International Clinical and Medical Case Reports Journal
Case Report (ISSN: 2832-5788)

Water-Clear Cell Parathyroid Adenoma: A Rare Entity in Tertiary Hyperparathyroidism

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Citation: Sheenam Azad, Saqib Ahmed, Anita Jaiswal. Water-Clear Cell Parathyroid Adenoma: A Rare Entity in Tertiary Hyperparathyroidism. Int Clinc Med Case Rep Jour. 2026;5(7):1-3.

Received Date: 13 July 2026; **Accepted Date:** 14 July 2026; **Published Date:** 16 July 2026

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ABSTRACT

Water-clear cell parathyroid adenoma (WCCA) is an exceptionally rare histological variant of parathyroid adenoma, representing less than 1% of cases. It is composed of cells with abundant glycogen-rich clear cytoplasm and often poses a diagnostic dilemma due to its resemblance to metastatic clear-cell neoplasms. We present a case of a 61-year-old male with end-stage renal disease and tertiary hyperparathyroidism. Imaging revealed a lesion posterior to the left thyroid lobe. Histopathological examination demonstrated sheets of clear cells with distinct borders and hyperchromatic nuclei, consistent with WCCA. Careful exclusion of other clear-cell tumors was essential for diagnosis. Awareness of this entity is crucial to avoid misdiagnosis and ensure appropriate clinical management.

INTRODUCTION

Water-clear cell parathyroid adenoma is a rare morphological subtype of parathyroid adenoma, accounting for approximately 0.15% of all parathyroid lesions. It is characterized by large polygonal cells containing abundant clear cytoplasm due to intracellular glycogen accumulation.

Clinically, these tumors are often associated with relatively low hormonal activity compared to their size, large tumor size at presentation, diagnostic overlap with other clear-cell neoplasms, particularly metastatic renal cell carcinoma. Due to these features, WCCA represents a significant diagnostic challenge in endocrine pathology and requires careful clinicopathological correlation.

CASE REPORT

A 61-year-old male presented with end-stage renal disease with tertiary hyperparathyroidism unresponsive to medical therapy. Biochemical Findings revealed markedly elevated serum parathyroid hormone (PTH) levels with disturbed calcium phosphate homeostasis consistent with tertiary hyperparathyroidism. Radiological findings magnetic resonance imaging (MRI) of the neck showed a well-defined lesion located posterior to the left thyroid lobe. The

excised specimen was sent for histopathological examination. Gross examination showed a well circumscribed nodular mass with cut surface showing homogeneous area without areas of necrosis or hemorrhage. Microscopic examination showed sheets and nests of large polygonal cells with abundant clear to vacuolated cytoplasm, distinct cell borders with small, hyperchromatic nuclei and absence of significant atypia, mitosis, or capsular/vascular invasion (Figure 1a, b and c). Based on these findings a final diagnosis of water-clear cell parathyroid adenoma was given.

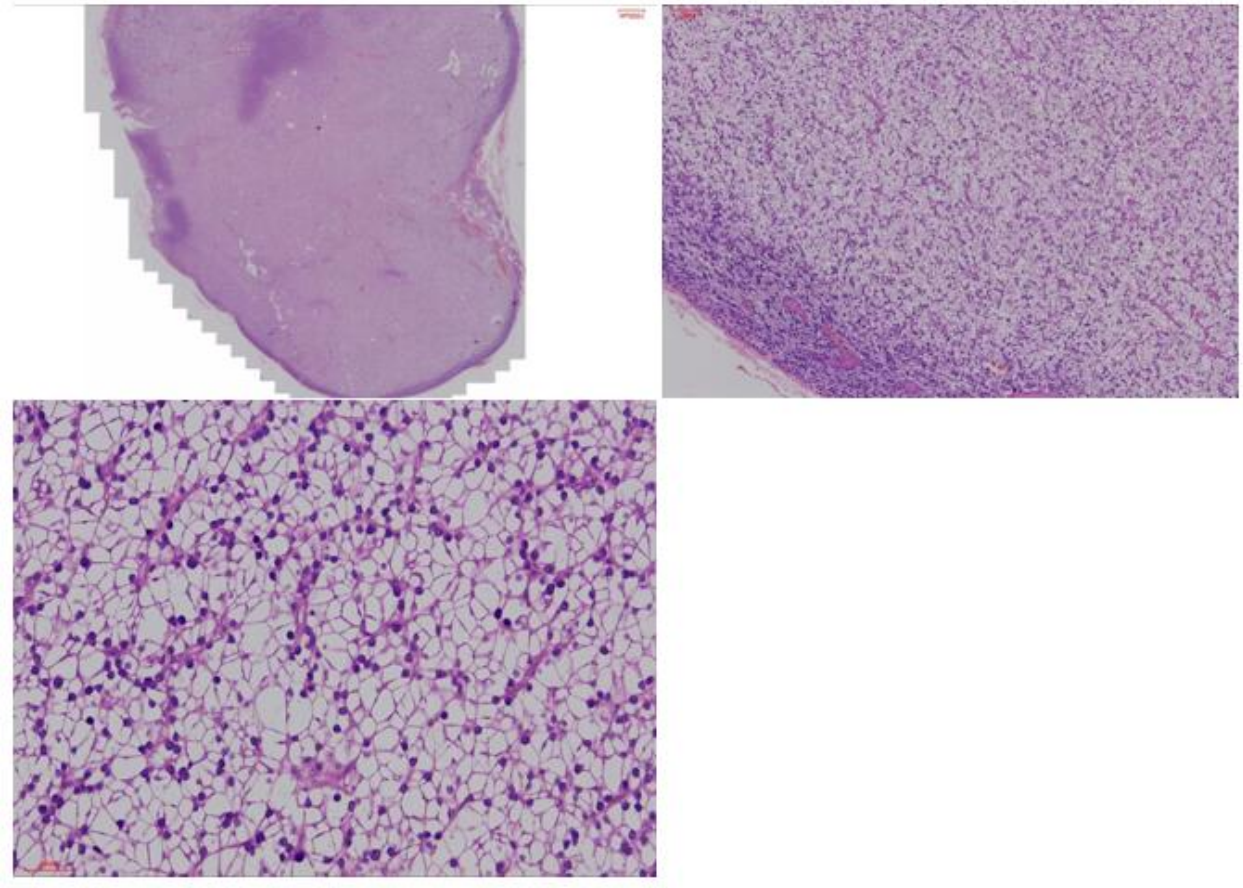

Figure 1a,b,c: Microscopic examination showed a well ciscumscibed lesion (a-X4) with sheets and nests of large polygonal cells with abundant clear to vacuolated cytoplasm, distinct cell borders with small, hyperchromatic nuclei and absence of significant atypia, mitosis, or capsular/vascular invasion (b-X40, c- X100, H and E).

DISCUSSION

Water-clear cell parathyroid adenoma is a rare but well-recognized entity with distinct histomorphological characteristics. The clear cytoplasm observed in these tumors is attributed to accumulation of glycogen, which can be demonstrated using periodic acid–Schiff (PAS) staining. The pathogenesis of WCCA is not completely understood; however, in patients with chronic renal failure, prolonged hypocalcemia and secondary hyperparathyroidism may lead to sustained stimulation of parathyroid glands. Over time, this persistent stimulation can result in nodular transformation and eventual adenoma formation. Metabolic alterations within tumor cells may contribute to the development of the characteristic clear-cell morphology.

A major diagnostic challenge lies in distinguishing WCCA from metastatic clear-cell renal cell carcinoma (RCC), especially in small biopsy samples. Both entities share overlapping morphological features, including clear cytoplasm and nested architecture. However, WCCA typically lacks significant cytological atypia and shows positivity for parathyroid hormone (PTH) on immunohistochemistry, whereas RCC expresses markers such as RCC antigen and CD10. Another important consideration is differentiation from water-clear cell hyperplasia, which usually involves multiple glands, whereas adenomas are typically solitary lesions. Additionally, parathyroid carcinoma must be excluded by the absence of invasive features such as capsular or vascular invasion and significant mitotic activity. From a clinical standpoint, WCCA tends to exhibit lower endocrine activity relative to tumor size, which may delay diagnosis. However, in the setting of tertiary hyperparathyroidism, as in the present case, the biochemical abnormalities are often pronounced due to underlying renal pathology. Recognition of this rare entity is essential for pathologists to avoid misinterpretation as metastatic malignancy, which could lead to unnecessary investigations and inappropriate management.

CONCLUSION

Water-clear cell parathyroid adenoma is a rare and diagnostically challenging lesion. Accurate diagnosis relies on a multidisciplinary approach incorporating clinical history, biochemical parameters, radiological findings, histopathological examination with adjunct immunohistochemistry. Early and precise identification is crucial to prevent misdiagnosis and guide appropriate surgical management.

Acknowledgement: None

Source of Support: None

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