

Carotid Body Paraganglioma with Prominent Lymphocytic Infiltration Mimicking Metastatic Lymph Node: A Case Report

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ABSTRACT

Carotid body paraganglioma is a neuroendocrine neoplasm of the mandibular region. Due to its prominent stromal alternations, carotid body paraganglioma is a great emulator of other neoplasms in the head and neck region especially in metastatic tumors and its definite diagnosis is a great challenge. To the best of our knowledge, the most frequently reported variant is sclerosing and paraganglioma with a prominent lymphoplasmacytic infiltration is extremely rare. We report a rare case of a carotid body lymphoplasmacytic paraganglioma presented as a single asymptomatic mass of the right mandibular region in a 45-year-old woman. In order to exclude other possibilities, the use of immunohistochemistry is essential which shows a strong positive immunoreaction for chromogranin and synaptophysin. Surgical resection is the treatment of choice which is replaced with radiotherapy in contraindications. Overall, the tumor has a favorable clinical outcome.

KEYWORDS: Head and neck neoplasms, Carotid body tumor, Neuroendocrine tumor

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Introduction

Extra adrenal paraganglioma is a neuroendocrine neoplasm originating from paraganglionic cells of the autonomic nervous system with a slow growing pattern (1). This tumor predominantly occurs in the abdominal cavity in 85% of the cases and only 3% of cases occur in the head and neck region (1,2). Paraganglioma in the head and neck is most frequently seen in the carotid body (3).

The tumor usually occurs in the fifth decade of one's life with a marginally higher incident rate in women (4). It is often presented as a single asymptomatic or painless mass on the mandibular region, but bilaterality and multiplicity have also been reported in 4-8% of patients mostly in hereditary syndromes, especially in Multiple Endocrine Neoplasia 2 (MEN2) and Von Hippel Lindau Syndrome (VHL) disease (3,5).

Hormonal disorders are detectable in 1-3% of cases that develop the same clinical symptoms as pheochromocytoma (1).

Because of its prominent stromal alternations, in microscopic examinations this tumor is observed as a great emulator of other neoplasms, especially metastatic lymph node, which means that the definite diagnosis could be pathologically challenging (3,4,6).

In order to exclude other possibilities, the use of immunohistochemistry is essential, which shows a strong positive immunoreaction for chromogranin and synaptophysin.

The presence of a positive reaction for S100 protein in sustentacular cells located at the periphery of the nests is highly resourceful (5,6). Surgical resection is the treatment of choice which is replaced with radiotherapy in contraindications (7). Overall, the tumor has a favorable clinical outcome. A malignant transformation in the carotid body is rare and has been reported only in 2% of the cases (8).

Case Report

We report, a case of carotid body paraganglioma, presenting as a single asymptomatic mass of right mandibular region in a 45-year-old woman, with no evidence of other abnormalities in physical examinations. In MRI, a well-defined hypervascular mass was visualized. The patient underwent surgery and the resected well-circumscribed mass showed tan nodular cut surfaces resembling lymphoid tissue ([Figure 1](#)). A neoplasm made of cell nests with round to oval nuclei was observed in microscopic examination, granular eosinophilic cytoplasm

surrounded by sustentacular cells embedded in a dense lymphoplasmacytic stroma containing few collagen bundles (Figure 2). According to clinicopathological findings, paraganglioma and certain differential diagnoses such as metastatic neuroendocrine carcinoma, or metastatic medullary thyroid carcinoma to a lymph node tumor were also taken into account. The cells showed diffuse positive

immunoreaction for chromogranin and synaptophysin, S100 protein and Neuron-Specific Enolase (NSE) with negative reaction for estrogen receptor, thyroid transcription factor-1(TTF-1) and thyroglobulin and cytokeratin (Figure 3). Unfortunately the tyrosine hydroxylase marker was not available in our laboratory. The follow-up of the patient one year later revealed no tumor recurrence.

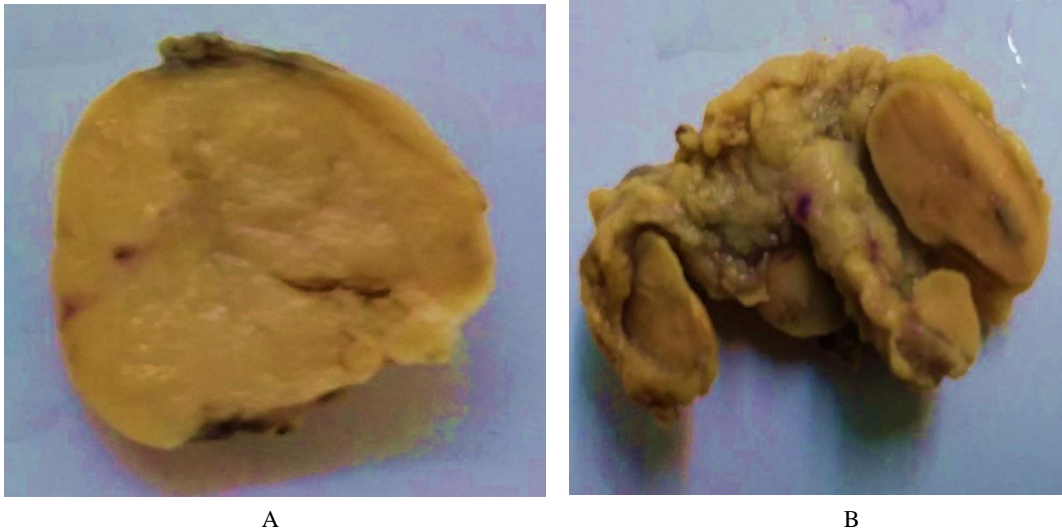


Fig. 1. A: Macroscopic examination show an encapsulated tan nodular mass resembling lymphoid tissue. B: Macroscopic examination show an encapsulated tan nodular mass resembling lymphoid tissue

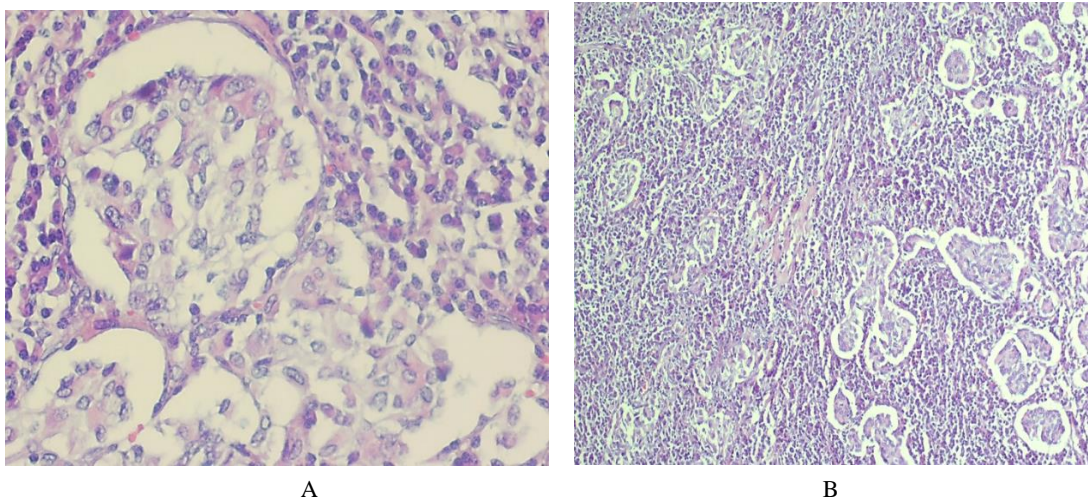


Fig. 2. A (hematoxylin-eosin, magnification 400X), B (hematoxylin-eosin, magnification 100X), section shows nests of the cells with eosinophilic cytoplasm surrounded by sustentacular cells in a dense lymphoplasmacytic stroma

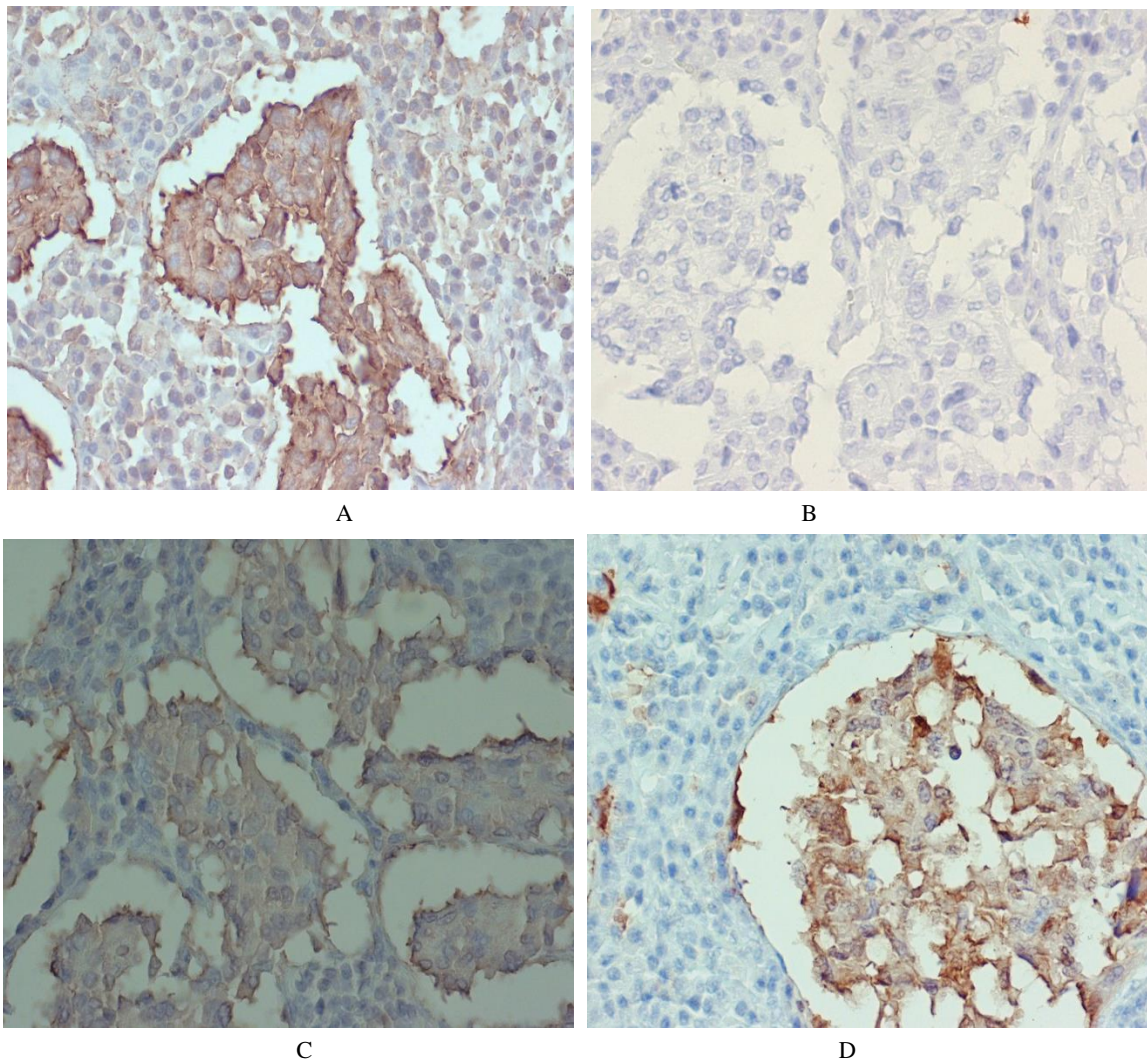


Fig. 3. Positive immunoreaction for chromogranin (A), synaptophysin (B), and S100 protein in peripheral sustentacular cells (C) with negative reaction for cytokeratin markers (D).

Discussion

The most reported variant of paraganglioma (PG) is a sclerosing that accounts for 16 cases in accordance to previous studies, and to the best of our knowledge, cases with prominent lymphoplasmacytic infiltration are extremely rare. (4,8,9,10). As observed in our reported case and similar to other variants like sclerosing, the site and onset of the carotid body may be typical in middle-aged women for PG with prominent lymphoplasmacytic infiltration.

Some studies show a considerable predilection of the carotid body PG in middle-aged women (mean age of 50.5 years) (4). The differential diagnosis of PG with prominent lymphoplasmacytic infiltration may be extensive in the head and neck region (9,10). The stroma embedding the tumor cells accompanied by cytological atypia, possibly infiltrating the lesion, may be interpreted as malignant, even though substantial mitotic activity and necrosis are absent (6,8,9). Prominent lymphoplasmacytic infiltrated stroma may also develop in metastatic carcinoma involving regions such as the larynx, breast, and lung.

In equivocal cases, immunostains can confirm the diagnosis. Carcinomas show a diffuse positive reaction to cytokeratin and epithelial membrane antigen (EMA), whereas, the majority of PGs are cytokeratin-negative (5,6,9). A new marker, Tyrosine hydroxylase, as an enzyme in catecholamine synthetic pathway is also positive in PGs. Although this marker plays an important role in its confirmation, it could be negative in nonfunctional paragangliomas, especially when occurred in the head and neck region. So, in these challenging conditions (keratin and tyrosine hydroxylase negative tumors) another new marker named as trans-acting T-cell-specific transcription factor (GATA-binding protein 3 [GATA-3]) may be helpful, although this marker could be also expressed in tumors like nonendocrine and parathyroid tumors. (11,12)

Metastasis of neuroendocrine carcinomas to a lymph node and PGs with prominent lymphoplasmacytic infiltration share the usual nesting pattern of a ribbon-like or trabecular arrangement (13). Generally, PGs exhibit a more dominant *zellballen* architecture than neuroendocrine carcinomas (8).

Relatively few ultrastructural studies have been conducted on the human carotid body and other head and neck paraganglia (8). In a case reported by Robertson and coworkers, a malignant carotid body PG was observed in which a large number of cells had ample mitochondria resembling oncocytes (14).

In summary, despite being rare, a PG with prominent lymphoplasmacytic infiltration can challenge the diagnosis and result of the over diagnosis. Pathologically, a correct diagnosis will be more possible by gaining information about the uncommon growth pattern of PG and the appropriate immune-stains.

Conclusion

Our case indicates that although carotid body paraganglioma is a neuroendocrine tumor, the condition involves a favorable behavior. However, because of its varied histologic features, especially a dense lymphoplasmacytic infiltration, it stimulates other neoplasms. A metastatic lymph node must be considered in a differential diagnosis of the head and neck tumors with lymphocytic infiltration.

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Conflict of Interest

The authors declared that there is no conflict of interest regarding the publication of this article.

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