CASE REPORTS

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Chemodectoma and Tetralogy of Fallot

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ABSTRACT

Objectives: To describe a rare case of chemodectoma, its clinical features and management and to discuss its relationship chronic hypoxia from Tetralogy of Fallot.

Methods:

Design: Case Report
Setting: Tertiary Government Hospital
Patient: One

Results: A 23-year-old woman presented with a painless, slow growing, movable right submandibular mass, initially diagnosed as a lipoma by fine needle aspiration biopsy. Computed tomography scan showed a solid nodule with ill-defined margins from the angle of the mandible to the level of the hyoid bone along the carotid sheath. There was also an incidental finding of patent ductus arteriosus and Tetralogy of Fallot on pre-operative clearance. Excision of the mass under general anesthesia revealed adherence to the posterior portion of the carotid trunk enveloping both the internal & external carotid artery. Final histopathological diagnosis was chemodectoma.

Conclusion: Although rare, chemodectoma should be considered as one of the differentials in a patient with a submandibular mass. Hyperplastic chemodectoma may result from chronic hypoxia due to Tetralogy of Fallot. Surgical excision is the treatment of choice.

Keywords: *Carotid Body Tumor, Chemodectoma, Paraganglioma, Tetralogy of Fallot*

Paragangliomas arise from extra-adrenal paraganglionic cells of the neural crest.[1] Various terminologies have been used to describe these tumors based on their location and histology. A chemodectoma is a paraganglioma arising from the chemoreceptors of the carotid body. It is a rare carotid body tumor, accounting for 0.5% of masses occurring in the head and neck region.[2,3]

We present a case of chemodectoma initially diagnosed as a lipoma by fine needle aspiration biopsy and discuss its clinical features, management and its relationship with chronic hypoxia from Tetralogy of Fallot.

Case Report

A 23-year-old woman presented with a painless, slow-growing right submandibular mass that started seven years before as a 2 x 2 cm soft, non-tender, mobile mass with well-circumscribed borders. No consult was sought nor medications taken until she visited a physician five years prior to admission due to a progressive enlargement of the mass.

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CT scan revealed a solid nodule measuring 5.0 x 3.0 x 4.0 cm in the right neck with ill-defined margins extending from the mandibular angle to the level of the hyoid bone along the carotid sheath (*Figure 1*). A fine needle aspiration biopsy revealed lipoma (*Figure 2)* but she did not follow-up until seventeen months prior to admission, when she was finally admitted for surgery.

On routine pre-operative cardiopulmonary examination, a patent ductus arteriosus (PDA) and a Tetralogy of Fallot (TOF) were discovered. She was started on carvedilol and was cleared for surgery.

Intraoperatively, a 5 x 4cm, dark brown, rubbery mass was seen attached to the carotid bifurcation (*Figure 3*). Despite careful dissection of the mass from the carotid, massive blood loss amounting to 1.8L ensued. As the working diagnosis was a lipoma, no blood had been prepared for perioperative use and the procedure was aborted.

Four days later, reoperation resulted in complete gross excision of the mass with preservation of the carotid arteries (*Figure 4*). Blood loss of 1.7L was replaced by transfusion of 2 units pRBC. At the post-anesthesia care unit (PACU), several bouts of oxygen desaturation resolved with oxygenation and completion of the blood transfusion. Hoarseness on the 1st post-operative day was attributed to right vocal cord paralysis diagnosed by indirect video laryngoscopy. The rest of the post-operative course was unremarkable and the patient was discharged on the 5th post-operative day.

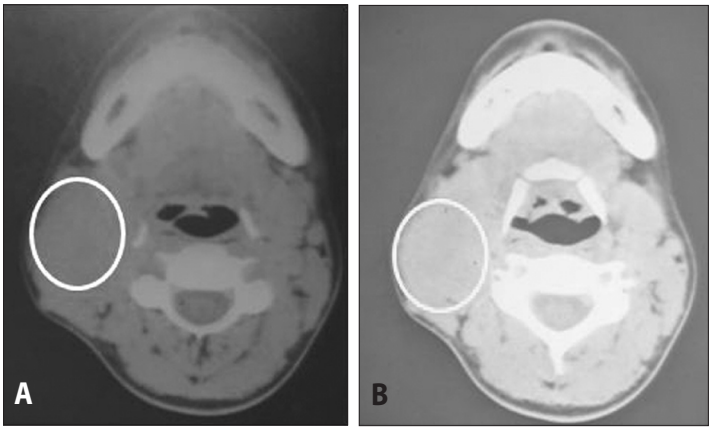
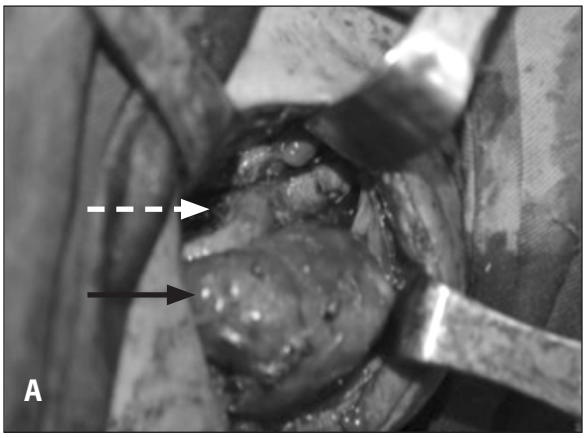


Figure 1. CT scan of the neck, axial view, at the level of the **A.** mandible **B.** hyoid bone, showing an ill-defined mass with intact nasopharyngeal retropharyngeal spaces. Carotid sheath not seen.



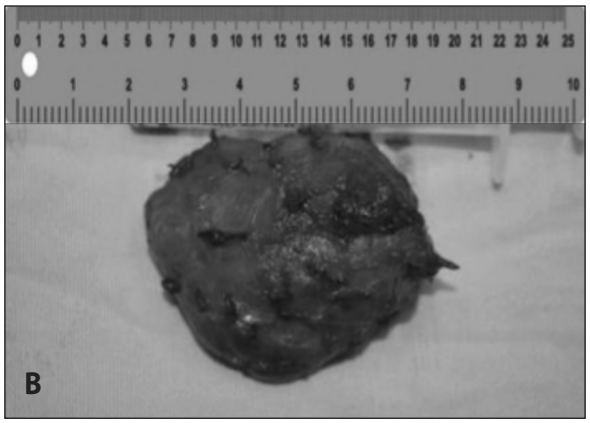


Figure 3 A. Intraoperative view showing reddish-brown mass (arrow) attached to the carotid bifurcation (dotted arrow). **B.** Gross specimen after excision.

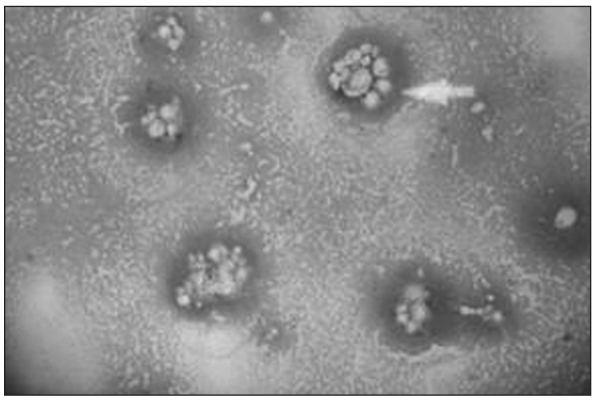


Figure 2. Fine needle aspiration biopsy photomicrograph (high power magnification, 40X) showing clusters of adipose tissue (yellow arrow) in a background of pink amorphous material, interpreted as lipoma.

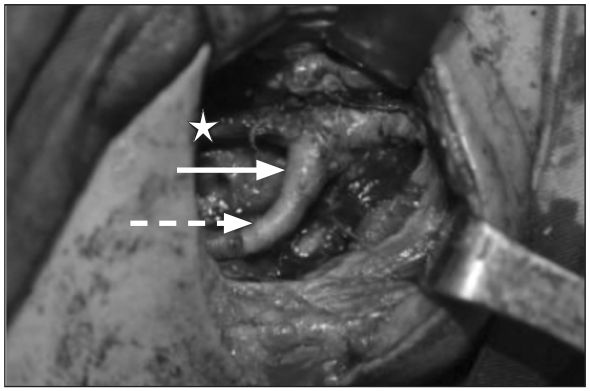


Figure 4. Common carotid artery bifurcation (arrow) after excision of the mass showing preserved External Carotid (dotted arrow) and Internal Carotid arteries (star).

Histopathologic gross examination revealed light to dark brown, irregular and rubbery tissue measuring 4.5 x 3 x 2.5 cm. Microsections disclosed epithelioid cells arranged in an organoid pattern exhibiting pleomorphism with course chromatin pattern, prominent nucleoli and scanty to ample cytoplasm in a fibrocollagenous stroma. Mitotic figures were rare (*Figure 5*). These findings were interpreted as consistent with a chemodectoma.

The patient was seen every 6 months for a year after her surgery with improvement of hoarseness in just 3 months post-operatively. There was no aspiration or recurrence of the mass.

DISCUSSION

The priority in our case of a submandibular mass that was mobile, slow growing, soft, painless and non-pulsatile was to establish the diagnosis. Our differentials based on location and presentation included branchial cleft cyst, TB adenitis, a submandibular new growth, or lymphoma. Fine needle aspiration cytology revealed lipoma ruling out our other considerations. Review of the aspirate by another cytopathologist still diagnosed a lipoma.

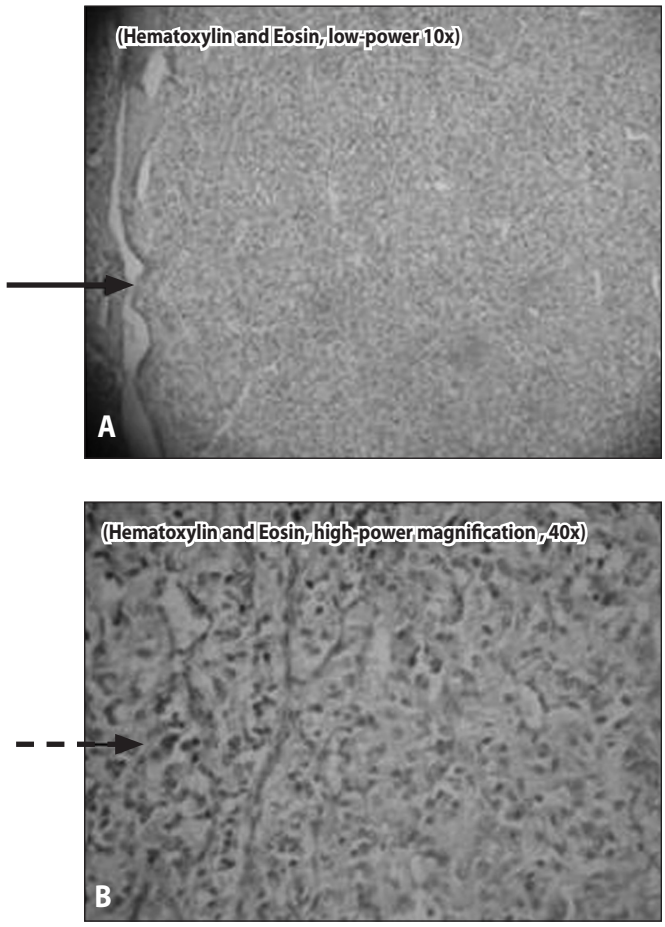


Figure 5 A. Histopathologic section, Hematoxylin-Eosin (low-power,10X) showing epitheliod cells in an organoid pattern seen in chemodectoma (arrow). **B.** High-power magnification (40X) shows cells exhibiting pleomorphism, with coarse chromatin pattern and scanty cytoplasm (dotted arrow).

In our case, "a chemodectoma was not entertained due to the absence of typical signs such as (1) a pulsatile slow growing mass that would have been mobile laterally and less mobile in a cranio-caudal direction because of its adherence to the carotid arteries (positive Fontaine sign), and (2) a bruit on auscultation."[1]

Although our fine-needle biopsy may have aspirated subcutaneous fat or cervical fibrofatty tissue, the aspirate of a chemodectoma, according to Masilamani *et al*., is hemorrhagic with clusters of round to oval cells showing anisokaryosis.[4] Delicate fibrous strands with spindle cells are observed within these clusters. These round to oval cells are seen as balloon-like which on poor fixation with ethyl alcohol and longer exposure to air-drying may result in poor slide quality and cellular degeneration. This can be read as a lipoma aspirate as by a cytopathologist.

According to O'Neill *et al.* "biopsy of a chemodectoma is rarely employed because of the risk of carotid injury or hemorrhage in these highly vascular tumors and open biopsy is clearly contraindicated due to the risk of catastrophic hemorrhage."[3] Also, according to Tayyab *et al*., fine needle aspiration cytology for chemodectomas is usually inconclusive.[2]

O'Neill *et al.* opined that "diagnostic modalities such as a Magnetic Resonance Imaging (MRI) and CT scan are useful for determining the extent of tumor and demarcating soft tissue planes to provide the anatomic detail crucial for planning the surgical approach."[3] A crucial, and curiously absent finding on the CT scans of our patient was the lack of enhancement typically found in chemodectomas (since they are intensely enhancing due to their extensive vascularity). Neither was splaying of the internal and external carotid arteries (the so-called "lyre sign") seen.

Our working diagnosis was a submandibular pleomorphic adenoma since the physical examination was not consistent with a lipoma. It was only intraoperatively when we noted that the mass surrounded the common carotid, internal & external carotid arteries that a chemodectoma was considered.

There are three treatment modalities for carotid body tumor-- tumor embolization, radiotherapy and surgical excision. According to Tayyab *et al.,* "tumor embolization has been questioned because of potential neurologic complications. Radiotherapy has been used in patients with metastatic lesions or tumors presumed to be malignant in certain series but recurrence has been observed after initial control."[2] Thus, Rekha *et al*. state "surgical excision is the best option but tumors with greater than 5 cm diameter have a 67% risk of complications versus 15% for tumors less than 5 cm in diameter."[5]

Tayyab *et al*. further say "cranial nerve palsies still remain one of the

major complications and occur in 10-40% of cases."[2] They found "that 0.6% resulted in mortality, stroke in 2.3%, and postoperative peripheral nerve dysfunction in 29% of patients."[2] Our patient manifested with hoarseness, aspiration and right vocal cord palsy as a result of vagus nerve injury.

Duran *et al*. reported that "paragangliomas arising from the carotid bodies account for 60% of all head and neck paragangliomas."[6] According to Rekha *et al*., "there is an increased incidence of these tumors in high altitude dwellers," which is not exactly seen in our patient, "and an in increased preponderance in females with a female to male ratio of 5:1."[5]

According to Rekha *et al*. and Aydogan *et al*., "there are three types of chemodectomas-- sporadic, which is the most common, familial, and hyperplastic. Chemodectomas are generally sporadic in nature, accounting for 85% of carotid body tumors and are more frequently multicentric in 30% - 40 % of cases. Familial cases occur in 7% to 10%. The inheritance pattern is autosomal dominant and passed on by the father."[5,8] There was no known family history of a similar tumor in our patient.

As Sajid *et al.* state, "the hyperplastic form is very common in patients with chronic hypoxia which includes patients living at high altitude (>5,000 feet above sea level) and in those with cyanotic heart disease."[9] Our patient was diagnosed with congenital heart disease-- a Patent Ductus Arteriosus and Tetralogy of Fallot (TOF). The development of her carotid body tumor may be attributed to these congenital heart diseases.

Several authors agree that "patients with congenital heart disease particularly TOF suffer chronic hypoxia. This can overburden the carotid body leading to hypertrophy, hyperplasia and neoplasia of the chief cells."[10-13] As Lopez-Barneo and colleagues said, "the carotid body is a peripheral chemoreceptor whose primary function is to detect changes in arterial oxygen tension in hypoxia. It is composed of neuron-like glomus, type I cells, which are enveloped by processes of glia-like sustentacular, type II cells that have the ability to proliferate and differentiate into glomus cells in response to hypoxia. These type I cells are the chemoreceptive elements that contain O_2 sensitive K^+ channels whose open probability decreases during hypoxia."[16]

Exposure to chronic hypoxia predisposes these glomus cells to undergo mitosis with resultant marked enlargement of the carotid body caused by dilatation and multiplication of blood vessels, as well as expansion of the parenchyma, with increased number of glomus cell clusters, thus resulting in hypertrophy and cellular hyperplasia of the carotid body. Tumorigenesis has been attributed to a defect in sensing environmental O_2 levels which is due to a decrease by 50% mitochondrial comples II activity.[16]

Post-operatively, it is recommended to follow-up the patient and monitor for tumor recurrence both on the ipsilateral and contralateral carotid body. The question of treating the patent ductus arteriosus and tetralogy of fallot arises because they might cause regrowth of a chemodectoma. This relationship is just an association at present and not entirely proven due to lack of published documents supporting this theory. This case report, however, supports this association. The question of whether the chemodectoma of this patient was brought about by the presence of a cardiac problem or was just merely coincidental remains unanswered.

Chemodectoma is a rare vascular neoplasm of the head and neck and it should be considered as one of the differentials in a patient with a submandibular mass particularly in the background of congenital heart disease. Chronic hypoxia brought about by TOF may have an association with hyperplasia of the chief cells of the carotid body leading to neoplasia and chemodectoma development. Surgical excision is the treatment of choice. Massive blood loss and cranial nerve damage are common complications of surgical excision and should be anticipated.

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