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**Pituitary Metastasis of Malignant Melanoma misdiagnosed as Pituitary Adenoma: a case report and
systematic review of the literature.**

**Métastase hypophysaire d'un mélanome malin mimant un adénome hypophysaire : un case report et une
revue systématique de la littérature**

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1 Pituitary Metastasis of Malignant Melanoma misdiagnosed as Pituitary Adenoma: a case report and
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4 revue systématique de la littérature
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Abstract

We report a case of malignant melanoma revealed by a metastasis to the pituitary gland. The tumor was misdiagnosed as a pituitary adenoma and aggressive transsphenoidal surgery was complicated by a cerebrospinal fluid fistula. Nine weeks later, the patient presented multiple leptomeningeal and brain metastases spreading from the sellar region. Regarding these observations, we conducted a systematic review of the literature in order to investigate clinico-radiological features that should lead clinicians to suspect pituitary metastasis and how it should impact the surgical management.

Key words

Pituitary; Metastasis; Leptomeningeal carcinomatosis; Melanoma; Transsphenoidal; Endoscopic surgery

Résumé

Nous rapportons un cas de mélanome malin révélé par une métastase hypophysaire. La tumeur a été diagnostiquée à tort comme un adénome hypophysaire et une chirurgie transsphénoïdale agressive a été compliquée par une fistule de liquide céphalorachidien. Neuf semaines plus tard, le patient a présenté plusieurs métastases leptoméningées et cérébrales se propageant à partir de la région sellaire. Aux vues de ces constats cliniques, nous avons conduit une revue systématique de la littérature afin de déterminer les caractéristiques clinico-radiologiques qui devraient conduire les cliniciens à soupçonner une métastase hypophysaire et en quoi cela doit impacter la gestion chirurgicale.

Mots-clés

Hypophyse; Métastase; Dissémination leptoméningée; Mélanome; Transsphénoïdal, Chirurgie endoscopique

Text

Introduction:

The pituitary gland is an unusual location for metastases, accounting for around 0.4% of all intracranial metastatic tumors [1] and representing less than 1% of surgically treated pituitary tumors [2]. Among histologically-proven cases, breast and lung cancers are the most common cancers disseminating to the pituitary gland [1,3], followed by prostate [4] and kidney cancers [1,5]. Pituitary metastases may reveal an unknown cancer in 40% of cases [3], leading to subsequent delay in diagnosis and therapeutic management. Here we report a rare case of pituitary metastasis of malignant melanoma misdiagnosed as a pituitary adenoma. Aggressive surgical treatment was complicated by a breach of the arachnoid membranes, then leading to an intracranial diffusion of the disease. Regarding these observations, we performed a systematic review of the literature in order to investigate clinicoradiological features that should lead clinicians to suspect pituitary metastasis and how it should impact the surgical management.

Case description:

Initial presentation

A 51-year-old woman without previous medical history, was admitted in our medical center for a rapid visual disturbance. These symptoms began few months ago and were associated with a general fatigue. The ophthalmological examination revealed a bitemporal hemianopsia. Endocrinological analysis showed modest hyperprolactinemia (908 uUI/mL, normal range: 102-496 uUI/mL), hypocortisolism and hypothyroidism. Computed tomography (CT) scans and brain magnetic resonance imaging (MRI) revealed a sellar lesion with suprasellar expansion leading to a compression of the optic chiasm. The lesion had heterogeneous high signal intensity on T1-weighted images, mild homogeneous enhancement on T1-weighted images with gadolinium infusion and had low signal intensity on T2-weighted images (Figure 1A). There were no other brain abnormalities on these exams. The patient underwent an exploration through a transsphenoidal endoscopic approach to release optic chiasm compression. Intraoperatively, the tumor was gray-colored with a necrotic

component. There was no adjacent bone or dura invasion. A breach of the arachnoid membranes was observed and sealed with fibrin-coated collagen fleece. Postoperatively, the patient recovered from her bitemporal hemianopsia but developed a diabetes insipidus. Hydrocortisone, levothyroxine and desmopressin oral substitution were required to balance endocrinological impairments in the early postoperative course.

Histological examination

The histological examination revealed a malignant tumor with melanotic pigmentation and necrosis (Figure 2). The immunohistochemistry testing was positive for HMB45, Sox10 and MelanA proteins. The diagnosis was consistent with a pituitary metastasis of malignant melanoma. BRAF mutation was positive, while cKIT and NRAS mutations were negative.

Postsurgical cerebrospinal fluid fistula

The patient came back to the hospital 14 days after surgery with severe headache, drowsiness and signs of intracranial hypotension. The CT scan showed disseminate pneumocephalus (Figure 1B). An endonasal revision surgery was performed to seal the CSF fistula with an autologous fat graft.

Oncological management

The patient underwent a full-body skin exam and a full-body CT/PET scan: no primitive or other secondary lesions were found. A new brain MRI was performed 9 weeks after surgery. It revealed contiguous extensions of the pituitary metastasis to the frontal lobes. Other brain metastases were observed in the right frontal lobe and in the right cingulate lobe (Figure 1C). In addition, the residual sellar tumor volume significantly increased in comparison to the immediate postsurgical CT scan.

A combined targeted therapy with dabrafenib (anti-BRAF) and trametinib (anti-MEK) was then started for 3 months. Due to a rapid clinical deterioration and progression of the disease, the treatment was changed to a monotherapy with vemurafenib (anti-BRAF) for 3 weeks. This treatment was stopped due to severe bilateral uveitis and skin rash. A third-line treatment with pembrolizumab (anti-PD1 immunotherapy) was then introduced. This therapy was stopped after the second infusion due to panhypopituitarism, that could be related either to the tumor progression or to an immunotherapy-related hypophysitis.[6] The patient finally deceased 12 months after the initial surgery due to a diffuse progression of brain metastases, repeated seizures and intracranial hypertension.

99

100 Systematic review of the literature:

101 A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews
102 and Meta-analyses (PRISMA) statement [7].

103 A literature search was performed in MEDLINE and Cochrane Library on May 5, 2020. The search strategy
104 used for MEDLINE was ((Pituitary OR Sella OR Sellar OR Hypophysis OR Neurohypophysis OR
105 Adenohypophysis) AND Metastas*) OR ("Pituitary Neoplasms/secondary"[Mesh]). Only symptomatic and
106 histologically confirmed cases were eligible. All cases of metastasis to the pituitary were initially screened.
107 Then, non-melanoma metastases to the pituitary and pituitary carcinomas were excluded from analysis. The
108 PRISMA flow diagram is provided in Figure 3. Thirteen studies were selected, including 15 cases of melanoma
109 metastases to the pituitary. These results are presented in Table 1.

110 Overall, the mean age was 58.3+/-16.3 years. There were only 3 females (20.0%). Ten patients (66.7%) had
111 visual disturbances, 2 patients (13.3%) had ophthalmoplegia, 3 patients (20.0%) had diabetes insipidus and 10
112 (66.7%) patients had anterior pituitary deficiency. One patient presented with an apoplexy syndrome.

113

114 Discussion:

115

116 Pituitary metastases have been described in autopsy series, but they remain rare in clinical condition. Among
117 them, few cases require a neurosurgical approach [8,9] with only 2.5 to 18.2% of pituitary metastases being
118 symptomatic [10]. In 40% of cases, pituitary metastases are the revealing condition of an underlying cancer [3].
119 Patients without previous neoplasm do not share the same clinical presentation as pituitary adenomas, with a
120 very high prevalence of ophthalmoplegia, visual field defects, visual acuity disorders and diabetes insipidus. By
121 contrast, posterior pituitary dysfunction and cranial nerve palsy is rarely reported in patients with pituitary
122 adenomas, excepted in case of apoplexy [11]. In addition, anterior pituitary gland dysfunction is observed in
123 most patient, with a prevalence of ACTH deficiency up to 71% [12]. The combination of ophthalmoplegia,
124 diabetes insipidus and/or adenohypophyseal dysfunction, the rapid installation of these symptoms and the
125 presence of a lateral extension on neuroimaging must lead clinicians to suspect pituitary metastases [1,11].

126

127 The occurrence of pituitary metastasis of malignant melanoma is very rare, with less than 20 cases reported in
128 the literature. Among them, there are autopsy reports in patients with disseminated metastatic spread [13–18].

Fifteen cases of symptomatic and histologically confirmed pituitary metastases of malignant melanoma were reported in the literature [19–31]. Among them, visual disturbance was the most common presentation (10 cases). A biological antehypophyseal insufficiency was also very common (10 cases) while diabetes insipidus was reported in only 3 cases. In two cases, a cranial nerve palsy was describe [25,30] and in another case, the disease was revealed by an apoplexy [21]. Most patients had a previous history of melanoma.

Rare cases of primary melanocytic tumors of the sellar region are reported in the literature [32,33]. Differential diagnosis between these primary lesions arising from the meninges and skin melanoma metastases can be challenging in case of negative whole-body imaging. Nevertheless, BRAF mutations seem to be absent or very rare in primary melanocytic tumors, while it is a common mutation in metastases from skin melanoma.[34,35]

Distant frontal and cingulate metastases observed in the present case may be related to the systemic progression of the disease, independently of the pituitary metastasis. No other case of metastatic spread after transsphenoidal surgical approach in pituitary metastases was reported in the literature, but only mentions of a possible leptomeningeal spread after a breach of the arachnoid membranes, which were mainly related to an intraoperative breaching of the diaphragma sellae [36,37]. One case of cerebrospinal fluid dissemination was described after a transsphenoidal surgery for a pituitary adenoma [38] and another case was about a growth hormone-producing pituitary carcinoma with spinal metastases following multiple surgeries [39]. Leptomeningeal spread of pituitary adenoma has been widely reported in patients who underwent craniotomies before the era of mini-invasive endoscopic transsphenoidal approach [40–42].

There is no standardized treatment for pituitary metastases, and different approaches have been described, including surgical resection, radiosurgery, radiotherapy and chemotherapy. While surgery is indicated for a symptomatic purpose (including optic chiasm decompression in case of bitemporal hemianopsia) and histopathological confirmation, it does not impact survival results [3,43]. Regarding our observations, it seems crucial to prevent any breach of the arachnoid layer in order to avoid subsequent intracranial diffusion of the disease. A gross total resection should not be attempted in case of doubtful clinicoradiological presentation (including a rapid progression of symptoms, and/or an unusual combination of endocrine deficits, visual deficits and cranial nerve palsy) or unusual intraoperative findings (including unattended bleeding or unusual aspect of the tumor).

159

160 Conclusion:

161 We report a case of pituitary metastasis of malignant melanoma misdiagnosed as a pituitary adenoma.
162 Aggressive surgical treatment was complicated by a breach of the arachnoid membranes, then leading to an
163 intracranial diffusion of the tumor. As surgery does not impact survival in pituitary metastases, we suggest that
164 gross total resection should not be attempted in case of doubtful clinicoradiological presentation (including a
165 rapid progression of symptoms, and/or an unusual combination of endocrine deficits, visual deficits and cranial
166 nerve palsy) or unusual intraoperative findings. Indeed, a precautious conservation of the arachnoid membranes
167 is necessary to avoid local or distant brain metastatic diffusion.

168

Tables

Table 1: Symptomatic Pituitary Metastases of Malignant Melanoma: Systematic Review of the Literature

Images and legends

Figure 1: (A) Preoperative Magnetic Resonance Imaging. From left to right: coronal T2 -weighted image, coronal T1-weighted image without and with Gadolinium infusion and Sagittal T1-weighted image with Gadolinium infusion. (B) Postoperative CT scan (12 days after surgery) showing diffuse pneumocephalus. (C) Postoperative MRI (9 weeks from the surgery). From left to right: coronal T1-weighted images with Gadolinium infusion and axial T1-weighted images with Gadolinium infusion. a: suprasellar enhancement; b and e: right cingulate enhancement; c: bilateral basifrontal enhancements; d: right frontal enhancement.

Figure 2: Postoperative pathological studies. (A) Hematoxylin and eosin-stained section. Immunohistochemical specimens show positive staining for HMB45 (B), Sox10 (C) and BRAF (D).

Figure 3: PRISMA flow diagram.

Patient consent

The patient has consented to the submission of this case report.

Compliance with ethical standards

Conflict of interest. The authors declare that they have no conflict of interest.

References

- [1] Habu M, Tokimura H, Hirano H, Yasuda S, Nagatomo Y, Iwai Y, et al. Pituitary metastases: current practice in Japan. *J Neurosurg* 2015;123:998–1007. <https://doi.org/10.3171/2014.12.JNS14870>.
- [2] Fassett DR, Couldwell WT. Metastases to the pituitary gland. *Neurosurg Focus* 2004;16:E8.
- [3] Ng S, Fomekong F, Delabar V, Jacquesson T, Enachescu C, Raverot G, et al. Current status and treatment modalities in metastases to the pituitary: a systematic review. *J Neurooncol* 2020;146:219–27. <https://doi.org/10.1007/s11060-020-03396-w>.
- [4] Couldwell WT, Chandrasoma PT, Weiss MH. Pituitary gland metastasis from adenocarcinoma of the prostate. Case report. *J Neurosurg* 1989;71:138–40. <https://doi.org/10.3171/jns.1989.71.1.0138>.
- [5] Weber J, Gassel AM, Hoch A, Spring A. Concomitant renal cell carcinoma with pituitary adenoma. *Acta Neurochir (Wien)* 2003;145:227–31. <https://doi.org/10.1007/s00701-002-1060-0>.
- [6] Byun DJ, Wolchok JD, Rosenberg LM, Girotra M. Cancer immunotherapy — immune checkpoint blockade and associated endocrinopathies. *Nat Rev Endocrinol* 2017;13:195–207. <https://doi.org/10.1038/nrendo.2016.205>.
- [7] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. *PLoS Med* 2009;6:e1000100. <https://doi.org/10.1371/journal.pmed.1000100>.
- [8] Marsh JC, Garg S, Wendt JA, Giolda BT, Turian JV, Herskovic AM. Intracranial metastatic disease rarely involves the pituitary: retrospective analysis of 935 metastases in 155 patients and review of the literature. *Pituitary* 2010;13:260–5. <https://doi.org/10.1007/s11102-010-0229-4>.
- [9] Nelson PB, Robinson AG, Martinez JA. Metastatic Tumor of the Pituitary Gland: *Neurosurgery* 1987;21:941–4. <https://doi.org/10.1227/00006123-198712000-00030>.
- [10] Komninos J, Vlassopoulou V, Protopapa D, Korfias S, Kontogeorgos G, Sakas DE, et al. Tumors Metastatic to the Pituitary Gland: Case Report and Literature Review. *J Clin Endocrinol Metab* 2004;89:574–80. <https://doi.org/10.1210/jc.2003-030395>.
- [11] Arafah BM, Nasrallah MP. Pituitary tumors: pathophysiology, clinical manifestations and management. *Endocr Relat Cancer* 2001;8:287–305.
- [12] Schill F, Nilsson M, Olsson DS, Ragnarsson O, Berinder K, Edén Engström B, et al. Pituitary Metastases: A Nationwide Study on Current Characteristics With Special Reference to Breast Cancer. *J Clin Endocrinol Metab* 2019;104:3379–88. <https://doi.org/10.1210/jc.2019-00012>.

- [13] Neilson JMcE, Moffat AD. Hypopituitarism caused by a melanoma of the pituitary gland. *J Clin Pathol* 1963;16:144–9. <https://doi.org/10.1136/jcp.16.2.144>.
- [14] Chiang M-F, Brock M, Patt S. Pituitary metastases*. *Min - Minim Invasive Neurosurg* 1990;33:127–31. <https://doi.org/10.1055/s-2008-1053571>.
- [15] Max MB, Deck MDF, Rottenberg DA. Pituitary metastasis: Incidence in cancer patients and clinical differentiation from pituitary adenoma. *Neurology* 1981;31:998–998. <https://doi.org/10.1212/WNL.31.8.998>.
- [16] Kovacs K. Metastatic Cancer of the Pituitary Gland. *Oncology* 1973;27:533–42. <https://doi.org/10.1159/000224763>.
- [17] Benjamin L. Ein Krebsfall. *Arch Für Pathol Anat Physiol Für Klin Med* 1857;12:566–9. <https://doi.org/10.1007/BF01950081>.
- [18] Scholtz CL, Siu K. Melanoma of the pituitary. *J Neurosurg* 1976;45:101–3. <https://doi.org/10.3171/jns.1976.45.1.0101>.
- [19] Leung GKK, Chow WS, Tan KCB, Fan YW, Lam KSL. Metastatic melanoma of the pituitary gland. Case report. *J Neurosurg* 2003;99:913–5. <https://doi.org/10.3171/jns.2003.99.5.0913>.
- [20] Guzel A, Maciacyk J, Dohmen-Scheufler H, Senturk S, Volk B, Ostertag CB, et al. Multiple intracranial melanoma metastases: case report and review of the literature. *J Neurooncol* 2009;93:413–20. <https://doi.org/10.1007/s11060-008-9785-0>.
- [21] Masui K, Yonezawa T, Shinji Y, Nakano R, Miyamae S. Pituitary Apoplexy Caused by Hemorrhage From Pituitary Metastatic Melanoma: Case Report. *Neurol Med Chir (Tokyo)* 2013;53:695–8. <https://doi.org/10.2176/nmc.cr2012-0068>.
- [22] 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 (Baltimore)* 2017;96:e6483. <https://doi.org/10.1097/MD.00000000000006483>.
- [23] Wang J, Ma E, Wu P, and B, Wang Y. Multiple intracranial and spinal metastases from a nonfunctioning pituitary adenoma following multiple surgeries: an illustrative case with 16 years of follow-up. *World J Surg Oncol* 2014;12:380. <https://doi.org/10.1186/1477-7819-12-380>.
- [24] Jung S-M, Hsu Y-Y, Chuang C-C, Chang C-N, Hsueh C, Kuo T. A man in his mid-70s with a sellar mass. *Brain Pathol Zurich Switz* 2007;17:115–6, 121. https://doi.org/10.1111/j.1750-3639.2007.00044_1.x.
- [25] McCutcheon IE, Waguespack SG, Fuller GN, Couldwell WT. Metastatic melanoma to the pituitary gland. *Can J Neurol Sci J Can Sci Neurol* 2007;34:322–7.
- [26] Zoli M, Mazzatenta D, Faustini-Fustini M, Pasquini E, Frank G. Pituitary Metastases: Role of Surgery. *World Neurosurg* 2013;79:327–30.

- <https://doi.org/10.1016/j.wneu.2012.03.018>.
- [27] Goulart CR, Upadhyay S, Ditzel Filho LFS, Beer-Furlan A, Carrau RL, Prevedello LM, et al. Newly Diagnosed Sellar Tumors in Patients with Cancer: A Diagnostic Challenge and Management Dilemma. *World Neurosurg* 2017;106:254–65. <https://doi.org/10.1016/j.wneu.2017.06.139>.
- [28] Castle-Kirszbaum M, Goldschlager T, Ho B, Wang YY, King J. Twelve cases of pituitary metastasis: a case series and review of the literature. *Pituitary* 2018;21:463–73. <https://doi.org/10.1007/s11102-018-0899-x>.
- [29] Mayr NA, Yuh WTC, Muhonen MG, Koci TM, Tali ET, Nguyen HD, et al. Pituitary Metastases: MR Findings. *J Comput Assist Tomogr* 1993;17:432–7. <https://doi.org/10.1097/00004728-199305000-00018>.
- [30] Kano H, Niranjana A, Kondziolka D, Flickinger JC, Lunsford LD. Stereotactic radiosurgery for pituitary metastases. *Surg Neurol* 2009;72:248–55. <https://doi.org/10.1016/j.surneu.2008.06.003>.
- [31] Burkhardt T, Henze M, Kluth LA, Westphal M, Schmidt NO, Flitsch J. Surgical management of pituitary metastases. *Pituitary* 2016;19:11–8. <https://doi.org/10.1007/s11102-015-0676-z>.
- [32] Tüttenberg J, Fink W, Back W, Wenz F, Schadendorf D, Thomé C. A rare case of primary sellar melanoma. *J Neurosurg* 2004;100:931–4. <https://doi.org/10.3171/jns.2004.100.5.0931>.
- [33] Wang F, Ling S. Primary Meningeal Melanocytoma in Sellar Region, Simulating a Nonfunctioning Pituitary Adenoma: Case Report and Literature Review. *World Neurosurg* 2018;112:209–13. <https://doi.org/10.1016/j.wneu.2018.01.145>.
- [34] Küsters-Vandeveld HVN, Klaasen A, Küsters B, Groenen PJTA, van Engen-van Grunsven IACH, van Dijk MRCF, et al. Activating mutations of the GNAQ gene: a frequent event in primary melanocytic neoplasms of the central nervous system. *Acta Neuropathol (Berl)* 2010;119:317–23. <https://doi.org/10.1007/s00401-009-0611-3>.
- [35] Gessi M, Hammes J, Lauriola L, Dörner E, Kirfel J, Kristiansen G, et al. *GNAI1* and *N-RAS* mutations: alternatives for MAPK pathway activating GNAQ mutations in primary melanocytic tumours of the central nervous system. *Neuropathol Appl Neurobiol* 2013;39:417–25. <https://doi.org/10.1111/j.1365-2990.2012.01288.x>.
- [36] Wang YY, Norris A, du Plessis D, Gnanalingham KK. Melanoma of the sellar region. *J Clin Neurosci* 2011;18:154–6. <https://doi.org/10.1016/j.jocn.2010.07.111>.
- [37] Wang D, Li T, Tian Y, Wang S, Jin C, Wei H, et al. Effects of atorvastatin on chronic subdural hematoma: A preliminary report from three medical centers. *J Neurol Sci* 2014;336:237–42. <https://doi.org/10.1016/j.jns.2013.11.005>.
- [38] Tanaka Y, Tsuda M, Sato M, Kanno H, Tokoro K, Yamamoto I, et al. CSF Dissemination of a Pituitary Adenoma : A Case Report. *Jpn J Neurosurg* 1996;5:391–7.

<https://doi.org/10.7887/jcns.5.391>.

[39] Tanaka T, Kato N, Aoki K, Watanabe M, Arai T, Hasegawa Y, et al. Long-term follow-up of growth hormone-producing pituitary carcinoma with multiple spinal metastases following multiple surgeries: case report. *Neurol Med Chir (Tokyo)* 2013;53:707–11.

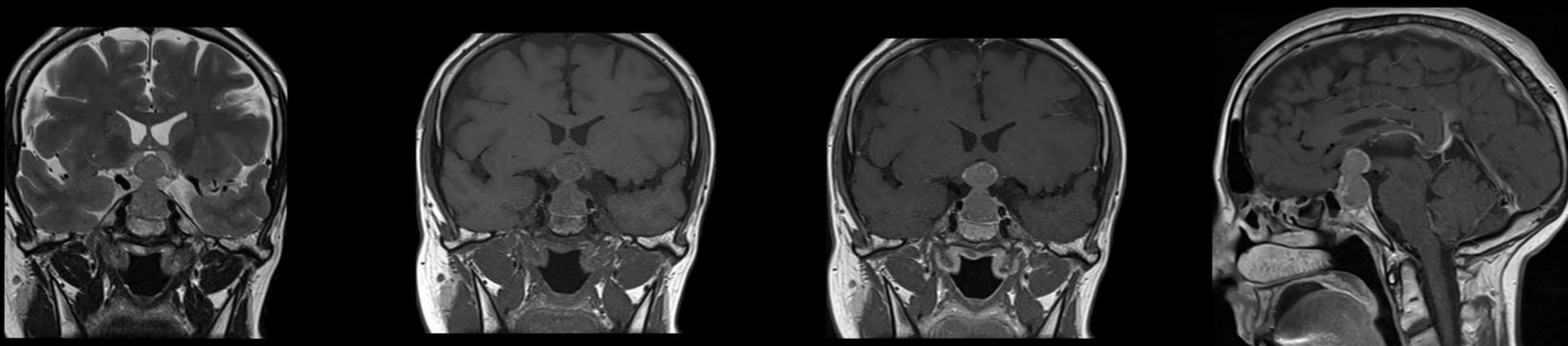
[40] Kuroki M, Tanaka R, Yokoyama M, Shimbo Y, Ikuta F. Subarachnoid dissemination of a pituitary adenoma. *Surg Neurol* 1987;28:71–6. [https://doi.org/10.1016/0090-3019\(87\)90210-2](https://doi.org/10.1016/0090-3019(87)90210-2).

[41] Gasser RW, Finkenstedt G, Skrabal F, Twerdy K, Grunert V, Mayr U, et al. Multiple intracranial metastases from a prolactin secreting pituitary tumour. *Clin Endocrinol (Oxf)* 1985;22:17–27.

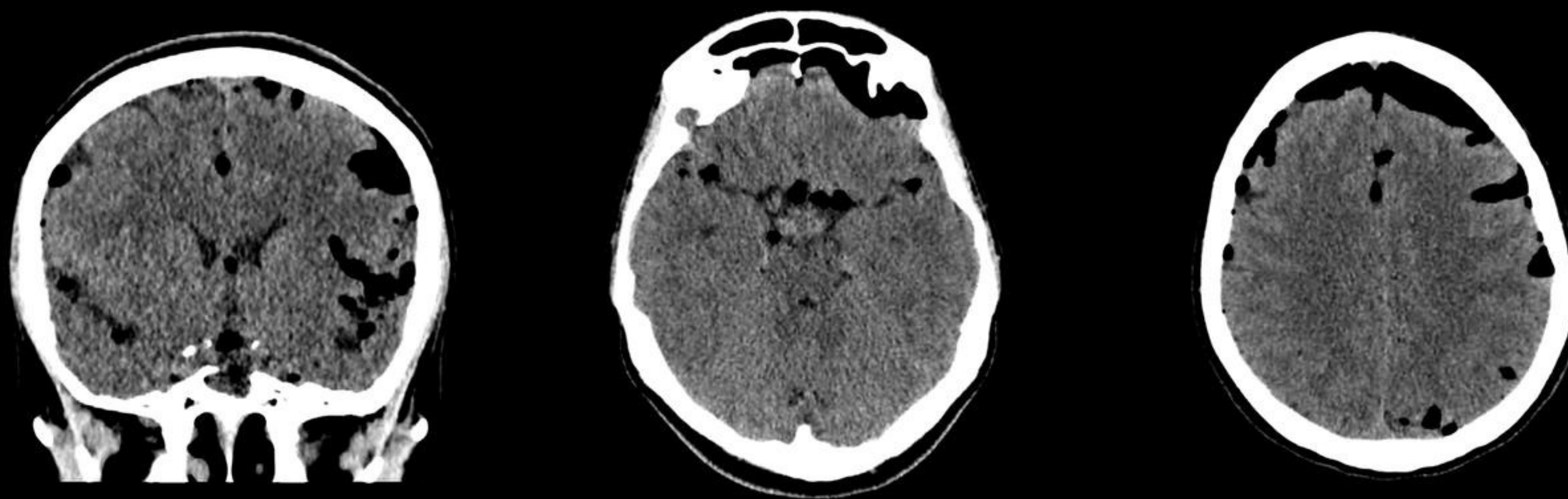
[42] Taylor WAS, Uttley D, Wilkins PR. Multiple dural metastases from a pituitary adenoma. *J Neurosurg* 1994;81:624–6. <https://doi.org/10.3171/jns.1994.81.4.0624>.

[43] Gilard V, Alexandru C, Proust F, Derrey S, Hannequin P, Langlois O. Pituitary metastasis: is there still a place for neurosurgical treatment? *J Neurooncol* 2016;126:219–24. <https://doi.org/10.1007/s11060-015-1967-y>.

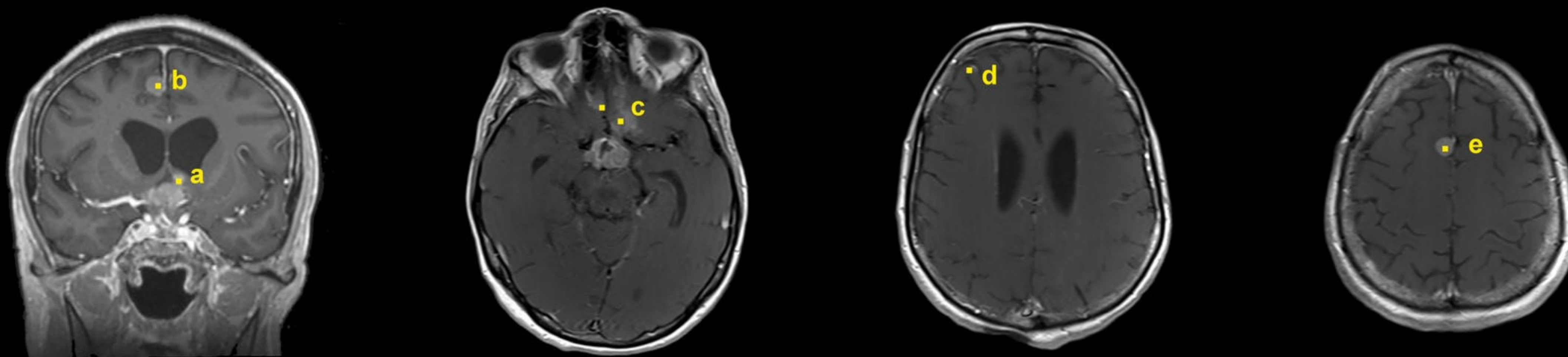
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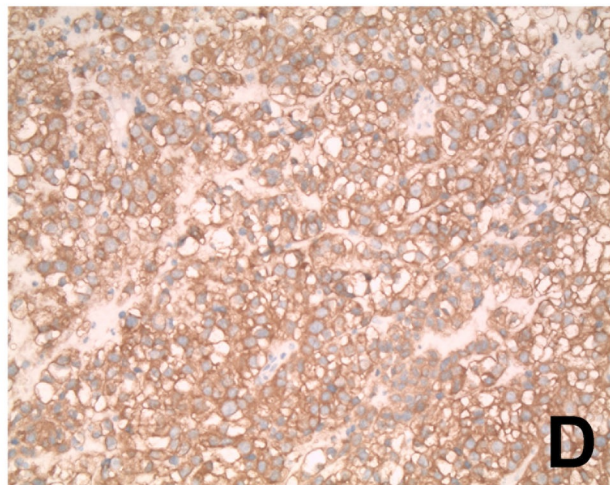
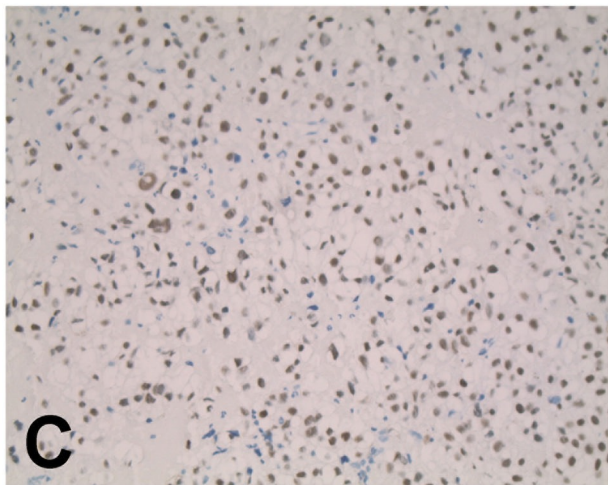
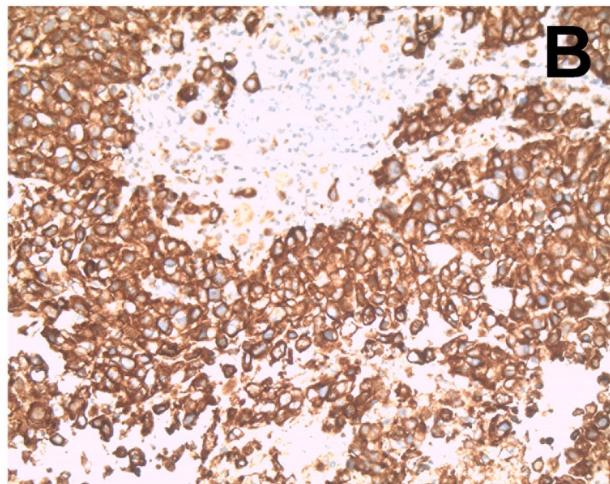
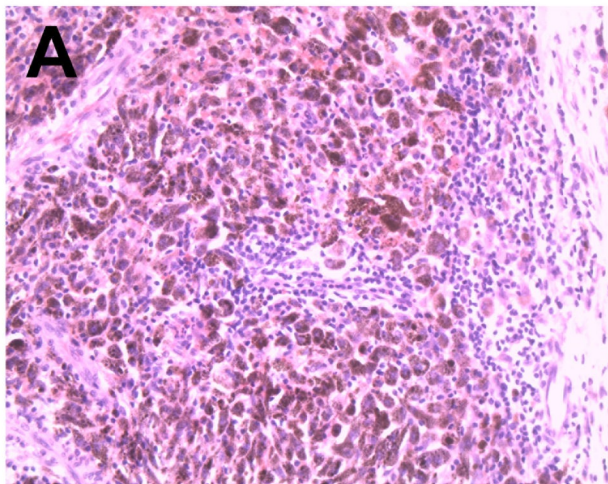


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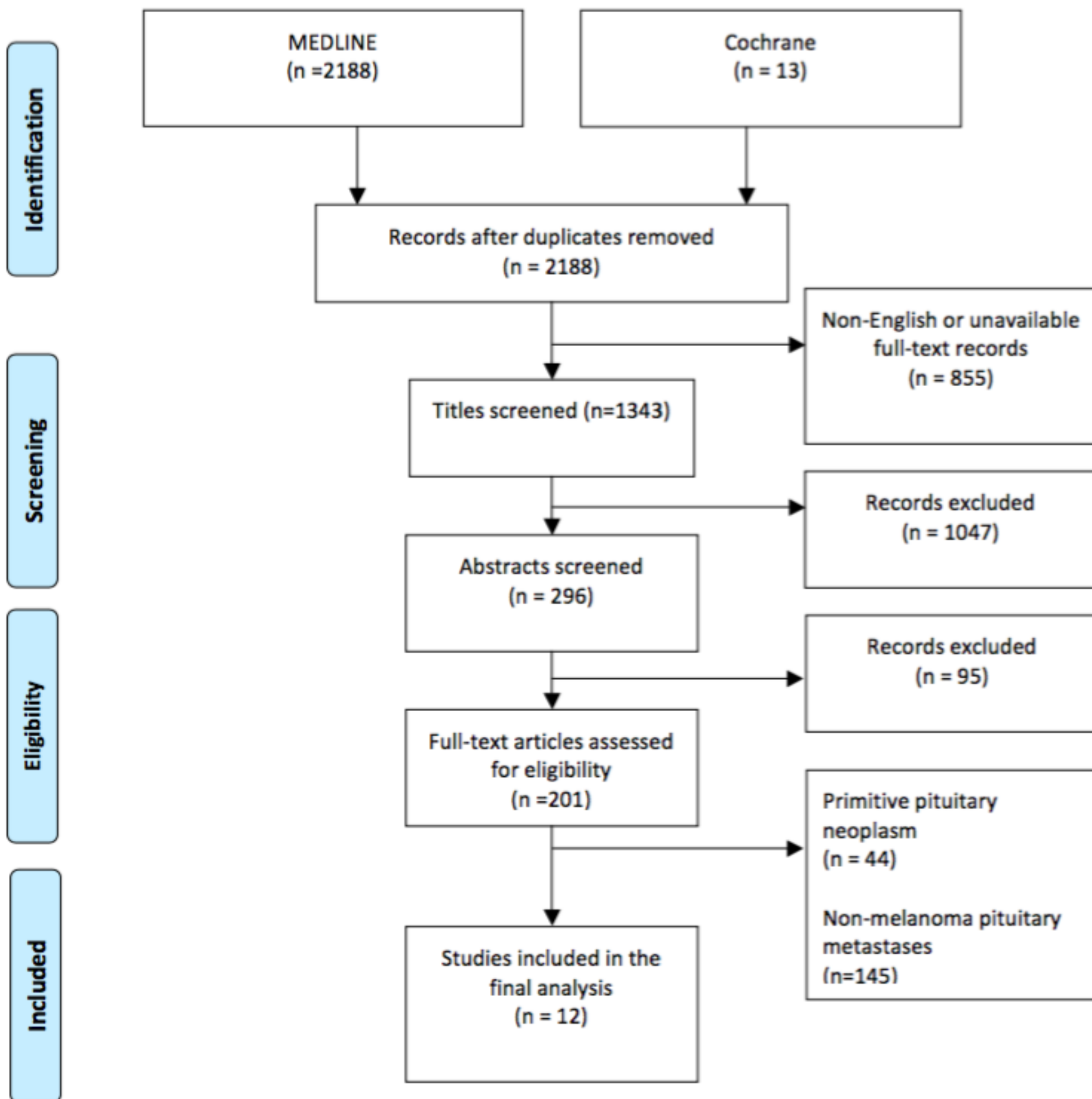


Table 1: Symptomatic Pituitary Metastases of Malignant Melanoma: Systematic Review of the literature

Case No	Authors & Year	Age (years), gender	Clinical presentation	Pituitary dysfunction	MRI findings Anterior / posterior lobe / sellar invasion	Histopathology and Immunocytochemistry	Melanoma Past history	Concomitant metastases or primary tumor at diagnosis	Treatment	Last follow-up
1	Mayr et al, 1993 (33)	25, male	Anterior pituitary dysfunction	Unknown	Sellar and suprasellar High T1, Low T2 signal Gadolinium enhancement	Details not provided	Unknown	Presence of systemic metastases and brain metastases	Details not provided	unknown
2	Leung et al, 2003 (8)	46, male	Diabetes insipidus Erectile dysfunction	Diabetes insipidus Decreased Testosterone, FSH, LH Decreased FT4 Decreased ACTH	Sellar Heterogeneous high T1 signal Low T2 signal Heterogeneous Gadolinium enhancement	Melanin pigmentation S-100 HMB-45	Right ear lobe melanoma. Clark IV. Lymphadenopathy. 5 years ago.	Negative whole-body FDG-PET	Transsphenoidal resection. Whole-brain irradiation.	7 months
3	Jung et al, 2007 (26)	70, male	Visual disturbance	Increased PRL Decreased ACTH Decreased FT4, FT3	Sellar and suprasellar Iso T1, High T2 signal Gadolinium enhancement	Melanin pigmentation S-100 HMB-45	Left big toe melanoma, T3N1M0, 15 months ago	Mediastinal, liver, inguinal and kidney lesions	Transsphenoidal resection. No adjuvant therapies	1 month. Death
4	McCutcheon et al, 2007 (27)	77, male	Ptosis and diplopia Visual disturbance	Decreased GH	Sellar, suprasellar, upper clivus extension	S-100 HMB-45	Anterior chest wall, Clark IV. Lymphadenopathy. 33 months ago.	Negative exploration	Transsphenoidal debulking. Radiotherapy.	6 months
5	McCutcheon et al, 2007	42, male	Diabetes insipidus Visual disturbance	Diabetes insipidus, Decreased GH Decreased FT4,3 Decreased ACTH	Sellar and suprasellar	Melanin pigmentation HMB-45	Anterior chest wall, Clark IV. 77 months ago.	Subcutaneous chest nodules Cervical, lung and retroperitoneal lymphadenopathy	Transsphenoidal debulking. Whole-brain irradiation (30 Gy). Thalidomide and temozolomide.	4 months Death
6	Guzel et al, 2009 (9)	46, female	Headache	No abnormalities	Sellar Iso T1, Iso T2 signal Gadolinium enhancement	S-100 HMB-45	Left shoulder melanoma 7 years ago. Lymphadenopathy 1 year ago.	Right pontocerebellar angle lesion	Stereotactic Biopsy. Whole-brain irradiation. Temozolomide	9 months Death
7	Kano et al, 2009	47, male	Diabetes insipidus	Diabetes insipidus.	unknown	Details not provided	Unknown	Unknown	Surgery. Stereotactic radiosurgery	34.8 months Death
8	Kano et al, 2009 (32)	52, female	Ophthalmoplegia	No pituitary dysfunction	unknown	Details not provided	Unknown	Unknown	Stereotactic radiosurgery	21.8 months Death
9	Wang et al, 2011 (14)	78, male	Visual disturbance, weight loss	Decreased Testosterone Decreased FT4, FT3 Decreased ACTH	Sellar and suprasellar High T1, low T2 signal Mild Gadolinium enhancement	Melanin pigmentation	-	Left frontal lobe lesion Liver and splenic lesions	Transsphenoidal debulking	1 week Death
10	Masui et al, 2013 (10)	68, male	Sudden headache and visual disturbance. Apoplexy	Decreased FT4, FT3	Sellar and suprasellar High T1, Low T2 signal, Heterogenous Gadolinium enhancement	Necrosis S-100 HMB-45	-	Stomach primary melanoma	Transsphenoidal debulking. No adjuvant therapies.	2 months
11	Zoli et al, 2013 (28)	unknown	Visual disturbance	unknown	unknown	unknown	unknown	unknown	Transsphenoidal resection	unknown
12	Burkhardt et al 2015	73, male	Visual disturbance, Anterior pituitary dysfunction, Diabetes insipidus	unknown	unknown	Details not provided	Unknown	Unknown	Surgery. Stereotactic radiotherapy (39Gy)	unknown
13	Yang et al, 2017 (11)	62, female	Visual disturbance	Increased PRL Decreased FT4, FT3	Sellar and suprasellar Iso T1, Iso T2 signal, Homogeneous Gadolinium enhancement, Bone destruction	Melanin pigmentation No necrosis S-100 HMB45	Left heel melanoma diagnosed 2 years ago. Stage III	Portal and retroperitoneal lymphadenopathy, Liver lesions	Transsphenoidal debulking. No adjuvant therapies.	22 months
14	Goulart et al, 2017 (29)	52, male	Visual disturbance	Panhypopituitarism	Suprasellar Gadolinium enhancement	Details not provided	Unknown	Unknown	Transsphenoidal debulking. No adjuvant therapies.	5 months
15	Castle-Kirsbaum et al, 2018 (30)	78, male	Visual disturbance	Increased ACTH Decreased FT4, FT3	Sellar and suprasellar High T1, Low T2 signal Gadolinium enhancement	Details not provided	Unknown	Disseminated lesions	Transsphenoidal debulking. No adjuvant therapies (palliation)	unknown-