Head and Neck Pathology (2019) 13:677–680
https://doi.org/10.1007/s12105-018-0972-9

SINE QUA NON RADIOLOGY-PATHOLOGY

Null Cell Adenoma of the Pituitary: Pseudo-rosettes Say It Best When Immunohistochemistry Says Nothing At All!

Vikram Singh[1] · Kirti Gupta[1] · Pravin Salunke[2] · Sivashanmugam S. Dhandapani[2]

Received: 7 August 2018 / Accepted: 24 September 2018 / Published online: 24 September 2018

Abstract
Null cell adenoma is composed of adenohypophyseal cells that show no evidence of any specific cell type differentiation by immunohistochemistry or transcription factors like pituitary-specific positive transcription factor 1 and steroidogenic factor 1. Though rare, pituitary ependymoma and germinoma are also known to occur at sellar region and in such instances, it is challenging to differentiate them from a pituitary null cell adenoma featuring papillary architecture and perivascular pseudo-rosettes. We describe a case of an elderly diabetic lady presenting with headache and blurring of vision for past 3 months due to a sellar tumour. The histology was diagnostically challenging with notable presence of numerous perivascular pseudo-rosettes and negative immunoreactivity for all pituitary hormones. The differential diagnosis and importance of ancillary techniques is discussed.

Keywords Null cell adenoma · Pseudo-rosettes · Sellar tumour · Pituitary tumor

Introduction

The recent WHO classification of endocrine organs has abandoned the concept of 'hormone-producing adenoma' and adopted a pituitary adenohypophyseal cell lineage designation of adenomas with subsequent categorization of histological variants according to the hormone content and specific histological and immunohistochemical features. Consequently, this new classification emphasizes immunohistochemistry as the main ancillary tool for diagnosis, and reliance on ultrastructural analysis in very rare, unusual instances [1].

Null cell adenoma is an adenoma composed of adenohypophyseal cells that show no evidence of cell type specific differentiation by immunohistochemistry and transcription factors like pituitary-specific positive transcription factor 1 and steroidogenic factor 1 [2, 3]. Rarely pituitary ependymoma and germinoma occur in the sellar region and closely mimic pituitary null cell adenoma predominantly featuring papillary architecture with perivascular pseudo-rosette [4, 5]. The case underscores the importance of histomorphology and electron microscopy (EM) in solving challenging cases of sellar tumours, especially when immunohistochemistry is of limited help.

Case Summary

A 60-year-old lady, who had a known case of type 2 diabetes, presented with complaints of headache and blurring of vision of 3 months duration. On examination, her visual acuity was—right 6/60 and left 6/24 with bilateral superior temporal field loss. All of the hormones (T3, T4, TSH and cortisol) levels were normal. Contrast enhancing magnetic resonance imaging (CE-MRI) showed a sellar tumour (2.7 × 2.1 × 2.5 cm) extending into sphenoid sinus (Fig. 1a–f). With pre-operative diagnosis of pituitary macroadenoma, *trans*-sphenoidal sinus surgery gross total resection of tumor was performed.

Microscopy revealed a cellular tumour, with tumour cells predominantly arranged around the vessels forming prominent perivascular pseudo-rosettes and papillae. The tumour cells were relatively monomorphic with round to oval nuclei,

✉ Kirti Gupta
kirtigupta10@yahoo.co.in

[1] Department of Histopathology, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

[2] Department of Neurosurgery, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

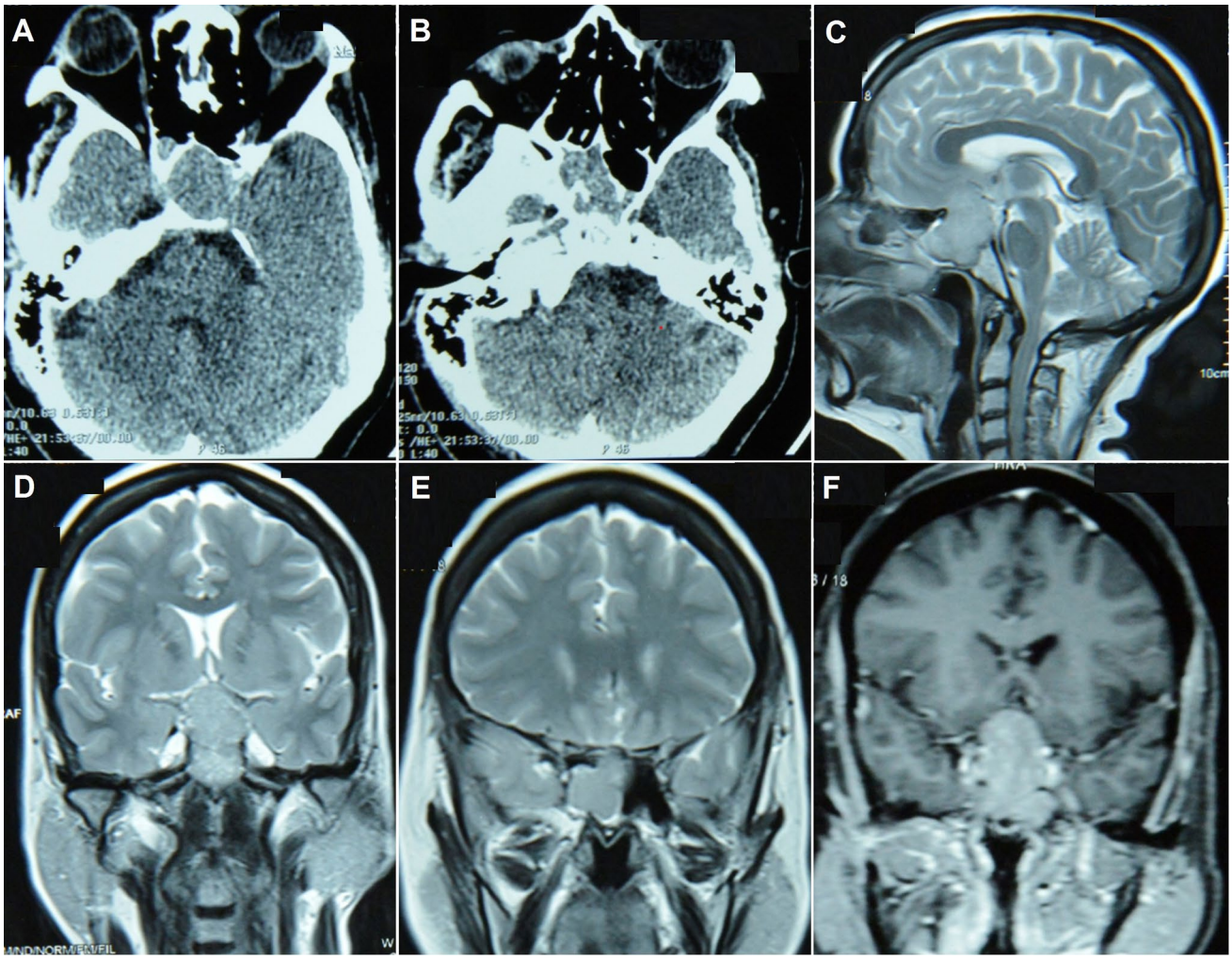

Fig. 1 **a, b** CT images showing expansion of sella with tumor eroding the floor into the sphenoid sinus; **c** mid sagittal T2 MR image showing sellar/suprasellar *iso*-hyperintense mass eroding the floor and upper clivus; **d, e** coronal T2 MR images showing sellar/suprasellar mass with wide waist between sellar and suprasellar component, reaching up to the carotids on either side and eroding inferiorly into the right sphenoid sinus; **f** post contrast coronal MR image showing contrast enhancing mass

stippled chromatin and moderate eosinophilic cytoplasm (Fig. 2a–c). Fragments composed of normal pituitary were also evident. No significant atypia, mitosis or necrosis was seen. On immunohistochemistry, the cells showed focal positivity for synaptophysin but were negative for GFAP, Pan-cytokeratin (Pan CK), GH, PRL, TSH, ACTH, FSH and LH (Fig. 2d, e). Immunopositivity within the normal pituitary gland served as positive internal control. Epithelial membrane antigen (EMA) was negative; no dot-like positivity, characteristic of ependymoma was noted. Ki67 index was < 3%. Absence of strong p53 nuclear staining and Ki67 index < 3% excluded the possibility of atypical adenoma. EM performed on formalin-fixed paraffin embedded tissue block demonstrated presence of sparse and small neurosecretory granules measuring up to 200 nm as described in null cell adenoma (Fig. 2f) [1]. Based on the characteristic histology, immunohistochemistry and EM features, a diagnosis of null cell adenoma was given. Her symptoms dramatically improved, postoperatively.

Discussion

Null cell adenomas are mostly macroadenoma with suprasellar extension and patients usually present with visual disturbances and headache [1]. Histologically, presence of perivascular pseudo-rosettes is consistent and distinctive feature of gonadotroph adenomas and null cell adenomas [6]. It is important to differentiate null cell adenoma from other rare sellar mass with similar histology, such as pituitary ependymoma, germinoma and metastatic carcinoma. Pituitary ependymoma is rare with very few cases reported

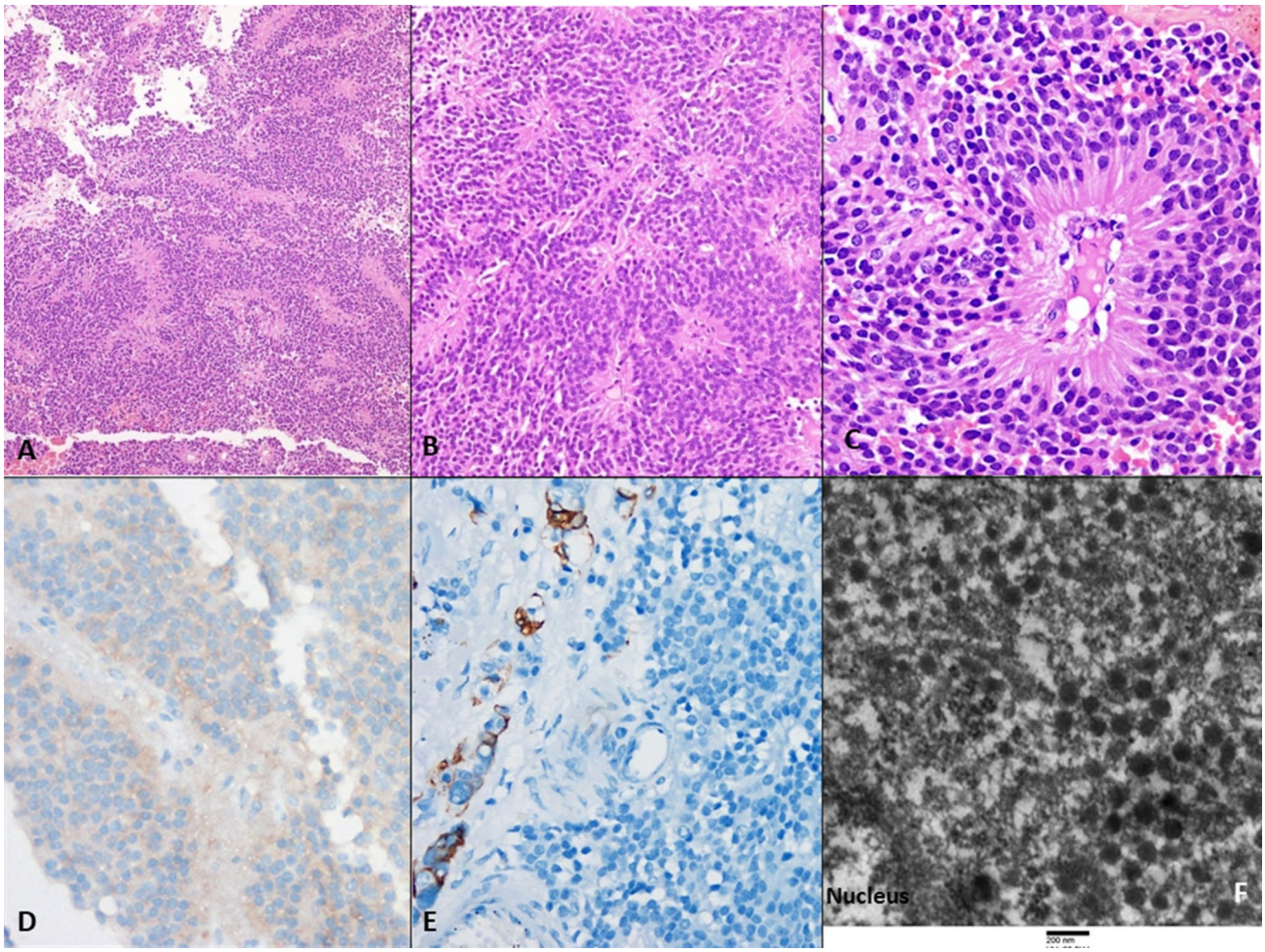

Fig. 2 **a** Low magnification demonstrates striking perivascular and papillary pattern of the tumor (H&E ×40); **b** ependymal-like perivascular pseudo-rosettes (H&E ×200); **c** high magnification demonstrates moderately pleomorphic round to oval cells forming perivascular pseudo-rosettes (H&E ×400); **d** granular positivity for synaptophysin (immunoperoxidase ×400); **e** representative image of tumor cells negative for GFAP, EMA, and all pituitary hormones (immunoperoxidase ×400); **f** sparse and small intracytoplasmic neurosecretory granules ranging in size from 89 to 110 nm (original magnification ×12,000, uranyl acetate with lead citrate)

in the literature [6]. GFAP and dot-like EMA immunopositivity favour a pituitary ependymoma. Apart from characteristic positivity for OCT3/4, CD117, the tumour cells demonstrate typical features similar to testicular seminomas or ovarian dysgerminomas. Negativity for Pan CK rules out metastatic carcinoma with papillary architecture. In conclusion, the case emphasizes the peculiar histology of hormone immunonegative, pituitary null cell adenoma with presence of perivascular pseudo-rosettes and the underscores the need for EM in clinching the correct diagnosis which is of prognostic relevance.

Compliance with Ethical Standards

Conflict of interest We do not have any financial disclosures and no conflicts of interests.

References

1. Lloyd RV, Osamura RY, Klöppel G, Rosai J, editors. WHO classification of tumours of endocrine organs. 4th ed. IARC: Lyon, 2017. pp. 34–38.
2. Nishioka H, Inoshita N, Mete O, Asa SL, Hayashi K, Takeshita A, Fukuhara N, Yamaguchi-Okada M, Takeuchi Y, Yamada S. The complementary role of transcription factors in the accurate diagnosis of clinically nonfunctioning pituitary adenomas. Endocr Pathol. 2015;26:349–55.
3. Nishioka H, Inoshita N. New WHO classification of pituitary adenomas (4th edition): assessment of pituitary transcription factors and the prognostic histological factors. Brain Tumor Pathol. 2018;35:57–61.
4. Ramesh VG, Karthikeyan KV, Rajaraman S, Rao R. Pituitary ependymoma: report of a rare case with an insight into the histogenesis. Neurol India. 2013;61:545–6.

5. Kontogeorgos G, Thodou E. The gonadotroph origin of null cell adenomas. Hormones (Athens) 2016;15:243–7.
6. Kontogeorgos G, Kovacs K, Horvath E, Scheithauer BW. Null cell adenomas, oncocytomas, and gonadotroph adenomas of the human pituitary: an immunocytochemical and ultrastructural analysis of 300 cases. Endocr Pathol. 1993;4:20.