Case Report

Hypercalcemia secondary to parathyroid hormone secretion from metastatic lesions in liver

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Parathyroid cancer is a rare malignancy with a prevalence of 0.005% of all registered cancer cases in the United States. Metastases are rare but when they occur the metastatic lesions are usually in the lungs and lymph nodes. There has been only one reported metastasis to the liver in the 233 combined year experience of several major medical centers. A 35-year-old man had 9 metastatic lesions in his liver which produced approximately 1500 mg/dl PTH and sustained hypercalcemia (12.3 mg/dl) even after surgical resection of the parathyroid cancer and a transient hypocalcemia.

Key words: Hypercalcemia, parathyroid hormone, liver secretion, metastases, parathyroid cancer.

INTRODUCTION

Parathyroid cancer is a rare endocrine malignancy with a prevalence of 0.005% of all registered cancer cases in the United States (Hundahl et al., 1999). It is also an uncommon cause of hypercalcemia in persons with parathyroid disease with only 0.4 to 3% of patients with hyperparathyroidism having parathyroid cancer (Cohn et al., 1985; Wang and Gaz, 1985; Sandelin et al., 1991; Hakaim and Esselstyn, 1993). The incidence of parathyroid cancer in parathyroidectomy patients is about 1% (Ruda et al., 2005). Metastases are rare but when they occur they most commonly involve the lymph nodes and lungs (Shane, 2001; Lang and Lo, 2006). Metastasis to liver is extremely rare with only one reported metastasis to the liver in the 233-years combined experience of the Massachusetts General Hospital (Wang and Gaz, 1985), University of Texas M.D. Anderson Hospital (Busaidy et al., 2004), Mayo Clinic (Wynne et al., 1992), University of California, San Francisco (Kebebew et al., 2001), University of Michigan (Sandelin et al., 1991), the Lahey Clinic (Cohn et al., 1985) and the Cleveland Clinic (Hakaim and Esselstyn, 1993).

This is the first case of a parathyroid cancer metastasis to liver that produced functional parathyroid hormone (PTH) and hypercalcemia. It is, thus, important to remember that hypercalcemia secondary parathyroid disease may not involve lesions in the neck but lesions elsewhere.

CASE STUDY AND DISCUSSION

A 35-years-old Caucasian man presented in 2008 to an outside hospital with anorexia, nausea and vomiting. He was found to have calcium of 14.7 mg/dl (reference range, 8.5 to 10.5 mg/dl), parathyroid hormone (PTH) of 1500 pg/ml (reference range 15 to 75 pg/ml) and a technetium (Tc)-99 me- thoxyisobutylisonitrile (MIBI) sestamibi scan revealed what appeared to be a parathyroid adenoma in the right neck. Pathological evaluation after removal of the right anterior neck mass revealed it was a parathyroid carcinoma (7 x 6 x 5 cm) that had marked nuclear anaplasia associated with multiple areas of tumor necrosis. This tumor infiltrated the capsule with multiple foci of lymphatic and vascular invasion. 2 out of 3 lymph nodes examined had partial replacement by metastatic carcinoma. The parathyroid carcinoma was focally infiltrating the capsule of the right lobe of the thyroid; however, the thyroid parenchyma...
itself was not replaced by carcinoma. The right lobe of the thyroid was surgically removed. Two years after his first parathyroid surgery, he presented with 3 days of nausea, vomiting and weakness. His serum calcium was elevated to 15.6 mg/dl and his PTH value was 1479 pg/ml. One year earlier his PTH was 143 pg/ml. On his current presentation his physical exam revealed a palpable mass in the neck as his only positive finding. Laboratory on admission: blood urea nitrogen 28 mg/dl (reference range, 6 to 20 mg/dl), serum creatinine 2.30 mg/dl (reference range, 0.5 to 1.7 mg/dl), Ca\(^{++}\) of 15.6 mg/dl (reference range, 8.5 to 10.5 mg/dl) and a decreased serum phosphorous of 1.8 mg/dl (reference range, 2.7 to 4.5 mg/dl). His potassium was decreased to 2.8 mmol/L (reference range, 3.5 to 5.3 mmol/L) with a sodium of 140 meq/L (reference range, 135 to 148 meq/L) and a serum osmolality of 284 mOsm/kg (reference range, 270 to 290 mOsm/kg). His total serum protein was 7.3 g/dl (reference range, 6.1 to 7.9 g/dl). 25-Hydroxy vitamin D was 47 ng/ml (reference range, 30 to 85 ng/ml). His alkaline phosphatase was elevated at 146 IU/L (reference range, 34 to 128 IU/L) with liver function tests within normal limits. A Tc-99 m sestamibi scintigraphy revealed a mass in the right tracheal groove. A computed tomogram of the thorax with upper abdominal images indicated 9 low density lesions in the liver consistent with metastatic lesions with the largest in the posterior segment of the right hepatic lobe being 3.8 × 3.1 cm (Figure 1). There was also a 3 × 1.9 cm mass in the left hepatic lobe and a 1.2 cm gastrohepatic lymph node (Figure 1).

The pathologic examination of the 2nd neck exploration revealed a 2.7 × 2.0 × 1.7 encapsulated mass weighing 5.6 g that was a parathyroid carcinoma, oxyphile type, with vascular invasion and the tumor present at the margins of the resection. His calcium decreased to 8.6 mg/dl by 48 h post surgery with PTH decreasing to 942 pg/ml. His calcium was in the hypocalcemic range at 6.2 mg/dl by the 4th day post-op. By the second week postoperatively, however, his calcium increased again to
12.3 mg/dl with a PTH of 1500 pg/ml. Parathyroid cancer is a rare malignancy with an estimated prevalence of 0.005% in the general population (Hundahl et al., 1999). Parathyroid cancer is usually an indolent tumor that tends to invade locally and commonly recurs in locoregional patterns after surgical resection (Shane, 2001; Lang and Lo, 2006; Dudney et al., 2010) as in the present patient. Metastasis is rare and occurs late in the disease with spread by both lymphatic and hematogenous routes (Shane, 2001; Lang and Lo, 2006) as in the present patient with invasion of both vascular and lymphatic systems in both the primary and recurrent parathyroid carcinomas on pathological exam. If a metastasis occurs, it most commonly involves the lymph nodes (30%) and lung (40%) (Lang and Lo, 2006). As an example of how rare liver metastases are, there has been only one reported case of liver metastasis and hypercalcemia was not reported with this metastasis, in the 233-years, combined experience of the University of Texas M.D. Anderson Hospital (Busaidy et al., 2004), Mayo Clinic (Wynne et al., 1992), Massachusetts General Hospital (Wang and Gaz, 1985), Cleveland Clinic (Hakaim and Esselstyn, 1993), University of Michigan (Sandelin et al., 1991), Lahey Clinic (Cohn et al., 1985) and the University of California, San Francisco (Kebebew et al., 2001). After the second removal of the parathyroid cancer in the right neck, he developed hypocalcemia but within 2 weeks postoperatively, his calcium increased to 12.3 mg/dl with a PTH of 1500 pg/ml, strongly suggesting that the large lesions in the liver were producing a biologically active PTH to cause his hypercalcemia. With respect to treatment of parathyroid cancer, several reports have stressed the importance of an en bloc resection including thyroid lobectomy with the isthmus and paratracheal and central neck nodal dissection for parathyroid carcinoma (Shane, 2001; Dudney et al., 2010). This procedure, when performed as the initial therapeutic step, offers patients the best chance for cure (Dudney et al., 2010).

Controversy exists as to whether patients without obvious tumor extension should be taken back to the operating room; the ipsilateral thyroidectomy, isthmusectomy, and excision of paratracheal and central neck nodes after the diagnosis of parathyroid carcinoma is determined pathologically (Dudney et al., 2010). Recurrent tumors that can be identified and are amenable to resection should be excised, even multiple times if necessary, for palliative relief from hypercalcemia (Fujimoto and Obara, 1987; Wynne et al., 1992; Kebebew et al., 2001; Shane, 2001). Because parathyroid carcinoma patients have multiple relapses over extended time periods, they should be monitored for life using serum calcium and PTH levels. If elevations of these disease markers are noted, signs of recurrence should be evaluated with localizing imaging studies such as ultrasonography, CT, MRI, sestamibi scanning or positron emission tomographic (PET) scanning (Busaidy et al., 2004). Recurrence after surgical excision of parathyroid carcinoma as in the present patient is common with rates ranging from 33 to 78% (Wynne et al., 1985; Sandelin et al., 1991; Kebebew et al., 2001).

Conclusion

This case study is important as it illustrates that hypercalcemia secondary to parathyroid disease may not be restricted to disease in the neck but may also be in other organs such as the liver. The hypercalcemia and markedly elevated parathyroid hormone level occurred 2 weeks after removal of the parathyroid cancer in the neck; that is presumably long before local recurrence. Therefore, the markedly elevated parathyroid hormone level was due to tumor progression at a distant site.

REFERENCES


