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Mini-Review

Parathyroid carcinoma; an updated mini-review on current trends

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Abstract

Parathyroid carcinoma is an infrequent endocrine disorder, commonly producing severe primary hyperparathyroidism. This is mainly a sporadic disorder, but it may occur in family primary hyperparathyroidism. Patients with parathyroid carcinoma regularly present with markedly elevated serum calcium and parathyroid hormone (PTH). Obviously, owing to the rarity of this cancer, there are no generalized procedures for its management; however, surgery remains to be the mainstay of treatment.

Keywords: Parathyroid carcinoma, Tertiary hyperparathyroidism, Neck radiation, Parathyroid adenoma, Parathyroid hormone

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Introduction

Behind of the thyroid, there are four glands named parathyroid which help the management of the calcium levels amid the human body (1). Parathyroid carcinoma is a scarce endocrine malignancy, accounting for an assessed 0.005% of all cancers (2). It was first explained by the Swiss surgeon Fritz De Quervain (3). In 1904, he illustrated a case of nonfunctioning metastatic parathyroid cancer, and 26 years later, Sainton and Millot explained the first case of operational metastatic parathyroid carcinoma (4). Additionally, Armstrong in 1938 explained another patient with metastatic parathyroid carcinoma and hypercalcemia (5), and in 1968, Holmes and colleagues (6) studied 50 cases of parathyroid carcinoma stated in the literature. It is commonly accepted that parathyroid carcinoma accounts for below 1% of cases of primary hyperparathyroidism (7), though, this number has been described to be higher in some studies, reaching up to 5% (8). Actually, parathyroid carcinoma frequently has an indolent growth with a trend for local invasion, and it appears with equal frequency in women and men (9). The age at demonstration for parathyroid carcinoma compared with adenoma is described to be a decade previous (10). It usually affects the ageing women and men and its clinical look is characterized by mild hypercalcemia, kidney manifestations, traditional classic bone disease and elevation of parathyroid hormone (PTH) and often subsequent in severe hypercalcemia (1).

It is noteworthy that, less than 10% of parathyroid carcinoma cases current as nonfunctional tumors (11). Though most patients with parathyroid carcinoma appear with hyperparathyroidism, a diagnosis of hyperparathyroidism ascribable to carcinoma may be problematic to arrive at preoperatively or even intraoperatively (12). In many situations, because of the rarity of the disorder and clinical topographies mimicking benign parathyroid pathology, preoperative diagnosis of parathyroid carcinoma is problematic. Furthermore, the pathologic diagnosis of malignancy is stimulating; nevertheless, severe hypercalcemia joined with high PTH levels and gross operative discoveries should arouse suspicion of parathyroid carcinoma. Hence, owing to its rarity and the paucity of large-scale available series of patients with parathyroid cancer, there still is an absence of understanding of the natural course and prognostic implications of this disorder.

The aim of this review is to examine and summarize the accessible literature on parathyroid cancer.

Materials and Methods

For this review, we used a diversity of sources by search¬ing through PubMed/Medline, Scopus, EMBASE, EBSCO and directory of open access journals (DOAJ). The search was conducted, using combination of the following key words and or their equivalents; parathyroid carcinoma, tertiary hyperparathyroidism, neck radiation and parathyroid adenoma.

Etiology and pathogenesis of parathyroid carcinoma

The etiology of parathyroid carcinoma is unidentified, and to date, no recognized predisposing factors have been recognized. Nevertheless, history of neck radiation is a recognized risk factor of head and neck carcinoma, and cases of patients with parathyroid cancer who earlier received radiation treatment to the neck have been designated (13). For example, In the describe by Koea and Shaw (14), 1.4% of the individuals with parathyroid cancer had prior history of neck irradiation; however, robust causal relationship between parathyroid (8). Other related factors previously designated contain secondary and tertiary hyperparathyroidism produced by chronic renal failure (15).

Carcinoma and radiation or way of life factors has not been explained. Other somatic gene mutations have been associated in the development of parathyroid carcinoma, counting abnormal expression of the retinoblastoma and p53 proteins. Likewise, the presence of an extra tumor suppressor gene on chromosome 13 in the vicinity of retinoblastoma gene has been suggested (16). But, no clinically significant deductions have been reached, and

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Implication for health policy/practice/research/medical education

Patients with parathyroid carcinoma regularly present with markedly elevated serum calcium and parathyroid hormone (PTH). Obviously, owing to the rarity of this cancer, there are no generalized procedures for its management; however, surgery remains to be the mainstay of treatment.

further examination is still required (17).

Diagnosis

The diagnosis of parathyroid cancer is quite problematic. It may be supposed during pre- or intraoperative phases however it is particularly made postoperatively through histological check. In some equivocal situations, pathology may also be inconclusive in place of the use of molecular markers, and the diagnosis must be verified only by the clinical course at a prolonged follow-up by the happening of distant metastasis (18).

In the other words, the preoperative diagnosis of parathyroid cancer can be very challenging. Many patients experience surgery for an assumed parathyroid adenoma with suspicion for a parathyroid cancer being elevated only during surgery. In others, the diagnosis becomes evident only later pathological inspection of the excised gland. In one study, in 14 out of 27 parathyroid cancer patients (52%), the verdict was made postoperatively based on histopathologic inspection (19). In spite of this finding, as previously mentioned, certain clinical, test center, and radiological answers should significantly increase clinical suspicion of malignant disorder. These include signs of severe hypercalcemia on presentation, counting profound renal and skeletal disorder (6), or parathyrotoxicosis. The attendance of a palpable neck mass in a sick with hyperparathyroidism should greatly increase suspicion of parathyroid cancer, as should the simultaneous advent of recurring laryngeal nerve paralysis and hyperparathyroidism. Calcium levels more than 3.5 mmol/l (14 mg/dl) (6) and an very elevated parathyroid hormone (PTH) (2) are also greatly indicative. Lastly, certain radiological results as mentioned above may be indicative of the presence of a malignant parathyroid cancer (17). Moreover, when a postoperative pathological endorsement of parathyroid cancer is obtained, a thorough examination to rule-out metastatic disorder involving the abdomen, chest, and skeletal system should be carried out. These examinations may include, whole body MRI, CT, and possibly FDG-PET/CT. A bone scan should be done to preclude bone metastasis (20).

Treatment

Parathyroid cancer tends to attack the nearby structures and to spread to regional lymph nodes (30% of instances). It may also distribute hematogenously, with liver (10%), lung (40%) and bones metastases (21). The prediction is quite variable, though it usually has a slow, lethargic but progressive course owing to the rather low malignant possible, with a described cumulative 5 and 10-year existence of 86% and 49%, one-to-one (12).

As mentioned above, parathyroid cancer is a slow-developing, however, aggressive malignant tumor and most patients expire of the metabolic problems of hypercalcemia. Consequently, the goals of therapy of the primary lesion, local recurrence, or metastatic disorder should be to reduce all demonstrable disorder when possible and to manage the metabolic problems of hyperparathyroidism (22).

In parathyroid cancers, hypercalcemia should be treated with vital and aggressive restoration of fluid volume (these patients are significantly dehydrated). Furosemide (loop diuretics) are given to rise renal calcium excretion after appropriated rehydration. Bisphosphonates (drugs which prevent osteoclast-mediated bone resorption by combination into the bone matrix) are efficient but they lose effectiveness over time (21). Pamidronate, infused in amounts of 30–90 mg/day over 2–4 times, is efficient, at least briefly, replies last for 1–3 weeks and the therapy can be repeated. On the other hand, possible problems of bisphosphonates are signified by avascular necrosis of the jaw and critical renal failure.

Recently, novel drugs (calcimimetics) have been industrialized for PTH-related hypercalcemia. Cinacalcet performances as an effective allosteric modulator of calcium sensing receptors that are responsible for the management of PTH secretion. It attaches to the calcium receptors on the surface of parathyroid cells and rises the receptor sensitivity to extracellular calcium and subsequently decreases serum PTH and calcium levels. Cinacalcet is administered orally (30–60 mg/daily) and it is well tolerated. However, it does not adapt the course of parathyroid carcinoma. Consequently, it cannot substitute surgical intervention in the case of resectable disorder. This medicine can potentially alleviate the consequences of hypercalcemia in patients with extensively metastatic disorder or renal insufficiency (23).

Obviously, the only most effective treatment for parathyroid cancer is complete resection of the main lesion at the time of primary operation (21). Parathyroid cancer is not a radiosensitive tumor (21). In the same way, because of the rarity of parathyroid cancer, few investigators have sufficient numbers of patients to certification a large scale clinical experimental. Attempts to management tumor with chemotherapy have been upsetting (21). In fact, complete surgical resection with microscopically negative limits is the recommended therapy and offers the best chance of remedy. Persistent or recurrent disorder occurs in over 50% of patients with parathyroid cancer. Surgical resection is similarly the primary mode of treatment for recurrence since it can offer noteworthy palliation for the metabolic derangement produced by hyperparathyroidism and permits hypercalcemia to become more therapeutically manageable. On the other hand, reoperation is hardly curative and eventual revert is likely. Chemotherapy and external ray radiation therapies have been generally unsuccessful in the treatment of parathyroid cancer. Usually, these patients need repeated operations that incline them to accumulated surgical risks with each interference (7).

As a matter of fact, the prediction of parathyroid carcinoma is quite adjustable. Indeed, no one characteristic correlates probably with consequence. Primary recognition and complete resection at the time of the early surgery carry the best prediction. The mean time between surgery and the first recurrence is about three years, though intervals of up to 20 years have been described. After the tumor has recurred, complete treatment is unlikely (21).

Conclusion

Parathyroid cancer is a very infrequent endocrine malignancy, however, in patients with early hyperparathyroidism is very essential (24), especially due to its mortality (25). Parathyroid cancer could appear equally between two genders (26) but the occurrence of parathyroid cancer is rising worldwide despite its rare incidence, with youth and being female as two vital related factors (27). There is no accessible lifestyle factor associated with parathyroid cancer (2). Actually, the cause of parathyroid cancer is yet to be established and there is no data to verify causal

relations between parathyroid cancer and any risk factor (28), though it may be some relatives with familial and irregular forms (12).

Furthermore, parathyroid carcinoma is normally related to a prolonged clinical course, with numerous recurrences the majority of which happen locally. Owing to limited value of adjuvant treatments, the recommended therapy for relapses and metastases is similarly surgical resection, when technically possible. Additional multi-centric investigations are required in order to further comprehend this rare clinical entity, and to advance more effective therapy methods.

Author's contribution

MRA is the single author of the manuscript.

Conflicts of interest

The author declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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References

1. Gupta SP, Mittal A, Sathian B. Significance of HCG to distinguish parathyroid carcinoma from benign disease and in adding prognostic information: a hospital based study from Nepal. Asian Pac J Cancer Prev. 2013;14:325-7.
2. Dudney WC, Bodenner D, Stack BC. Parathyroid carcinoma. Otolaryngol Clin North Am. 2010;43:441-53.
3. DeQuervain F. Parastruma maligna aberrata [Malignant aberrant parathyroid]. Deusche Zeitschr Chir. 1904; 100:334-52.
4. Sainton P, Millot J. Malegne dun adenoma parathyroidiene eosinophile. Ann Anat Pathol. 1933;10:813-4.
5. Armstrong H. Primary carcinoma of the parathyroid gland with report of a case. Bull Acad Med Tor. 1938;11:105-10.
6. Holmes EC, Morton DL, Ketcham AS. Parathyroid carcinoma: a collective review. Ann Surg. 1969;169:631.
7. Wei CH, Harari A. Parathyroid carcinoma: update and guidelines for management. Curr Treat Options Oncol. 2012; 13:11-23.
8. Mohebati A, Shaha A, Shah J. Parathyroid carcinoma: challenges in diagnosis and treatment. Hematol Oncol Clin North Am. 2012;26:1221-38.
9. Rao SR, Shaha AR, Singh B, Rinaldo A, Ferlito A. Management of cancer of the parathyroid. Acta Otolaryngol. 2002;122:448-52.
10. Cohn K, Silverman M, Corrado J, Sedgewick C. Parathyroid carcinoma: the Lahey Clinic experience. Surgery. 1985; 98:1095-100.
11. Wilkins BJ, Lewis JS Jr. Non-functional parathyroid carcinoma: a review of the literature and report of a case requiring extensive surgery. Head Neck Pathol. 2009;3:140-9.
12. Hundahl SA, Fleming ID, Fremgen AM, Menck HR. Two hundred eighty-six cases of parathyroid carcinoma treated in the US between 1985–1995. Cancer. 1999;86:538-44.
13. Obara T, Fujimoto Y. Diagnosis and treatment of patients with parathyroid carcinoma: an update and review. World J Surg Oncol. 1991;15:738-44.
14. Koea JB, Shaw JH. Parathyroid cancer: biology and management. Surg Oncol. 1999; 8:155-65.
15. Khan MW, Worcester EM, Straus FH, Khan S, Staszak V, Kaplan EL. Parathyroid carcinoma in secondary and tertiary hyperparathyroidism. J Am Coll Surg. 2004;199:312-9.
16. Shattuck TM, Kim TS, Costa J, Yandell DW, Imanishi Y, Palanisamy N, et al. Mutational analyses of RB and BRCA2 as candidate tumour suppressor genes in parathyroid carcinoma. Clin Endocrinol. 2003;59:180-9.
17. Al-Kurd A, Mekel M, Mazeh H. Parathyroid carcinoma. Surg Oncol. 2014;23:107-14.
18. Iacobone M, Lumachi F, Favia G. Up-to-date on parathyroid carcinoma: Analysis of an experience of 19 cases. J Surg Oncol. 2004;88:223-8.
19. Busaidy NL, Jimenez C, Habra MA, Schultz PN, El-Naggar AK, Clayman GL, et al. Parathyroid carcinoma: A 22-year experience. Head Neck. 2004;26:716-26.
20. Evangelista L, Sorgato N, Torresan F, Boschin IM, Pennelli G, Saladini G, et al. FDG-PET/CT and parathyroid carcinoma: Review of literature and illustrative case series. World J Clin Oncol. 2011;2:348-54.
21. Shane E. Clinical review 122: parathyroid carcinoma. J Clin Endocrinol Metab. 2001;86:485.
22. Rodgers SE, Perrier ND. Parathyroid carcinoma. Curr Opin Oncol. 2006;18:16-22.
23. Favia G, Iacobone M. Parathyroid Carcinoma. Primary, Secondary and Tertiary Hyperparathyroidism. Springer; 2016. p. 183-91.
24. Kassahun WT, Jonas S. Focus on parathyroid carcinoma. Int J Surg. 2011;9:13-9.
25. Talat N, Schulte KM. Clinical presentation, staging and long-term evolution of parathyroid cancer. Ann Surg Oncol. 2010;17:2156-74.
26. Schoretsanitis G, Daskalakis M, Melissas J, Tsiftsis DD. Parathyroid carcinoma: clinical presentation and management. Am J Otolaryngol. 2009;30:277-80.
27. Lee PK, Jarosek SL, Virnig BA, Evasovich M, Tuttle TM. Trends in the incidence and treatment of parathyroid cancer in the United States. Cancer. 2007;109:1736-41.
28. Ohe MN, Santos RO, Hojaij F, Neves MC, Kunii IS, Orlandi D, et al. Parathyroid carcinoma and hungry bone syndrome. Arq Bras Endocrinol Metabol. 2013;57:79-86