Case Report

Chemoradiotherapy In Locally Invasive Parathyroid Cancer

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Abstract
Parathyroid carcinomas (PTC) are very rare and have a poor prognosis. A 48 year old case with locally invasive PTC that was positive for close surgical removal margin was treated with chemoradiotherapy after surgery. Even though this required bimodal chemo and radio adjuvant therapy, the patient was treated by chemoradiotherapy with some modifications, including oral administration of capecitabine. These treatments were well tolerated with minimal side effects, which have proven to be very effective in freeing the patient from the invasive tumor for the following twenty six months of monitoring. This treatment method could be adopted in place of the widely preferred surgical therapy. We believe that this case report will guide future studies concerning with similar cases.

Keywords
Parathyroid carcinoma; Chemo radiotherapy; Low toxicity; Positive surgical margin

Introduction
Parathyroid carcinomas are present in fewer than 1% of patients admitted to the hospital with hyperparathyroidism [1] and are often together with signs of hypercalcemia and high levels of serum calcium and parathormone [2,3]. The natural course of this disease is usually silent and shows progression in time. Surgery is usually the choice of treatment although there hasn’t been any conclusive treatment protocol for PTC. Death due to recurrences, local invasions, distant metastases and hypercalcemia crisis related with difficulties in diagnosis and inadequate surgery could be seen [4-6].

Even though adjuvant radiotherapy decreased local recurrences, radiotherapy and chemotherapy failed to provide a cure for PTC [7-11]. Since there has not been any further improvement in the overall and disease-free survival rates for the last thirty years [12], we set out to investigate the efficacy of adjuvant therapy of this disease.

In this report, we present a case with parathyroid carcinoma that was treated with chemoradiotherapy after surgery to improve overall and disease-free survival and to contribute to current literature since there hasn’t been any conclusive treatment protocol for this disease.

Case Report
A 48-year-old male patient with hypertension had hypercalcemia and high parathyroid hormone level. He was admitted to the Oncology Clinic. His serum calcium and parathyroid hormones were 14.5 mg/dL and 890 pg/dL, respectively. Since the thyroid and neck ultrasonography revealed isechoic solid nodules containing cystic degenerative fields in the left lobe of thyroid gland, parathyroidectomy and left thyroid lobectomy were performed. The pathology report was parathyroid carcinoma with a diameter of 3 cm after surgery. There were vascular invasion and positive surgical margins. Computed tomography scans of the neck, thorax and abdomen showed a hypodense lesion that was 2 cm in diameter in the liver, a few lytic lesions in the left ala of iliac bone with suggestion of Brown tumor or metastasis. For the verification of these lesions magnetic resonance imaging of the abdomen was performed and it showed simple hepatic cyst and bilateral renal cortical cysts. Focal activity increase in the parietal bone and the 6th left rib was defined in whole-body bone scintigraphy. There wasn’t any abnormal finding concerning malignancy in PET-CT imaging ordered for the discrimination of the lesions. The serum calcium and parathormone levels were 9.5 mg/dL (normal range: 8.8 – 10.6 mg/dL) and 87.5 pg/mL (normal range: 15-68.3) after operation. For the positive surgical margins, 64 Gy radiotherapy concurrent with capecitabine therapy (825 mg/m2/day) was given to the tumor bed.

The patient tolerated chemoradiotherapy well and there wasn’t any grade 3 or 4 toxicity during the treatment. One month after the treatment, ultrasonography of the thyroid and scintigraphy of the parathyroid were normal.

Bone scintigraphy revealed persistence of the calvarial lesions and disappearance of the left sixth costal lesion. Computed tomography of abdomen and thorax did not show any abnormality. The patient has been followed post-discharge without any recurrence and metastasis for the following 26 months. The findings of the patient during follow-up are summarized in Table 1.

There isn’t any staging for parathyroid cancers in the American Joint Committee on Cancer System [3]. Shaha et al. [13] made a staging according to being limited to parathyroid gland, extra glandular involvement and distant metastasis. The disease was staged as locally invasive.

Discussion
Carcinomas of the parathyroid gland are rare with non-specific symptoms like bone pain, arthralgia, head and neck pain, myalgia, loss of weight, paresthesia, polyuria, polydipsia, and constipation [3]. It is usually encountered in the fourth decade and slightly more in men than women [14]. The patient was male and 48 years-old, consistent with the literature.

Although parathyroid carcinoma has a slow and silent course, the prognosis of patients is worse in whom local recurrence and distant metastasis develop [15]. Even though some patients with parathyroid carcinoma present with severe clinical conditions such as bone lesions, renal disease and hypercalcemia crisis, some may not display any clinical signs [16]. This patient had cystic bone lesions, renal and hepatic cysts.
Laboratory findings in our case consistently showed elevated levels of serum Ca and PTH. The average Ca levels are reported to be 14.6 mg/dL [9]. The serum Ca level of the patient on admission was 14.5 mg/dL and the level of PTH was 13 fold higher than average. Their levels dropped to normal immediately after surgery. However, during the treatment after surgery, there was a slight elevation of PTH. We believe that this was because of PTH secretion by the marginal presence of residual tumor tissue. Near the end of the treatment, the PTH levels fell to normal as a result of the intervention.

In these patients, neck imaging by USG, BT, MRI, technetium-99m-sestamibi scintigraphy and PET are used to investigate the tumor and invasion of the peripheral tissues [17-20]. We sought PET CT scanning for our patient for the presence of distant metastasis.

It has been reported that parathyroid cancer (PTC) can occur as a result of secondary or tertiary hyperparathyroidism caused by multiple endocrine neoplasia I & II A and the end stage of renal failure [21-24]. However, none of these were present in our patient.

The prognosis of PTC is variable. It has been reported in some studies that removal of the tumor is the most important prognostic determinant and that the status of the surgical margin determines local or regional progression [17]. There is data indicating that Ki-67 levels bear prognostic value for PTC [25]. In a study concerning PTC survival, gender, age at the time of diagnosis, size of tumor, and preoperative serum Ca levels were monitored as prognostic factors for 22 years and no significant correlation was found [3].

The best curative treatment of PTC is reported to be the total excision of the tumor along with its margin [7]. While a recurrence rate of 8% has been reported postoperatively for comprehensive excision, the rate rose to 50% for excisions limited to the tumor mass only. In line with this, disease-free survival rate is reported to be 89% in wide surgical removals, which falls to 50% in mass excisions [24]. It has been reported that survival rates are 40-86% for 5 years and 49% for 10 years and that disease progression is through local invasion and recurrence [6]. Radiotherapy has been proposed for the reduction of the high postoperative recurrence rate of PTC, which is 30-67% [9, 17]. However, even though RT is reported to reduce the recurrence rate, it does not influence the prognosis [3].

Since PTC is RT responsive, it is recommended for curtailing tumor growth after incomplete surgical resection. In addition, since RT increases the disease-free survival time in high risk patients, adjuvant RT is recommended [26]. Since PCT is rare, it has not been investigated extensively and there is no tailored treatment protocol.

Several studies reported no clinical benefits of chemotherapy [3,8,26]. Even though nitrogen mustard, dacarbazine, cyclophosphamide, actinomycin D, Adriamycin, and 5-fluouracil have been recommended for the treatment of metastatic disease, their contribution to survival is unclear [11]. The results of adjuvant chemotherapy and RT of metastatic or recurrent disease have been disappointing [7].

In a recent comprehensive study that lasted 33 years data on 340 PTC patients have been analyzed [12]. While all patients underwent surgical therapy, only 8.9% received adjuvant RT and no chemotherpay was provided. In this study, survival rates ten years before and after 1997 were compared and no significant difference was found. As these cases received hardly any RT, the implication is that adjuvant RT may be of benefit. In the past survival rates of breast carcinoma cases that underwent surgical treatment only were improved only after chemotherapy and RT.

In summary, PTC is rare whose diagnosis is difficult and therapy remains inefficient. It seems that treatment by wide surgical excision combined with RT to minimize recurrence is the best available approach. Since adjuvant chemoradiotherapy reduces the incidence of local recurrence and improves survival, tolerable low toxicity adjuvant chemoradiotherapy may represent a treatment option. This case represents the short term results of chemoradiotherapy of PTC, which may be indicative of the long term outcome and shed light on its therapeutic management.

### References


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