Primary Sellar Melanoma Simulating Hemorrhagic Pituitary Adenoma: MR and Pathologic Findings

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Primary intracranial melanoma is uncommon, and primary malignant melanoma of the sella turcica is exceedingly rare. We describe a 35-year-old woman who presented with endocrine dysfunction and CT findings suggestive of a prolactin-secreting macroadenoma. Subsequent MR findings revealed homogeneously short T1 and T2 relaxation times, yielding uniformly bright signal on T1-weighted images and dark signal on T2-weighted images. At high field strength (1.5 T), these characteristics seemed to implicate either paramagnetic effects suggestive of subacute hemorrhage or the intrinsically short relaxation times of lipidlke or mucinous material that may accumulate in a dermoid or Rathke cleft cyst. Following surgery, a final pathologic review revealed deeply pigmented, nonhemorrhagic malignant melanoma. The paramagnetic effect of stable free radicals of melanin is thought to account for the confusing MR characteristics of this uncommon lesion encountered at an unusual location [1-3].

Case Report

A 35-year-old woman presented with a 3-year history of oligomenorrhea, intermittent galactorrhea, and headache. Her prolactin level was 102.5 ng/ml (normal range, 0–20 ng/ml). Contrast-enhanced CT revealed a homogeneously hyperdense lesion in the sella turcica with suprasellar extension. High-field-strength MR (GE 1.5 T) confirmed the presence of a pituitary mass, demonstrating very high signal intensity on T1-weighted images, and low signal intensity on T2-weighted images (Fig. 1). The CT and MR appearance of the mass suggested a histologically complex lesion harboring a paramagnetic substance. The combination of clinical findings, laboratory-documented hormonal derangements, and imaging results prompted consideration of hemorrhagic pituitary adenoma (the favored preoperative diagnosis) or a developmental inclusion tumor of dermal origin.

At transphenoidal hypophysectomy, a firm, dark black/purple mass was exposed and a biopsy was done. Frozen section specimens were interpreted as showing no evidence of tumor. Initially, the lesion was thought to represent an area of old hemorrhage with hemosiderin deposition. However, permanent histologic sections demonstrated a markedly pleomorphic tumor. Large amounts of melanin pigment were identified on both Fontana and melanin bleach stains. Prussian blue stains were negative for iron (Fig. 2). These distinctive histologic findings confirmed the final pathologic diagnosis as malignant melanoma.

Postoperatively, ophthalmoscopic, gynecologic, and dermatologic examinations were negative. Endoscopy of the gastrointestinal tract also failed to reveal an extracranial primary tumor. Complete hypophysectomy, followed by moderate-dose radiotherapy was recommended, but the patient refused further treatment. MR of the sella 3 months later showed regrowth of the tumor, filling the entire sella turcica and adjacent suprasellar cistern. Hyperintensity was again noted on T1-weighted images and hypointensity was seen on T2-weighted images.

Discussion

Malignant melanoma metastasizes commonly to the CNS, and knowledge of an extra-CNS primary lesion is usually at hand. Furthermore, distinctive CT and MR features related to cellular compactness, blood-brain-barrier defects, sequelae of hemorrhage, and melanin content of metastatic melanoma usually permit an accurate preoperative diagnosis. Our patient is extraordinary both because of the unusual MR signal changes exhibited by the tumor and the rarity of primary intracranial melanomas at this site.

Melans are naturally occurring paramagnetic photoprotective polymers [3]. Paramagnetism derives from the presence of stable organic free radicals in melanin. The unpaired electrons of these free radicals are accessible to water protons, and can enhance proton relaxation via proton-electron-dipole interactions [3]. These interactions result in shortening of both T1 and T2 relaxation times, producing hyperintensity on T1-weighted images and hypointensity on T2-weighted images.

In a series of six choroidal melanomas reported by Gomori et al. [2], all lesions displayed shortening of T1 and T2 relaxation times proportional to their melanin content. On T1-weighted images, hyperintensity of a deeply pigmented melanoma can mimic the behavior of methemoglobin, a more common biological molecule that exhibits paramagnetism.

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Fig. 1.—Coronal MR images show signal changes of primary intrasellar melanoma.
A, T1-weighted (600/20) image. Tumor (T) occupies entire sella turcica and extends superiorly into suprasellar cistern, uplifting the left side of the optic pathway (straight arrows). Note that the uniform hyperintensity of the tumor parallels the appearance of fat signal in the marrow space of the subjacent medial temporal bone (curved arrows).
B, Proton-density-weighted (2000/30) image. Lesion shows uniformly decreased signal intensity that appears isointense relative to normal neural tissue.
C, T2-weighted (2000/80) image. Lesion displays hypointensity relative to neural tissue, including normal white matter. Note that the melanoma is isointense with the fatty marrow space of the medial temporal bone (curved arrows). The pattern displayed is attributable to the paramagnetic effects of free radical contained in melanin pigment.

Fig. 2.—Histologic photomicrographs from surgical specimen.
A, Hematoxin and eosin (H and E) staining demonstrates components of rustlike material representing melanin pigment, which is difficult to differentiate from hemosiderin on H and E.
B, Fontana stain is positive for melanin pigment, evident by numerous components of darkly staining material.
C, Melanin bleach stain reveals pigmented areas as multiple sites of lightly staining material (arrows). Prussian blue stains were negative for iron.

Preferential T2 proton relaxation enhancement (PRE) is observed when a paramagnetic substance is heterogeneously distributed. Biologically, this effect is often caused by intracellular methemoglobin, a blood degradation product absent in our patient’s nonhemorrhagic lesion. Although melanin, heterogeneously distributed within melanosomes, might be expected to demonstrate this effect, its only significant paramagnetic effect in MR imaging is PEDD PRE. The absence of T2 PRE in melanomas may be related to the lack of sufficient quantities of paramagnetic melanin or to insufficient heterogeneity of distribution [2]. Melanomas are, as a result, relatively less hypointense than intracellular methemoglobin on T2-weighted images.

Lysis of red blood cells containing methemoglobin results in elimination of the T2 PRE. Undiluted, free methemoglobin (i.e., before partial resorption of the methemoglobin released from lysed cells) is mildly hypointense on T2-weighted images. Thus, melanotic melanomas may be difficult to distinguish from hemorrhagic areas, which can produce similar MR signal characteristics.

Lipidlike material could also produce the signal changes shown in Figure 1. Most aliphatic molecular species exhibit
intrinsically short T1 and T2 relaxation times in the absence of paramagnetic effects. For instance, note that the fatty marrow space of the petrous bone beneath the sphenoid sinus (curved arrows in Fig. 1) shows signal changes that closely parallel the appearance of the intrasellar lesion on T1-weighted images, proton-density-weighted images, and T2-weighted images.

The possibility that the pituitary fossa tumor represented a lipoma was dismissed because of its hyperdensity on CT scans. Other lipid-, cholesterol-, or mucin-containing lesions of developmental origin such as a dermoid, epidermoid, or Rathke cleft remnant cyst, warrant consideration [4, 5]. Among these, epidermoid and Rathke cleft cysts occasionally show increased density on CT scans and would therefore be more difficult to exclude.

Chemical shift misregistration is an MR finding that appears at interfaces of fat and hydrated tissue oriented perpendicular to the frequency-encoded direction. Chemical shift misregistration is especially prominent on high-field-strength images [6]. The absence of this distinctive MR artifact at the perimeter of the lesion shown in our patient argues against the possibility of a lipid-containing tumor.

The initial imaging study (CT), in conjunction with our patient's clinical history, prompted consideration of a prolactin-secreting macroadenoma as the favored diagnosis. Subsequent MR studies revealed signal changes that could plausibly and perhaps most likely be explained on the basis of tumoral hemorrhage, a not uncommon complication of pituitary adenomas on MR. Although other diagnoses were considered, the possibility of melanoma was never entertained, owing to the unexpected occurrence of such a lesion at this location.

Primary intracranial melanoma or melanocytoma can develop at the surface of the brain as a solitary lesion or in the form of diffuse meningeal melanosis [7]. Both forms affect the elderly, with peak incidence occurring in the seventh decade.

Only two intrasellar melanomas have been reported previously, both prior to the advent of CT and MR [8, 9]. As in our patient, exhaustive searches for extra-CNS primary lesions were negative.

Intrasellar pial elements or pigmented cells of the posterior pituitary gland are thought to give rise to pituitary melanomas. Melanotic pigment is often distributed irregularly amidst glial-origin pituicytes of the pars nervosa, a normal microscopic finding noted by Kernohan and Sayre [10]. These observations provide a histologic basis for oncogenic derivation of the tumor described in our patient.

Any tumefactive process occurring in proximity to the infundibular stem can disrupt the delicate hypothalamic-portal feedback mechanism. Because the main influence of the hypothalamus on anterior pituitary prolactin secretion is inhibitory, interruption of this pathway commonly produces hyperprolactinemia. Other anterior pituitary hormones may be deficient, owing to interference of stimulatory hypothalamic influences. Progressive tumor enlargement eventually causes panhypopituitarism, neurologic deficits, and headache, owing to direct compressive effects exerted upon the adenohypophysis and bordering neural tissue. Thus, the potential spectrum of nonspecific endocrinologic dysfunction caused by an intrasellar mass effect obviously incorporates the hormonal disturbance (hyperprolactinemia) and clinical symptoms observed in our patient.

This case provides a paradigm for the study of MR signal changes produced by the paramagnetic effects of melanin isolated from tumor hemorrhage, a frequent histologic accompaniment of metastatic melanoma.

REFERENCES