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An updated mini-review on parathyroid cancer

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Abstract

Parathyroid cancer is a rare malignancy originating from the parathyroid glands, which regulate calcium levels in the body. This review article aims to provide a comprehensive overview of parathyroid cancer, including its epidemiology, etiology, clinical presentation, diagnostic methods, treatment options, and prognosis. The article also highlights recent advancements in research and potential future directions for improving the management of this challenging disease.

Keywords: Parathyroid cancer, Parathyroid glands, Malignancy, Primary hyperparathyroidism, Multiple endocrine neoplasia type 1, Metastasis

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Introduction

Parathyroid cancer is a rare malignancy that arises from the parathyroid glands, which regulate calcium levels in the body (1,2). Parathyroid cancer's rarity presents unique diagnostic and therapeutic challenges (3). This mini-review aims to provide a comprehensive overview of parathyroid cancer, including its epidemiology, etiology, clinical presentation, diagnostic modalities, treatment options, and prognosis. Additionally, we will discuss the ongoing research efforts and future directions in managing this rare malignancy.

Search strategy

For this review, we extensively searched various databases including PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ), and Embase. We used a wide range of keywords to ensure comprehensive results, such as parathyroid cancer, parathyroid glands, malignancy, primary hyperparathyroidism, multiple endocrine neoplasia type 1, hypercalcemia, kidney stones, bone pain, neck masses, hoarseness, dysphagia, and metastasis.

Epidemiology

Parathyroid cancer is an extremely rare malignancy, accounting for less than 1% of all cases of primary hyperparathyroidism. It predominantly affects middle-aged adults, with a slight female predominance (2,3). Parathyroid cancer's exact incidence and prevalence are

difficult to determine due to its rarity and the lack of population-based studies (4).

Etiology of parathyroid cancer

The etiology of parathyroid cancer remains largely unknown. However, specific genetic syndromes, such as multiple endocrine neoplasia type 1 (MEN1) and hyperparathyroidism-jaw tumor syndrome (HPT-JT), have been associated with an increased risk of developing parathyroid cancer. Somatic mutations in genes such as CDC73 and HRPT2 have also been implicated in the pathogenesis of sporadic parathyroid cancer (2,5).

Clinical presentation

Parathyroid cancer often presents symptoms similar to primary hyperparathyroidism, including hypercalcemia, kidney stones, bone pain, and fatigue. However, patients with parathyroid cancer may also experience more severe manifestations, such as palpable neck masses, hoarseness, dysphagia, and respiratory distress (2,6).

Diagnosis of parathyroid cancer

The diagnosis of parathyroid cancer is challenging and relies on a combination of clinical, biochemical, radiological, and histological findings. Serum calcium and parathyroid hormone levels are typically elevated in patients with parathyroid cancer. Imaging modalities such as ultrasound, computed tomography, magnetic resonance imaging, and technetium-99m sestamibi scintigraphy can

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■ Implication for health policy/practice/research/medical education

Parathyroid cancer is an uncommon malignancy originating from cells of the parathyroid glands. Despite its rarity, cases of parathyroid cancer are increasing, necessitating a comprehensive understanding of its clinical presentation, diagnosis, and treatment.

aid in localizing the tumor (7,8). Definitive diagnosis requires histopathological examination of the resected tissue, which may reveal characteristic features such as capsular invasion, vascular invasion, and mitotic activity (9,10).

Clinical features and diagnosis

Parathyroid cancer usually affects adults, with a slight female predominance. Patients often present with symptoms related to hypercalcemia, such as fatigue, kidney stones, bone pain, and neuropsychiatric manifestations (2,8). However, these symptoms can overlap with those of benign parathyroid disease, making diagnosis challenging. Radiological imaging, including neck ultrasound, computed tomography, and technetium sestamibi scan, are helpful in localization. Still, a definitive diagnosis typically needs histological examination through fine-needle aspiration or surgical biopsy (11,12).

Molecular Pathways and prognostic factors

The molecular pathways involved in parathyroid cancer are still being elucidated. Common genetic alterations, such as cyclin D1 (CCND1) and retinoblastoma 1 (RB1) gene mutations, have been identified, along with alterations in the Wnt signaling pathway (13,14). These insights into the molecular basis of parathyroid cancer may aid in the development of targeted therapies in the future. Additionally, several prognostic factors, including tumor size, presence of lymph node or distant metastases, and histological characteristics, have been identified to guide treatment decisions and predict patient outcomes (15,16).

Treatment

Surgical resection is the mainstay of treatment for parathyroid cancer. However, due to the rarity and aggressiveness of the disease, complete resection is often challenging, and local recurrence and distant metastasis are common. Adjuvant therapies, including radiation therapy and chemotherapy, have shown limited efficacy in improving outcomes. Targeted therapies, such as tyrosine kinase inhibitors and mammalian target of rapamycin (mTOR) inhibitors, are currently being investigated in clinical trials (17,18).

Multidisciplinary approach

Managing parathyroid cancer necessitates a collaborative

effort from a multidisciplinary team consisting of endocrinologists, surgeons, pathologists, radiologists, and oncologists. This collaboration is crucial for ensuring an accurate diagnosis, optimizing surgical intervention, and developing personalized treatment plans tailored to each patient's circumstances (1,19).

Prognosis of parathyroid cancer

Parathyroid cancer is associated with a poor prognosis with a high risk of recurrence and metastasis. The 5-year survival rate ranges from 50% to 80%, depending on the stage of the disease. Prognostic factors include tumor size, extent of invasion, lymph node involvement, and distant metastasis (17,20).

Conclusion

Parathyroid cancer is a rare, aggressive malignancy with significant diagnostic and therapeutic challenges. Further research is needed to improve our understanding of the underlying molecular mechanisms, develop effective targeted therapies, and identify reliable prognostic markers. Multidisciplinary collaboration and international registries are crucial for advancing the management and outcomes of patients with parathyroid cancer.

Authors' contribution

Conceptualization: MAEP, AK.

Validation: MAEP, AK.

Investigation: MAEP, AK.

Resources: MAEP, AK.

Data Curation: MAEP, AK.

Visualization: MAEP, AK.

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Writing—original draft preparation: MAEP, AK.

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Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

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References

- Byrd C, Kashyap S, Kwartowitz G. Parathyroid Cancer. [Updated 2022 Jul 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK519038/>
- Sharretts JM, Kebebew E, Simonds WF. Parathyroid cancer. *Semin Oncol.* 2010;37:580-90. doi: 10.1053/j.seminoncol.2010.10.013.
- Marcocci C, Cetani F, Rubin MR, Silverberg SJ, Pinchera A, Bilezikian JP. Parathyroid carcinoma. *J Bone Miner Res.* 2008;23:1869-80. doi: 10.1359/jbmr.081018.
- Ferraro V, Sgaramella LI, Di Meo G, Prete FP, Logoluso F, Minerva F, et al. Current concepts in parathyroid carcinoma: a single Centre experience. *BMC Endocr Disord.* 2019 May

- 29;19:46. doi: 10.1186/s12902-019-0368-1.
5. Sharretts JM, Simonds WF. Clinical and molecular genetics of parathyroid neoplasms. *Best Pract Res Clin Endocrinol Metab.* 2010;24:491-502. doi: 10.1016/j.beem.2010.01.003.
 6. Ziaeean B Md, Sohrabi-Nazari S Md. Huge Parathyroid Adenoma with Dysphagia Presentation; A Case Report from Southern Iran. *Iran J Med Sci.* 2016;41:446-9.
 7. Bao Y, Kang G, Wu X, Li J, Huang Y, Wang Y. Mediastinal parathyroid carcinoma: a case report and review of the literature. *BMC Endocr Disord.* 2023;23:130. doi: 10.1186/s12902-023-01363-w.
 8. Givi B, Shah JP. Parathyroid carcinoma. *Clin Oncol (R Coll Radiol).* 2010;22:498-507. doi: 10.1016/j.clon.2010.04.007.
 9. Sali AP, Motghare P, Bal M, Mittal N, Rane S, Kane S, et al. Parathyroid Carcinoma: A Single-Institution Experience with an Emphasis on Histopathological Features. *Head Neck Pathol.* 2021;15:544-554. doi: 10.1007/s12105-020-01244-x.
 10. Ghossein R. Update to the College of American Pathologists reporting on thyroid carcinomas. *Head Neck Pathol.* 2009;3:86-93. doi: 10.1007/s12105-009-0109-2.
 11. Obołończyk Ł, Karwacka I, Wiśniewski P, Sworczak K, Osęka T. The Current Role of Parathyroid Fine-Needle Biopsy (P-FNAB) with iPTH-Washout Concentration (iPTH-WC) in Primary Hyperparathyroidism: A Single Center Experience and Literature Review. *Biomedicines.* 2022;10:123. doi: 10.3390/biomedicines10010123.
 12. Gowrishankar SV, Bidaye R, Das T, Majcher V, Fish B, Casey R, et al. Intrathyroidal parathyroid adenomas: Scoping review on clinical presentation, preoperative localization, and surgical treatment. *Head Neck.* 2023;45:706-720. doi: 10.1002/hed.27287.
 13. Cardoso L, Stevenson M, Thakker RV. Molecular genetics of syndromic and non-syndromic forms of parathyroid carcinoma. *Hum Mutat.* 2017;38:1621-1648. doi: 10.1002/humu.23337.
 14. Arnold A. Major molecular genetic drivers in sporadic primary hyperparathyroidism. *Trans Am Clin Climatol Assoc.* 2016;127:235-244.
 15. Sawhney S, Vaish R, Jain S, Mittal N, Ankathi SK, Thiagarajan S, et al. Parathyroid Carcinoma: a Review. *Indian J Surg Oncol.* 2022;13:133-142. doi: 10.1007/s13193-021-01343-3.
 16. Ullah A, Khan J, Waheed A, Sharma N, Pryor EK, Stumpe TR, et al. Parathyroid Carcinoma: Incidence, Survival Analysis, and Management: A Study from the SEER Database and Insights into Future Therapeutic Perspectives. *Cancers (Basel).* 2022;14:1426. doi: 10.3390/cancers14061426.
 17. Alberti A, Smussi D, Zamparini M, Turla A, Laini L, Marchiselli C, et al. Treatment and outcome of metastatic parathyroid carcinoma: A systematic review and pooled analysis of published cases. *Front Oncol.* 2022;12:997009. doi: 10.3389/fonc.2022.997009.
 18. Machado NN, Wilhelm SM. Parathyroid Cancer: A Review. *Cancers (Basel).* 2019;11:1676. doi: 10.3390/cancers11111676.
 19. Benali K, Aarab J, Benmessaoud H, Nourreddine A, Majjaoui SE, Kacemi HE, et al. Intrathyroidal parathyroid carcinoma: a case report and literature review. *Radiat Oncol J.* 2021;39:145-151. doi: 10.3857/roj.2020.01060.
 20. Adam MA, Untch BR, Olson JA Jr. Parathyroid carcinoma: current understanding and new insights into gene expression and intraoperative parathyroid hormone kinetics. *Oncologist.* 2010;15:61-72. doi: 10.1634/theoncologist.2009-0185.