

# Metastasis of a Dorsal Melanoma to a Pituitary Adenoma Mimicking Pituitary Apoplexy

## *Metástase de um melanoma dorsal em um adenoma hipofisário imitando apoplexia pituitária*

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### Abstract

Metastases to pituitary adenomas are very rare. From the 20 cases found in the literature, none originated from a cutaneous melanoma.

We present the case of a 67-year-old man with a history of transcranial approach to treat a pituitary macroadenoma followed by adjuvant radiotherapy. Fifteen years later, he presented a dorsal nodular melanoma, and three years after that, he developed symptoms of pituitary apoplexy. He was submitted to transsphenoidal surgery, and the histology result revealed metastasis of the melanoma into a pituitary adenoma.

The similarity in the clinical presentation of the two entities—pituitary apoplexy and metastasis of the melanoma into a pituitary adenoma—and the rarity of this type of metastization alert to challenges in the differential diagnosis that may confound the neurosurgeon's decision.

### Keywords

- ▶ tumour-to-tumour metastasis
- ▶ pituitary adenoma
- ▶ melanoma
- ▶ apoplexy

### Resumo

As metástases em adenomas pituitários são muito raras. Dos 20 casos descritos na literatura, nenhum foi originado por um melanoma cutâneo.

Apresentamos um caso de um homem de 67 anos de idade, com história de abordagem transcraniana para tratar um macroadenoma pituitário, seguido de radioterapia adjuvante. Quinze anos depois, o paciente apresentou um melanoma nodular dorsal e 3 anos mais tarde desenvolveu sintomas de apoplexia pituitária. Ele foi então submetido a uma cirurgia transfenoidal, e o resultado histológico revelou tratar-se de uma metástase do melanoma em um adenoma hipofisário.

A semelhança na apresentação clínica entre as duas entidades—apoplexia pituitária e metástase do melanoma em um adenoma hipofisário—e a raridade deste tipo de metastização alertam para desafios no diagnóstico diferencial que podem confundir a decisão do neurocirurgião.

### Palavras-chave

- ▶ metástase tumor-tumor
- ▶ adenoma hipofisário
- ▶ melanoma
- ▶ apoplexia

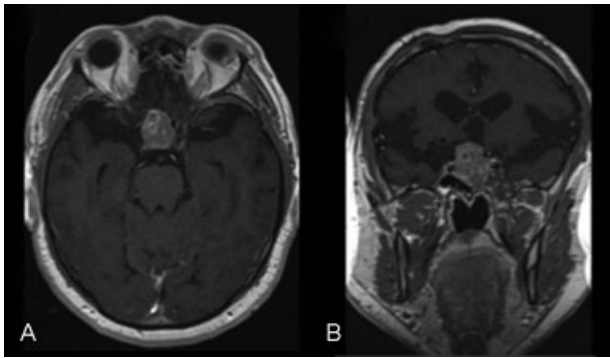
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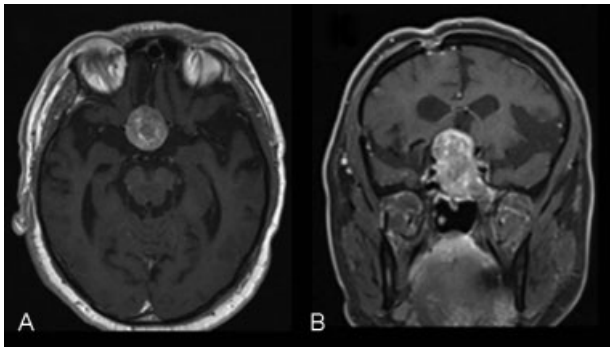
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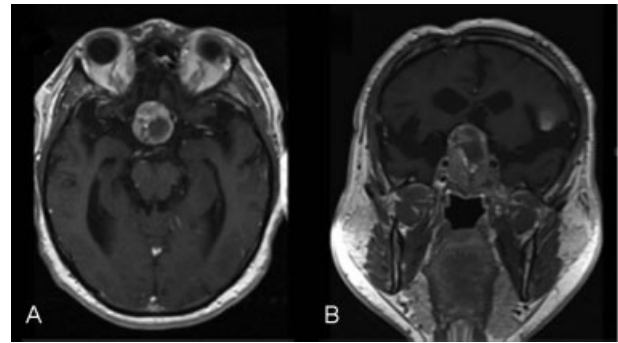




**Fig. 1** Brain MRI in December of 2012, 1 year before the apoplexy. Gadolinium-enhanced T1-weighted axial (A) and coronal (B) images showing a sellar/suprasellar/sphenoidal lesion measuring 21 × 30 mm, heterogeneous signal, compressing of the optic chiasm and invasion of the cavernous sinus.



**Fig. 2** Brain MRI in December of 2013, after the apoplexy and before the transsphenoidal surgery. Gadolinium-enhanced T1-weighted axial (A) and coronal (B) images showing a sellar/suprasellar/sphenoidal lesion measuring 26 × 42 mm and heterogeneous signal.



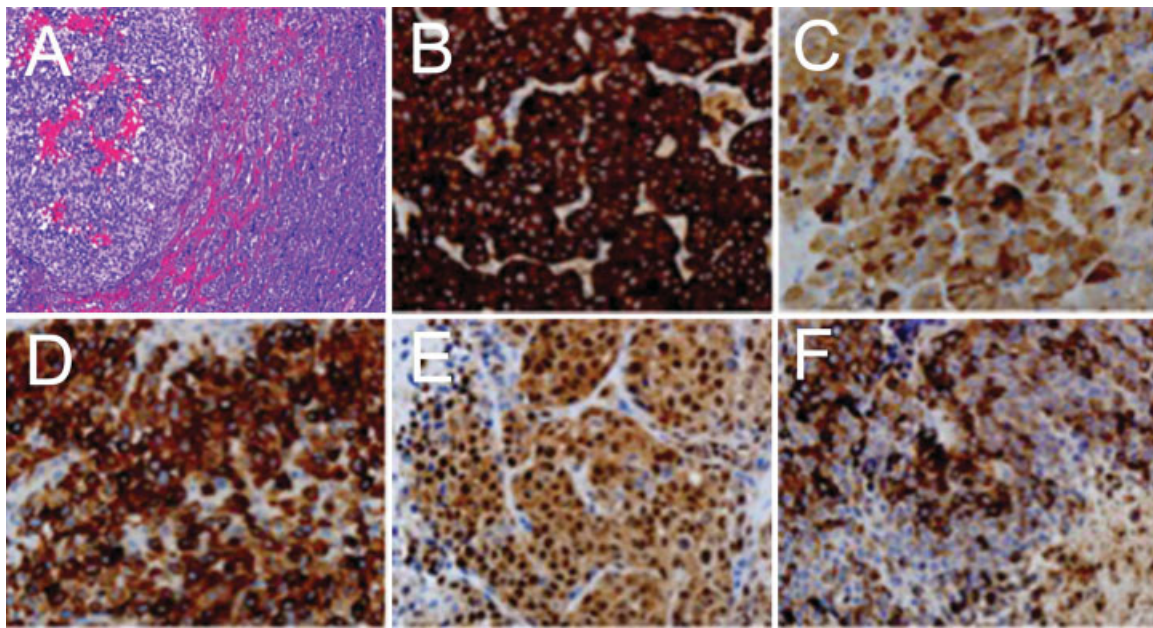
**Fig. 4** Brain MRI two months after the transsphenoidal surgery. Gadolinium-enhanced T1-weighted axial (A) and coronal (B) images showing regrowth of the sellar/suprasellar lesion and a new left frontal-opercular lesion.

## Introduction

Tumor-to-tumor metastasis is a well-known phenomenon since its first observation, in 1930, by Fried et al in a case of bronchogenic carcinoma metastasis to an intracranial meningioma.<sup>1</sup>

The definition of a tumor-to-tumor metastasis needs to meet the following criteria: 1.) presence of more than one primary tumor; 2.) the receiver tumor has to be a true neoplasm; 3.) the tumor donor should be a source of metastasis; 4.) tumors that metastasize through the lymphatic system where lymphoreticular tumors already exist are not included.<sup>1</sup>

The most common intracranial receptors for visceral metastasis are meningiomas, but other tumors like low grade gliomas, ependymomas, schwannomas, hemangioblastomas and pituitary adenomas have also been reported.<sup>2</sup>



**Fig. 3** Histologic tissue sections. Hematoxylin and eosin (A), 100× original magnification showing melanoma cells on the left and adenoma cells on the right. Synaptophysin (B) and follicle-stimulating hormone (FSH) (C) positive staining in the adenoma cells. Melan-A (D), microphthalmia transcription factor (Mitf) (E) and human melanoma black (HMB)-45 (F) positive staining in the melanoma cells.

**Table 1** Reported cases of metastases to pituitary adenomas until August of 2016

Year	First author	Gender	Age	Symptoms	Apoplexy	Type	Primary tumor	Cancer spreading	Sellar lesion treatment	Survival
1971	Richardson <sup>8</sup>	F	70	Headache, hemiparesis	?	NS	Breast	Yes	Autopsy case	?
1971	Van Der Zwan <sup>9</sup>	F	73	Loss of vision	?	NS	Breast	Yes	Transcranial	28 days
1973	Burns <sup>10</sup>	M	78	Fever, nausea, diarrhea	?	NS	Renal/ureter	?	Autopsy case	5 weeks
1981	Max <sup>11</sup>	F	61	Loss of vision	No	NS	Lung	Yes	Transcranial and RT	?
1984	James <sup>4</sup>	M	75	Loss of vision	No	NS	Kidney	No	Tsf	?
1984	Molinatti <sup>12</sup>	F	71	Loss of vision	?	NS	Lung	?	?	?
1985	Seters <sup>13</sup>	F	66	Obesity, seizures, loss of vision	No	PRL	Stomach	No	Transcranial	12 days
1987	Zager <sup>14</sup>	F	56	Diplopia	No	NS	Breast	Yes	RT	3 weeks
1988	Post <sup>15</sup>	F	61	Headache, loss of vision	No	ACTH	?	No	Tsf and RT	?
1988	Post <sup>15</sup>	M	77	Headache, loss of vision	Yes	Oncocytic adenoma	Lung	No	Tsf and RT	6 months
1988	Ramsay <sup>16</sup>	M	57	Autopsy case	No	NS	Prostatic	Yes	Autopsy case	?
1988	Ramsay <sup>16</sup>	F	50	Exophthalmos, truncal and facial obesity	No	ACTH	Pancreas	Yes	Tsf, RT and CT	8 months
1992	Hurley <sup>17</sup>	M	76	Loss of vision, lethargy, nausea, emesis	No	GH	Renal	Yes	Tsf	6 months
1997	Abe <sup>18</sup>	F	46	Headaches, loss of vision	No	PRL	Mediastinal	Yes	Tsf	6 months
1999	Hanna <sup>5</sup>	F	42	Headaches	No	PRL	Lung	Yes	Tsf	?
2000	Bret <sup>2</sup>	F	75	Loss of vision	No	NS	Breast	No	Tsf	> 18 m
2000	Bret <sup>2</sup>	F	87	Loss of vision	No	NS	?	?	Tsf	> 6 m
2001	Noga <sup>19</sup>	M	60	Loss of vision	No	NS	Gastrointestinal	Yes	Transcranial	Shortly after surgery with pulmonary embolism
2009	Hoelling <sup>20</sup>	M	71	Loss of vision	No	NS	Lung	Yes	Tsf	13 days
2014	Thewijtharoen <sup>3</sup>	M	65	Loss of vision, ptosis, headache	Yes	NS	Colon	Yes	Tsf	?

Abbreviations: ?, unknown; ACTH, adrenocorticotropic hormone; CT, chemotherapy; F, female; GH, growth hormone; M, male; NS, nonsecretory; PRL, prolactin; RT, radiotherapy; Tsf, transsphenoidal approach.

The rare phenomenon of metastasis to a pituitary adenoma may be explained by different factors: 1.) the abnormal vasculature and the hormonal effect of the adenoma with the ability to increase cellular proliferation;<sup>3</sup> 2.) the increased microvasculature produced by surgery or radiation to an adenoma;<sup>2</sup> 3.) the slow growth of the adenomas, which creates an environment without competition to the growth of the metastasis.<sup>3</sup> Finally, due to its rarity, the tumor-to-tumor metastasis can be a simple coincidence.<sup>3</sup>

The clinical and imaging features of pituitary metastasis are often similar to those of a pituitary adenoma.<sup>3</sup> In many cases, the pituitary metastases are asymptomatic.<sup>4</sup> In symptomatic patients, the most frequent presentations are diabetes insipidus, visual disturbances, cranial nerves palsy, and anterior hypopituitarism.<sup>5</sup> Another possible clinical presentation is pituitary apoplexy. The apoplexy occurs as result of hemorrhaging or infarction of a rapidly growing preexisting adenoma.<sup>6</sup> It manifests as an acute-onset headache, vomiting, decreased visual acuity, ophthalmoplegia and decreased level of consciousness.<sup>7</sup> It usually occurs in pituitary macroadenomas, but it has also been described in normal pituitary gland, craniopharyngiomas, lymphocytic hypophysitis and pituitary metastasis.<sup>3</sup>

On the magnetic resonance imaging (MRI), the pituitary metastases are similar to pituitary adenomas and present as intra and suprasellar homogeneous masses without ring enhancement and areas of necrosis.<sup>2</sup> They may present isosignal in T1- and T2-weighted images and loss of the neurohypophysis bright signal.<sup>3</sup> On the other hand, melanin appears with hypersignal on T1 and hyposignal on T2-weighted images.<sup>7</sup> Lastly, hemorrhagic metastases can result in the same type of signal on T1- and T2-weighted images, but they have a more heterogeneous pattern.<sup>7</sup>

The intraoperative findings are not different between the two lesions, but some authors have reported an atypical presentation of the metastasis, exhibiting hard texture, hemorrhage or both components.<sup>2</sup>

The poor prognosis in case of metastasis to a pituitary adenoma depends on the fact that many patients already have extensive metastatic spread when diagnosed.<sup>3</sup> The average survival of a pituitary metastasis is about 6 months.<sup>3</sup>

The treatment options are limited, but the patients may be given palliative radiotherapy, hormone replacement therapy and chemotherapy for the primary tumor.<sup>3</sup>

## Case Report

We describe the case of a 67-year-old male patient followed up in our pituitary group outpatient clinic since 1995, after a pituitary macroadenoma had been diagnosed as the cause of visual amputation. He underwent a craniotomy followed by adjuvant radiotherapy and started on levothyroxine, hydrocortisone, and testosterone because of hypopituitarism. Since then his clinical state was stable.

In 2010, a dorsal nodular melanoma, Clark level IV, was excised.

The baseline images of the adenoma remained stable over the years, the last one dated from December 2012 (► Fig. 1).

In December of 2013, he entered the emergency room after a sudden onset of headache, vomiting and decreased visual acuity in the left eye. Brain computed tomography and MRI (► Fig. 2) suggested pituitary apoplexy, and he underwent partial removal of the lesion by transsphenoidal approach. During the procedure, we found a hemorrhagic lesion with heterogeneous consistency. Some areas were very soft and similar to adenoma and others were stiff with some foci of chronic hemorrhaging.

The histological result revealed a melanoma metastasis within the pituitary adenoma (► Fig. 3). After the surgery, the patient's clinical state improved, but 2 months later he presented with nausea and vomiting. The MRI revealed regrowth of the sellar/suprasellar lesion reaching similar dimensions to those before surgery, but a new left frontal opercular lesion was visible (► Fig. 4). The patient died 3 months later.

## Discussion

This patient had been previously submitted to surgery and radiotherapy due to a pituitary macroadenoma. He remained stable for 18 years, but 7 years ago he was diagnosed with a dorsal melanoma. Suddenly, he presented with unexpected symptoms suggesting pituitary apoplexy. The presence of a marked visual deficit conducted to an early surgical intervention.

Although apoplexy is more frequent in untreated macroadenomas, and tumor-to-tumor metastases are extremely rare, the severity of visual complications in this case misled the surgeons to an emergent surgical approach, since they attributed the symptoms to classic apoplexy.

A literature search conducted in PubMed until August of 2016 yielded 20 cases of metastasis to pituitary adenomas. The results have been summarized in ► Table 1. We did not find any cases of melanoma metastization to a pituitary adenoma, but only cases of melanoma metastasis to a normal pituitary gland. As in our case, the presenting symptoms were compatible with pituitary apoplexy and surgery or autopsy confirmed this very rare diagnosis.

## Conclusions

Two different clinical entities, such as pituitary apoplexy and a melanoma metastasis to a pituitary adenoma, present with very similar clinical, imagiological and surgical findings. The rarity of tumor-to-tumor metastasis and the need for an emergent decision facing acute visual loss compatible with pituitary apoplexy of a residual tumor led the surgeons to elect surgical intervention as the treatment of choice. The histology revealing a melanoma metastasis within the residual adenoma highlighted the need to value differential diagnosis that may confound the surgeon's decision.

This case alerts neurosurgeons to the possibility of a metastasis to a pituitary adenoma when there is the coexistence of another tumor highly prone to metastization.

## Conflict of Interest

Authors declare no conflict of interest.

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