lymph node dissection should be performed if there is lymph node metastasis. Local recurrences and distant metastases can be excised surgically to control the hyperparathyroidism and the serum calcium.<sup>12</sup> For localization of recurrences or metastatic spread, different modalities of radiological studies can be used. Sestamibi scan can be very accurate in localizing the local recurrence and lymph node metastasis.<sup>13</sup> Selective venous sampling for PTH can detect the lesions.<sup>14</sup> CT scan, MRI and ultrasonography can be helpful in detecting parathyroid carcinoma.<sup>15</sup>

The biphosphonates (osteoclast inhibitors) inhibit bone resorption.<sup>16</sup> Pamidronate is the most potent agent. It has been used to control hypercalcemia in case of metastatic

carcinoma.<sup>17</sup> These agents can be used to decrease the symptoms in cases where the tumor is inoperable.

We believe that adequate first surgery without rupture of the capsule should give the best result. Recurrences and distant metastases can be excised surgically. Chemotherapy and radiotherapy have failed to make improvements in these patients. DNA analysis or other cellular markers may help in the management of these patients in the future.

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