Diagnostic Cytopathology

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BRIEF REPORT

Extra-Adrenal Paraganglioma on Fine-Needle Aspiration Cytology: A Case Series

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Received: 26 February 2024 | **Revised:** 24 July 2024 | **Accepted:** 6 August 2024

Keywords: carotid body paraganglioma | extra-adrenal paraganglioma | FNAC

ABSTRACT

Paragangliomas (PGs) are rare tumors that most commonly occur in the head and neck region and along the sympathetic chain. Fine-needle aspiration cytology is not commonly used for the diagnosis of PG due to the potential risk of hemorrhage and hypertensive crisis. As a result, limited studies describe the cytological features of PGs. In this case series, we will discuss the fine-needle aspiration features of three cases of extra-adrenal PGs. The cellular arrangement in smears was either singly scattered or loosely cohesive clusters. The cells were polygonal with pleomorphic nuclei, abundant granular cytoplasm, and bland chromatin. Cellblock showed two types of cells with focal acinar formation. Immunohistochemistry also confirmed the diagnosis. These results were also in keeping with radiological findings. Fine-needle aspiration cytology, along with clinicoradiological findings, can help in making an accurate preoperative diagnosis of PG.

1 | Introduction

Paragangliomas (PGs) are rare tumors that develop from neural crest cells of the neuroendocrine system [1]. Some secrete catecholamines, while others may be hormonally inactive [2]. Functional PGs may cause symptoms such as diaphoresis, hypertension, flushing, hypertensive cardiomyopathy, and psychological issues [3]. Mediastinal PGs are uncommon, highly vascularized tumors developed from chromaffin tissue in the para-aortic ganglia [4]. PGs are uncommon tumors, accounting for less than 0.3% of mediastinal tumors and less than 2% of all PGs [5].

Although fine-needle aspiration cytology (FNAC) is not recommended for suspected PGs due to the risk of hypertensive crisis during the procedure, this tumor may still be diagnosed incidentally on FNAC [3]. This case series describes a rare example of extra-adrenal paraganglioma (EAP) diagnosed through FNAC.

2 | Case Presentation

2.1 | Case 1

In Case 1, we received ultrasound-guided fine-needle aspiration of the para-aortic lymph node of a 42-year-old female. She displayed clinical symptoms of lethargy, occasional bradycardia, and syncope. On radiology, a well-defined spherical, homogeneously enhanced soft tissue density mass measuring 3.0 × 2.5 cm was detected in the para-aortic region.

FNAC was performed, and two alcohol-fixed and two air-dried slides were sent to us, along with a cellblock. Cytomorphological evaluation of the smears and cellblock revealed clusters of polygonal to oval cells with eosinophilic coarsely granular cytoplasm against a hemorrhagic background (Figure 1). Subsequently, immunohistochemistry was performed on the cellblock. The cells were diffusely positive for synaptophysin, with some scattered sustentacular cells showing patchy S100 protein staining. Since

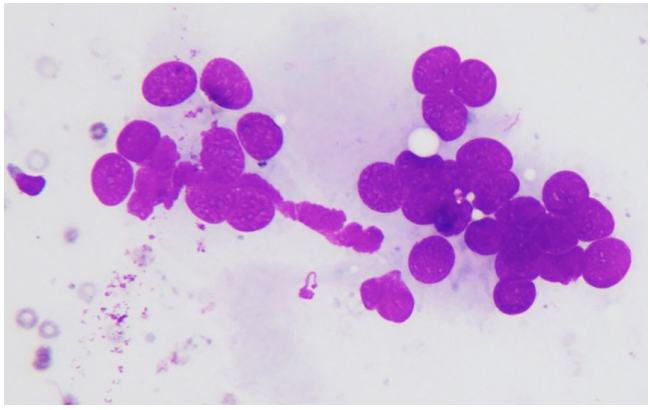

FIGURE 1 | Diff quik showing cells with loosely cohesive acini. Nuclei are slightly pleomorphic with abundant cytoplasm and granular chromatin. [Color figure can be viewed at wileyonlinelibrary.com]

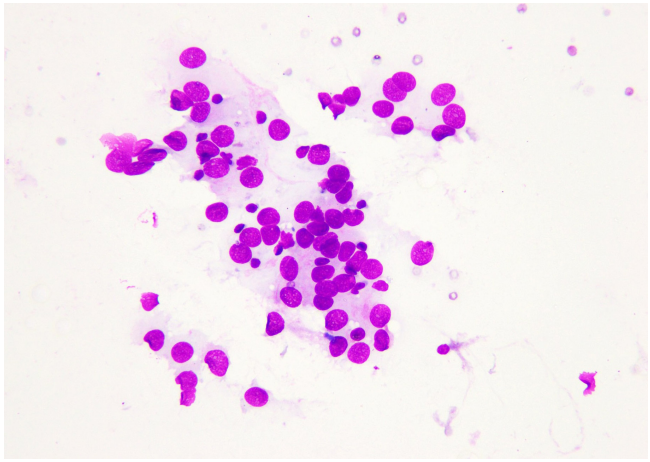

FIGURE 2 | Diff quik smear of Case 2 showing scant round to oval scattered cells with granular cytoplasm with vacuolations. Many singly scattered cells are seen in the background. [Color figure can be viewed at wileyonlinelibrary.com]

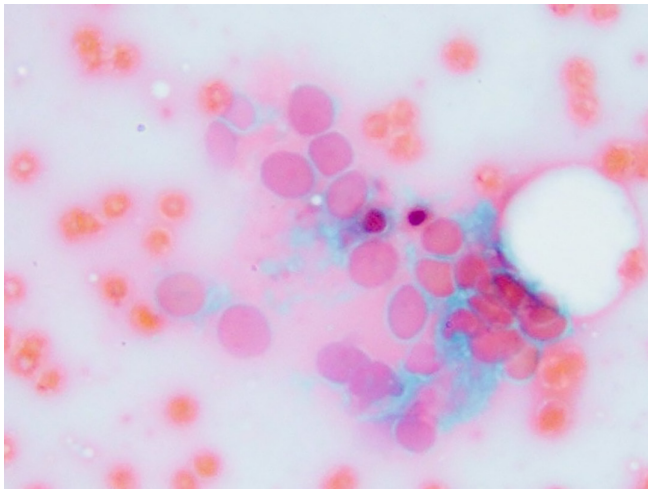

FIGURE 3 | Pap smear of Case 2 showing cells with stippled chromatin with inconspicuous nucleoli and mild variation in shape and size. [Color figure can be viewed at wileyonlinelibrary.com]

cytokeratin was negative, the neuroendocrine tumor was ruled out, and the case was reported as PG.

2.2 | Case 2

The second case we reported in the parapharyngeal space involved a 22-year-old male patient with a parapharyngeal mass. On radiology, it was a well-circumscribed, hypoechoic solid mass in the parapharyngeal space at the bifurcation of the carotid artery. FNAC was performed, and three alcohol-fixed and two air-dried smears have been prepared and sent to us. Analysis of smears revealed hemorrhagic aspirate with moderate cellularity. The cells are round to oval, singly scattered, and arranged in loose clusters. Individual cells show granular cytoplasm and stippled chromatin with rare nuclear inclusions. A few singly scattered spindled cells are also identified, most likely representing the sustentacular cells (Figures 2 and 3). No cellblock was available in this case. The final diagnosis of a carotid body tumor was made and further confirmed on histopathology.

2.3 | Case 3

Our third patient was a 36-year-old female with a solid, well-defined mass in the left carotid triangle measuring 47 × 32 mm. Ultrasonographic findings were suggestive of PG; however, MRI was consistent with vagal schwannoma. FNAC of the lesion was performed, and the material for the cellblock was also taken along with smear preparation.

Cytomorphological examination showed very cellular smears, with cells showing mild variation in shape and size. However, the nuclear contours were regular with abundant granular cytoplasm (Figure 4). Many transgressing vessels were also identified. The background showed abundant hemorrhage. Cellblock material was scant but showed cells with variation in size and shape. Cytology findings, along with clinical findings, were suggestive of PG, and hence the final diagnosis.

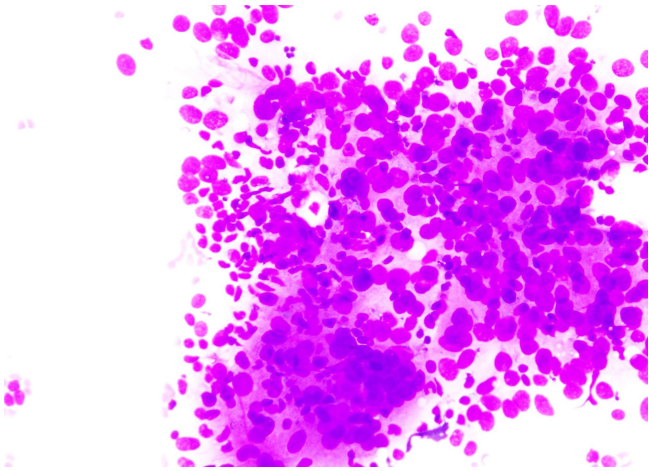

FIGURE 4 | Diff quik of Case 3 showing cellular smears with clusters of cells showing mild variation of shape and size with abundant granular cytoplasm. Abundant sustentacular cells are seen. [Colorfigure can be viewed at wileyonlinelibrary.com]

3 | Results

PGs are rare neoplasms that account for less than 0.05% of all neoplasms. The ratio of females to males affected by PGs is 2:1, with a mean age of 33 years. The symptoms experienced by patients depend on the location of the PG. In all cases, the smears were cellular, with cells distributed in clusters and singly scattered patterns. Cytomorphological features were consistent in almost all cases, with cells being round to polygonal in shape and showing variations in nuclear size and shape, as well as inconspicuous nucleoli. The cytoplasm was granular with focal vacuolation, and intranuclear inclusions were also observed. A cellblock was made and showed cells with abundant granular cytoplasm with prominent nuclei. Sustentacular cells were also identified. Cellblocks were made in two cases, and immunohistochemical stains were applied. In one case, where a cellblock was not available, the diagnosis was confirmed through histopathology. All cases were also confirmed through radiology. The comparison of cytological features of all the cases is given in Table 1.

4 | Discussion

PG is a rare type of neuroendocrine tumor that develops from neural crest cells. The World Health Organization (WHO) defines this tumor as one that produces, stores, and secretes catecholamine and can originate from extra-adrenal locations. Most PGs in the mediastinum arise from the sympathetic ganglia, located in the posterior region of the para-aortic or paravertebral ganglia [6]. In 17%–43% of cases, PGs in the thorax, abdomen, and pelvis are nonfunctional [7]. Most of these tumors grow slowly and tend to invade the surrounding tissue, with a high local recurrence rate after surgical removal [8]. According to Erickson et al.'s research, PGs (69%) are mainly located in the head and neck regions, while those in the mediastinum account for only 2% [7]. These tumors usually present between the ages of 30 and 60 years are sporadic and occur more frequently in women than men [9]. In our series, two cases are carotid body PGs. Among EAP, carotid body tumors are the most common. As they are located at the bifurcation of the carotid artery, they usually appear as a painless, lymph node–like mass in neck. Some patients may experience symptoms, but usually, there are not many symptoms.

Many cases found in the medical literature that was diagnosed using FNAC were either carotid body PGs or other EAPs diagnosed incidentally. Due to the risk of bleeding, FNAC is usually not recommended, especially when the patient is experiencing symptoms. EAP is typically diagnosed through a combination of clinical and radiological examinations. However, in the cases we observed, FNAC was performed because the patients were asymptomatic, and a tissue correlation was required to confirm the diagnosis.

EAPs exhibit a wide range of cytomorphological features. Upon comparing the cytological features of these three cases, it is evident that the cellular features are similar, except in one case, which is not a carotid body PG, there are scant sustentacular cells compared to the other two cases. The background is hemorrhagic in all cases.

Limited data are available about the cytological features of EAP and most of the cases described in the literature are of carotid body tumors. However, range of cytological and architectural characteristics can be observed, but there are some consistent findings in all cases, which can aid in making a confident diagnosis on FNAC. In our study, all cases displayed cells with nuclei of varying sizes, but nuclear membranes were smooth. The cytoplasm was abundant and had a fine pink texture. A few small spindly cells were also present, which are likely to be sustentacular cells. Other rare features included intranuclear pseudoinclusions and focal membrane irregularities. Varma, Jain, and Mandal [10], Handa, Kundu, and Mohan [11], and Dukkipati and Kumar [12] reported similar findings in their studies.

FNA has been a very useful diagnostic tool for detecting mass lesions. However, its effectiveness in diagnosing PG is debatable due to the risk of hemorrhage, which can be life-threatening. However, in our case, all the patients were stable after the procedure, and there were no complications. FNAC, along with

TABLE 1 | Comparison of cytomorphological features of three cases.

Features	Case 1	Case 2	Case 3
Cellularity	Good cellularity	Moderate cellularity	Very cellular
Cell arrangement	Clusters of round to oval cells	Round to oval cells, singly scattered, and arranged in loose clusters	Clusters with mild variation in size and shape
Cytoplasm	Eosinophilic, coarsely granular cytoplasm	Granular cytoplasm with vacuolations	Abundant granular cytoplasm
Nuclear features	Inconspicuous nucleoli	Stippled chromatin with inconspicuous nucleoli	Regular nuclear contours with stippled chromatin
Special cell types	Rare sustentacular cells	Many singly scattered spindled cells, likely sustentacular cells	Sustentacular cells present
Background	Hemorrhagic	Hemorrhagic	Abundant hemorrhage
Additional features	Not specified	Nuclear inclusions	Many transgressing vessels

radiological findings and clinical data, can aid in diagnosing PG. This observation has also been supported by other studies [13, 14]. The only limitation of FNA is that it cannot differentiate properly between benign and malignant lesions; however, increased mitotic rate and pronounced nuclear atypia would be associated with malignant lesions.

5 | Conclusion

Diagnosing PG on FNAC is highly challenging due to its great morphological variability. However, an accurate diagnosis depends on pertinent clinical history, exact anatomical location, cytomorphologic image, and ancillary tests. The patients had no adverse effects following FNA, thus supporting the reliability and safety of cytologic diagnosis.

Author Contributions

Aribah Atiq: conceptualization, writing – original draft, and review. **Zubaria Rafique:** writing – original draft. **Ujyara Maryam Lone:** pictures. **Azra Bashir:** writing – original draft. **Faria Waqar Khan:** review. **Akhtar Sohail Chughtai:** final review.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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