Case Report

Cytomorphology of pituitary carcinoma metastatic to liver diagnosed by fine-needle aspiration: A rare case report and review of literature

Pallavi Srivastava, MBBS, MD, PDCC, Anurag Gupta, MBBS, MD, MIAC, Kiran Preet Malhotra, MBBS, MD, PDCC, Nuzhat Husain, MBBS, MD

1Department of Pathology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh, India.

INTRODUCTION

Pituitary carcinoma (PC) is a rare neoplasm of adenohypophysis defined as a pituitary adenomas (PA) presenting with non-contiguous craniospinal or systemic metastasis. PC constitutes about 0.1–0.2% of all pituitary neoplasms. About 170 cases have been reported in the literature with adrenocorticotropic hormone and prolactin (PRL)-secreting adenomas being the most common. Fine-needle aspiration (FNA) has shown utility as a modality of diagnosis for such rare neoplasms in six cases till date; hence, the cytologic features are not well defined. Herein, we report a case of PA having high Ki-67 proliferation index and p53 expression, presenting with liver lesion 6 weeks post-surgery and diagnosed on FNA. Detailed cytomorphologic features are defined and compared. We emphasize that FNA, along with clinic-radiologic correlation, is a cost-effective, safe, and diagnostically accurate method of diagnosing PC metastases.

Keywords: Pituitary adenoma, Pituitary carcinoma, Fine-needle aspirate

CASE REPORT

A 60-year-old woman who was a diagnosed and treated case of PA on follow-up underwent a screening contrast-enhanced computed tomography of the whole abdomen 6 weeks post-surgery which revealed multiple well-defined hypoechoic lesions of varying size involving right, left,
and caudate lobes of liver with largest lesion measuring 7.0 × 7.0 cm in size, with few showing areas of central necrosis [Figure 1a]. Few variable size pre-/para-aortic and aortocaval lymph nodes were seen, largest measuring 1.7 × 1.2 mm. The previous history revealed that she underwent transnasal and transsphenoidal resection of an infiltrating sellar-suprasellar tumor (2.4 × 2.3 × 1.7 mm) at another institution 6 weeks back; however, resection was incomplete as tumor was invading the cavernous sinus [Figure 1b and c]. The patient presented with retro-orbital pain followed by blurring of vision and diplopia along with ptosis at the time of initial diagnosis; however, there were no abdominal symptoms. There was no history suggestive of pituitary hormone excess including unexplained weight gain, hirsutism, acromegaly, or sexual dysfunction. There was no family history of similar lesions or history of tumors at any other site.

Ultrasound-guided FNA was performed from the largest liver lesion using a 22-gauge needle. Wet fixed slides were prepared and stained with hematoxylin and eosin and papanicolaou stains. Cytosmears showed loose clusters and microacini of monotonous, small- to medium-sized plasmacytoid cells with moderate amphophilic cytoplasm, mildly pleomorphic, round to oval eccentrically placed nuclei, coarsely granular chromatin, and inconspicuous to prominent nucleoli [Figure 2a-c]. No immunocytochemistry could be performed on the liver aspirate due to limited aspirated material available. Review of previous sellar tumor biopsy revealed sheets and nests of monomorphic cells with similar morphology as seen in cytosmears [Figure 2d]. Immunohistochemical stains for synaptophysin and chromogranin were positive [Figure 2e and f] and all pituitary hormones including growth hormone, adrenocorticotropic hormone, PRL, and thyroid-stimulating hormone were tested and showed negative expression. Ki-67 labeling index was >3% and p53 showed wild-type expression [Figure 2g and h]. A cytologic

![Figure 1: Contrast-enhanced computed tomography whole abdomen (a) demonstrating multiple hypoenhancing lesions of various sizes noted in the right, left, and caudate lobes of liver. Magnetic resonance imaging brain – sagittal (b) and axial (c) images demonstrating low signal intensity lesions involving the sellar-suprasellar region.](image)

![Figure 2: Cytomorphological characteristics of the liver lesion (a-c) singly dispersed monotonous population of tumor cells (a), microacinar arrangement with cells exhibiting mild nuclear pleomorphism, stippled chromatin, and eccentric nuclei (b and c). Histopathology of pituitary lesion showing highly cellular sheets and nests of monotonous cells with intervening fibrovascular septae (d), positive expression for synaptophysin (e), chromogranin (f), Ki67 >3% (g), and increased expression for p53 (h). (Original magnifications, a: H&E; 200×, b: H&E; 400×, c: PAP; 400×, d: H&E; 200×, e-h: DAB; 200×).](image)
diagnosis of metastatic PC was rendered in the liver aspirate after clinical correlation with prior histologic diagnosis of PA in the sellar space-occupying lesion (SOL). Serum markers evaluated at the time of FNA cytology (FNAC) showed serum T3: 122 ng/dl, serum T4: 7.6 μg/dl, serum TSH: 4.8 μIU/ml, serum PRL: 20 ng/ml, and intact PTH level of 82.4 pg/ml.

### DISCUSSION

Lymphatic and hematogenous spread is more common in PC, with approximate frequency of 47% systemic metastases, 40% craniospinal metastases, and 13% exhibiting both. Hematogenous spread occurs through portal system of anterior pituitary into cavernous and petrosal sinuses, with venous

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**Table 1: Summary of cytologic features of pituitary carcinoma.**

| Case report       | Age/gender | Site of metastasis       | Cytomorphologic feature                                                                 | Treatment                  |
|-------------------|------------|--------------------------|----------------------------------------------------------------------------------------|----------------------------|
| Cartwright et al., 1994 | 28/F       | Cervical lymph node      | Pattern: Disposed in sheets Size/shape: Plasmacytoid Nuclei: Eccentric Cytoplasm: Moderate amount, homogeneous | Primary surgery+RT          |
|                   | 46/F       | Cervical lymph node      | Pattern: Disposed in small groups of individual cells Size/shape: Round to oval Nuclei: Prominent nucleoli evident Cytoplasm: Vacuolated | Primary surgery+RT          |
| Wang et al., 2017  | 67/F       | Cervical lymph node      | Pattern: Disposed in loosely cohesive clusters Size/shape: Pleomorphic epithelioid cells with marked cytologic atypia Nuclei: Intermediate to large nuclei, relatively irregular nuclear contours, coarse granular chromatin, prominent nucleoli Cytoplasm: Delicate finely granular cytoplasm | Primary surgery            |
|                   | 51/F       | Liver                    | Pattern: Disposed in loose clusters, microacini Size/shape: Monotonous population of moderate sized cells, mildly pleomorphic Nuclei: Round to oval eccentrically placed nuclei with coarsely granular chromatin and small nucleoli Cytoplasm: Moderate in amount, clear and ill-defined or absent due to its extreme fragility nucleus. Few with metachromatic dense granules | Primary surgery; adjuvant CRT |
| Ceyhan et al.      | 66/F       | C5 and C6 vertebral bodies | Pattern: Disposed in dyscohesive single cells or loose cell groups; small cords; and microacinar structures Size/shape: Monotonous, round to oval, plasmacytoid Nuclei: Moderate in size and round to oval. Mild nuclear membrane irregularities, coarsely granular chromatin pattern, and small, noticeable nucleoli: Few with eccentric nuclei Cytoplasm: Moderate amount of cytoplasm | Primary surgery+RT          |
| Chandler and Lin   | 59/F       | Right transverse T1 process, left lateral fifth rib, the left lateral aspects of L1 and L2 and the anterior left ilium | Pattern: A few loosely cohesive, singly or arranged in nests or acini Size/shape: Epithelial polygonal cells, plasmacytoid scant Nuclei: Eccentrically located round nuclei (plasmacytoid) with slight nuclear pleomorphism, evenly distributed fine granular chromatin, conspicuous nucleoli, and smooth nuclear membrane Cytoplasm: Moderate, vacuolated, and granular | Primary surgery+Gamma Knife |
| Present case       | 60/F       | Liver                    | Pattern: Loose clusters and microacini Size/shape: Monotonous medium sized plasmacytoid cells Nuclei: Round to oval eccentrically placed mildly pleomorphic nuclei with coarsely granular chromatin and inconspicuous to prominent nucleoli Cytoplasm: Moderate, amphophilic with well-defined cytoplasmic boundaries | Primary surgery+CT          |
return to the lungs. However, the reason of frequent liver metastasis still remains unclear.[6] The interval between PA and metastasis development is highly variable ranging between 4 months and 30 years; however, in the present case, metastasis developed within 6 weeks of the detection of primary tumor.

Cartwright et al. first described the cytomorphologic features of two cases of PC in 1994.[4] Since then, only a total of six cases have been reported, in which the cytomorphologic features of extracranial PCs have been described which are quite similar to our case [Table 1]. The cytologic diagnosis of metastatic lesion in PC is easy with classical clinical history. However, in the absence of relevant clinical history, diagnosis becomes a challenge due to overlapping cytomorphologic features with various other neoplasms including neuroendocrine carcinoma.[5-7] Hence, this differential should be taken care of with proper clinical workup when dealing with such overlapping cytomorphology. Since in previously reported cases, plasmacytoid appearance of the tumor cells was almost universally present, plasmacytoma is one of the important differential diagnoses. However, the presence of perinuclear hof/clearing, Russell bodies, clock-face chromatin, and Dutcher bodies may help in distinguishing the two entities on FNA.[8] In the presence of loose clusters and microacini along with epithelioid morphology, metastatic adenocarcinoma may also be considered in the differentials, particularly of lung or breast origin. However, the absence of marked pleomorphism, rare mitosis, and regular nuclear membrane differentiate PC from metastatic adenocarcinoma.

The recent 2017 WHO classification of CNS endocrine tumors suggests features of high-risk PAs predicting the recurrence and resistance to therapy which includes radiological or intraoperative evidence of invasion and increased tumor proliferative potential as determined by high mitotic and high Ki-67 proliferation index in addition to correct tumor subtyping. Such cases should be kept on high suspicion and under regular follow-up by serial MRI.[12] In the present case, FNAC assisted in the diagnosis as well as in the reclassification of previous diagnosis of PA on sellar SOL as a PC with metastasis to liver. We suggest that FNAC, along with clinical history, is a cost-effective, safe, and diagnostic method of diagnosing pituitary carcinoma metastases.

COMPETING INTEREST STATEMENT BY ALL AUTHORS
No competing interests.

AUTHORSHIP STATEMENT BY ALL AUTHORS
Drafting of manuscript: Pallavi Srivastava, Anurag Gupta. Literature search: Pallavi Srivastava. Case acquisition: Pallavi Srivastava, Anurag Gupta. Case analysis & interpretation: Anurag Gupta, Nuzhat Husain. Manuscript preparation: Pallavi Srivastava, Anurag Gupta, Kiran Preet Malhotra. Manuscript editing: Anurag Gupta, Kiran Preet Malhotra. Manuscript review and approval: Nuzhat Husain, Anurag Gupta.

ETHICS STATEMENT BY ALL AUTHORS
The informed and written consent was obtained from the patient. The case was submitted without identifiers.

LIST OF ABBREVIATIONS (In alphabetic order)
FNA – Fine needle aspiration
FNAC – Fine needle aspiration cytology
PA – Pituitary adenoma
PC – Pituitary carcinoma
PRL – Prolactin
SOL – Space-occupying lesion

EDITORIAL/PEER REVIEW STATEMENT
To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a double-blind model (authors are blinded for reviewers and vice versa) through automatic online system.

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