Endocrinology, Diabetes & Metabolism CASE REPORTS

M Darrat and others | Metastasis in a pituitary adenoma

ID: 20-0094; December 2020
DOI: 10.1530/EDM-20-0094

A very rare case of pituitary metastasis infiltrating a non-secretory gonadotroph adenoma

Milad Darrat[1], Mohammad Binhussein[1], Alan Beausang[2], Clare Faul[3], Michael W O'Reilly[1], Mohsen Javadpour[4,5] and **Amar Agha[1,5]**

[1]Deparments of Endocrinology, [2]Neuropathology, [3]Radiation Oncology, [4]Neurosurgery, Beaumont Hospital, Dublin, Ireland, and [5]School of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland

Correspondence should be addressed to M Darrat
Email
miladmustafa7@yahoo.com

Abstract

Pituitary adenomas are the commonest sellar tumours. Pituitary metastases are very rare, with the most common primaries being breast and lung cancers. We report the case of an 83-year-old man with a history of breast carcinoma who presented with recent-onset headaches and progressive deterioration of visual acuity. MRI brain showed a large sellar and suprasellar mass compressing the optic chiasm and involving the pituitary stalk. Transsphenoidal debulking resulted in symptomatic relief and visual recovery. Specimen examination revealed a combination of a gonadotroph pituitary adenoma that was infiltrated by metastatic breast carcinoma. He had no symptoms of diabetes insipidus. He was subsequently treated with pituitary radiotherapy. This is a very rare presentation of a pituitary mass with mixed pathology. To our knowledge, this is the third description of a breast carcinoma metastasis into a gonadotroph cell pituitary adenoma.

Highlight points:

- Infiltrating metastases into pituitary adenomas are very rare but do occur.
- To our knowledge this is the third case of breast adenocarcinoma metastasising to a gonadotroph pituitary adenoma.
- Pituitary metastases should always be considered in rapidly evolving pituitary symptoms in a cancer patient.
- Not all complex pituitary lesions are associated with panhypopituitarism.
- Early invasive local management (TSS and post TSS radiotherapy) can provide rapid satisfactory outcomes.

Background

Metastatic disease to the pituitary is reported to account for approximately 0.4% of all brain metastases and a carries a poor prognosis, with a median life span of 14 months (range 4 to 30 months) depending on the origin and stage of the primary cancer (1). Breast and lung cancers are the most common sites of origin (1, 2). Approximately 30% of pituitary metastases are silent, while the majority present with mass related symptoms such as retro orbital pain/headache, visual defects and ophthalmoplegia (3). The commonest endocrine manifestation is diabetes insipidus (70% of the symptomatic patients), followed by anterior hypopituitarism (15% of the symptomatic patients) (3).

Metastases to a pre-existing pituitary adenoma are extremely rare, with only 31 reported clinical cases in the world literature (4, 5). Endocrinological, visual and cranial nerve complications are found to be more frequent with a dual pituitary lesion. This is likely due

ID: 20-0094; December 2020
DOI: 10.1530/EDM-20-0094

to either hormonal hypersecretion from adenomas and/or hormonal deficiency caused by a greater mass effect (5).

In this paper we present a case of breast carcinoma metastasis to a pituitary adenoma and review the relevant literature.

Case presentation

An 83-year-old white man with a background history of metastatic breast carcinoma presented with a 2-week history of headache and bitemporal hemianopia. He was initially diagnosed with invasive ductal carcinoma of the right breast 5 years prior, which was treated with total mastectomy. His tumour was 4 cm in size, TNM stage PT2N0M0 and oestrogen receptor (ER) positive. Post-operatively, he was commenced on Tamoxifen. He later developed lymph node metastases and was switched to the Gonadotrophin releasing hormone (GnRH) analogue Goserelin 3.6 mg (GnRHA) monthly, in tandem with the aromatase inhibitor Letrozole 2.5 mg daily.

On presentation, brain and pituitary MRI revealed a 33 × 17 × 15 mm solid and cystic hyperintense lesion arising from the sellar and suprasellar regions with chiasmal compression (Fig. 1). His pituitary function tests revealed low random cortisol, morning testosterone (on GnRH analogue) and IGF-1 levels, with normal thyroid function and electrolytes (Table 1). He had no symptoms suggestive of diabetes insipidus (DI).

Differential diagnosis

Given his medical history of metastatic breast carcinoma, in addition to current use of GNRH analogue, our initial differentials included pituitary metastasis, pituitary adenoma or pituitary apoplexy.

Treatment

Initial treatment included IV followed by oral stress doses of hydrocortisone. Endoscopic transsphenoidal pituitary surgery was performed with an uneventful operative and post-operative course. Neuropathological examination of the resected tissue revealed a gonadotroph pituitary adenoma (demonstrating focal expression for follicular stimulating hormone (FSH) and luteinising hormone (LH), as well as widespread nuclear expression of gonadotroph transcription factor SF1), infiltrated by breast adenocarcinoma with positive oestrogen and progesterone receptors and HER2 (2+) similar to his primary breast carcinoma (Fig. 2).

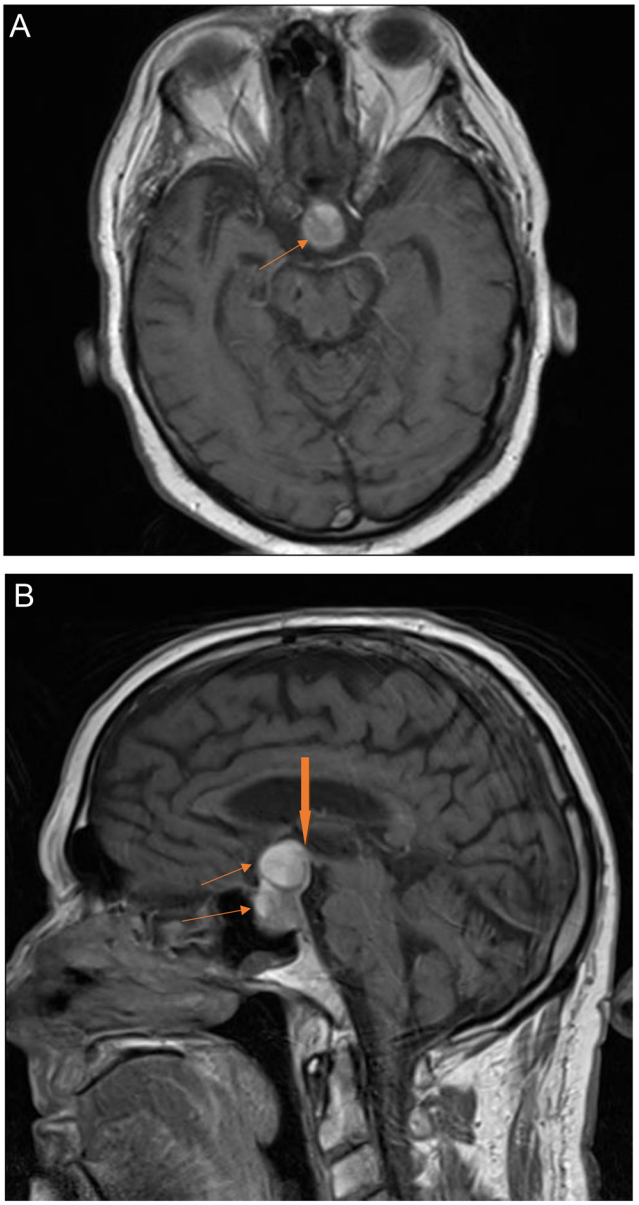

Figure 1
(A and B) Images are pre-operative, axial and sagittal T1 MRI showing 33 × 17 × 15 sold cystic hyperintense lesion arising from sellar and suprasellar regions (thin arrows) with left optic chiasm (thick arrow) compression.

Outcome and follow-up

He was discharged on hydrocortisone 10 mg in the morning and 5 mg afternoon. He was also educated about the glucocorticoid sick day rules and an educational leaflet was given. He underwent fractionated pituitary radiotherapy afterwards with a total dose of 25 Gy/5.

A post-operative (pre-radiotherapy) pituitary MRI in October 2019 showed a significant reduction in the tumour size of 13 × 14 × 9 mm without compression of the

Table 1 Pre-operative and post-operative pituitary blood results.

Tests	Pre-operative results	Post-operative results	Reference range
Random cortisol	36	-	
Short synacthen test			
0 min		321	>250–310
30 min		479	>450
LH, U/L	<1.0	1.0	1.7–8.6
FSH, U/L	3.7	4.0	1.5–12.4
FT4, pmol	15.7	14.1	12–22
TSH, mIU/L	0.57	2.15	0.27–4.2
Testosterone, nmol/L	<0.4	<0.4	6.7–25.7
IGF-1, ng/mL	28.1	28.3	183–37
Prolactin, mIU/L	109	185	56–278

optic chiasm. There was a significant improvement in his visual symptoms and resolution of his headache. Repeat pituitary assessment 4 months post-radiation showed normal corticotropin and thyroid function tests (Table 1). His gonadotropins and testosterone remained suppressed (iatrogenic) and his IGF-1 stayed low. Interestingly, he had no evidence of DI.

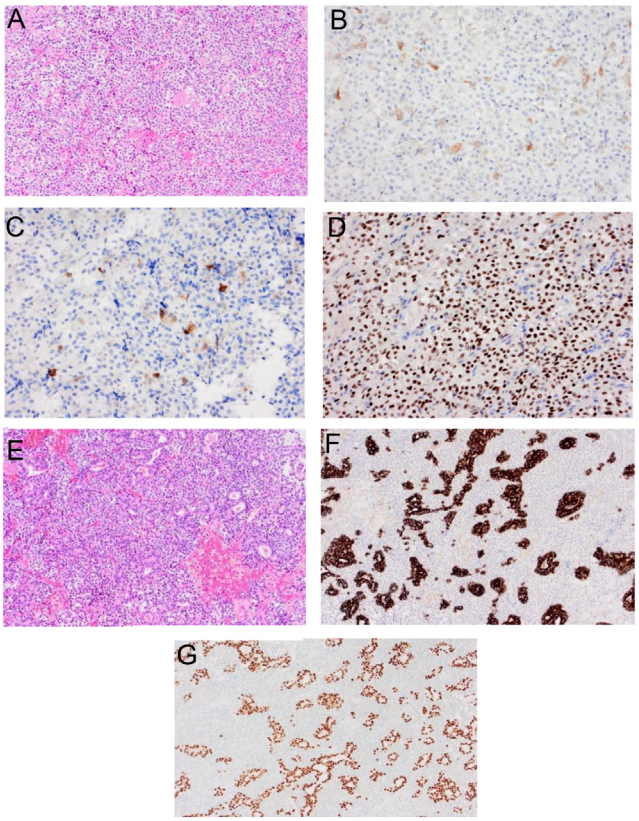

Figure 2
Histopathology slides showing a pituitary adenoma composed of monomorphic cells with round to oval nuclei and abundant pale eosinophilic cytoplasm (A) with expression for follicular stimulating hormone (FSH) (B), luteinising hormone (LH) (C) and SF1 (D), infiltrated by metastatic adenocarcinoma (E), which was cytokeration 7 (F) and GATA3 (G) positive, consistent with origin from breast primary.

Discussion

Metastatic disease to pituitary adenomas has been very rarely reported in the literature.Our case is the third description of a breast metastasis into a gonadotroph cell pituitary adenoma after that of Bret *et al.* and Mils *et al.* (5, 6). Differentiation between benign and metastatic pituitary gland lesions clinically can be difficult, but it is crucial for treatment options (1). Although diabetes insipidus (DI) occurs more frequently with metastatic disease, this is not always the case, as it did not occur with our patient. Ocular manifestations may not be helpful in differentiating between pituitary metastases and growing adenomas. However, the presence of rapidly progressive compressive symptoms on a background of malignancy, as in our patient, should always raise the suspicion of metastatic disease.

While imaging studies, including a dedicated pituitary scan, will show a sellar/stalk mass, it cannot confidently diagnose a metastasis or more rarely mixed tumours within the gland.The MRI in our case showed a large enhancing cystic solid lesion which was similar to earlier reported cases. Furthermore, intraoperatively, these pituitary lesions including our case have no characteristic features that may suggest the diagnosis of infiltrating neoplasm into an adenoma. Therefore, histopathology remains the definitive method to establish the diagnosis (1). Immunohistochemistry plays an essential role in the differentiation between the mixed components of a solitary lesion (1).

There are several theories that explain the occurrence of infiltrating metastases in pituitary adenomas. One attractive hypothesis relates to changes in the normal

ID: 20-0094; December 2020
DOI: 10.1530/EDM-20-0094

blood supply of the pituitary gland. It has been reported that pituitary adenomas can have additional arterial circulation, bypassing hypophyseal portal circulation, from carotid and meningeal arteries. This rich vascular supply of pituitary adenomas creates an extra access for metastases from the circulation. This has been observed specifically with metastases to non-functioning FSH/LH gonadotroph adenomas (7). Another proposed theory is the presence of certain growth factors produced by metastases which lead to direct binding and interaction with epithelial cell receptors of pituitary adenomas as was reported with metastatic renal cell carcinoma (8). Hormonal therapy, as in our patient, previous radiation and surgical intervention may also lead to significant changes in adenoma microstructures, resulting in the development of metastatic disease (9). Another interesting finding in our case, is the use of an GnRH analogue on a background of an undiagnosed pituitary lesion. GnRH analogues are currently used to treat prostate cancer and metastatic male breast cancer. There are several case reports of pituitary apoplexy with the use of GnRH. It was found that these agents may accelerate the growth of asymptomatic pituitary adenomas and cause haemorrhage/infarction (10). However, this was not a part of our patient's presentation.

Conclusion

Metastases to a pituitary adenoma is an extremely rare condition with no specific clinical manifestations. However, it should always be considered in the differential diagnosis of rapid progression of pituitary disease, in particular when the patient has underlying malignancy. To our knowledge, this is the third case of breast adenocarcinoma metastasising to a gonadotroph pituitary adenoma.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding
This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

Patient consent
Written informed consent has been obtained from the patient.

Author contribution statement
All authors included in this article made substantial contributions to the study, as well as assisted with critical revisions of the writing, and approved the final version for submission for publication.

References

1 Javanbakht A, D'Apuzzo M, Badie B & Salehian B. Pituitary metastasis: a rare condition. *Endocrine Connections* 2018 **7** 1049–1057. (https://doi.org/10.1530/EC-18-0338)
2 O'Halloran PJ, Hannon AM, Bartels C, McCawley N, Agha A, Brett F, Leader M, Broe P & Javadpour M. Gastrointestinal stromal tumor metastases to the pituitary: a rare entity. *British Journal of Neurosurgery* 2017 **31** 603–604. (https://doi.org/10.3109/02688697.2016.1173194)
3 Al-Aridi R, El Sibai K, Fu P, Khan M, Selman WR & Arafah BM. Clinical and biochemical characteristic features of metastatic cancer to the sella turcica: an analytical review. *Pituitary* 2014 **17** 575–587. (https://doi.org/10.1007/s11102-013-0542-9)
4 Yang C, Liu L, Lan X, Zhang S, Li X & Zhang B. Progressive visual disturbance and enlarging prolactinoma caused by melanoma metastasis: a case report and literature review. *Medicine* 2017 **96** e6483. (https://doi.org/10.1097/MD.0000000000006483)
5 Mills MT, Wharton SB, Connolly DJ, Mirza S & Sinha S. Pituitary apoplexy secondary to metastatic breast carcinoma into a gonadotroph cell adenoma of the pituitary. *British Journal of Neurosurgery* 2018 **19** 1–4. (https://doi.org/10.1080/02688697.2018.1540766)
6 Bret P, Jouvet A, Madarassy G, Guyotat J & Trouillas J. Visceral cancer metastasis to pituitary adenoma: report of two cases. *Surgical Neurology* 2001 **55** 284–290. (https://doi.org/10.1016/S0090-3019(01)00447-5)
7 Powell DF, Baker Jr HL & Laws Jr ER. The primary angiographic findings in pituitary adenomas. *Radiology* 1974 **110** 589–596. (https://doi.org/10.1148/110.3.589)
8 Magnoli F, Finzi G, Riva C & Capella C. Renal cell carcinoma metastatic to a pituitary FSH/LH adenoma: case report and review of the literature. *Ultrastructural Pathology* 2014 **38** 430–437. (https://doi.org/10.3109/01913123.2014.937843)
9 Yancopoulos GD, Davis S, Gale NW, Rudge JS, Wiegand SJ & Holash J. Vascular-specific growth factors and blood vessel formation. *Nature* 2000 **407** 242–248. (https://doi.org/10.1038/35025215)
10 Keane F, Egan AM, Navin P, Brett F & Dennedy MC. Gonadotropin-releasing hormone agonist-induced pituitary apoplexy. *Endocrinology, Diabetes and Metabolism Case Reports* 2016 **2016** 160021. (https://doi.org/10.1530/EDM-16-0021)

Received in final form 18 September 2020
Accepted 26 November 2020