Clinical Neurology and Neurosurgery 120 (2014) 120–123

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Case report

Multiple intracranial tumors: Coexistence of a glioblastoma and null cell pituitary adenoma within the same patient

Ersin Haciyakupoglu[a], Aydın Sav[b], Sebahattin Haciyakupoglu[a], Jan Walter[c,*]

[a] Acibadem University Hospital Adana, Department of Neurosurgery, Adana, Turkey
[b] Acibadem University Hospital Istanbul, Department of Pathology, Istanbul, Turkey
[c] Jena University Hospital, Friedrich Schiller University Jena, Department of Neurosurgery, Jena, Germany

ARTICLE INFO

Article history:
Received 14 October 2013
Received in revised form 4 March 2014
Accepted 5 March 2014
Available online 13 March 2014

Keywords:
Glioblastoma multiforme
Multiple intracranial tumors
Null cell pituitary adenoma

1. Introduction

The coexistence of a glioblastoma multiforme and a null cell pituitary adenoma within the same patient is presented. Although brain tumors are diagnosed in a slightly increasing number of patients, due to a broader availability of computer tomography and magnetic resonance imaging (MRI), the estimated frequency of primary brain tumors per year is as low as about 6–8 patients/100,000 people. Moreover, simultaneous existences of primary brain tumors with different pathologies were described in not more than 0.9% of all primary brain tumors, but the majority of those cases were seen after radiotherapy or are associated with familial tumor syndromes [1,3]. Furthermore it is known that in phacomatosis syndromes, mesodermal and neuroectodermal tumors can be seen together and occurrences of an ependymoma, chromophobe pituitary adenoma and an astrocytoma in those patients have been reported elsewhere [4]. But to our knowledge, this is the only case with two intracranial tumors of an essentially different histopathological nature within the same patient, who does not suffer from any known germ line mutation.

2. Case report

A 61-year-old patient was admitted to the outpatient department suffering from severe headache, completely resistant to analgesic drugs. He had a history of headache and easy fatigability for two weeks. Nausea and vomiting started 3 days ago. The patient neither had drinking nor smoking habits. No related familial or past history was discovered. Cranial MRI revealed two different types of intracranial tumors and the patient was admitted to our hospital. On admission, his general examination, except being somnolent, was found to be normal. Neurological examination revealed a bilateral primary optic atrophy and visual disturbances. Gadolinium enhanced cranial MRI showed a right frontal tumor mass of 4.3 cm × 5.2 cm with perifocal edema, and yet another suprasellar mass, which already had displaced the optic chiasm (Fig. 1). Pre-operative laboratory analysis showed all pituitary hormones within normal ranges, and no hormones were excessively secreted. Medication with dexamethasone (24 mg daily) was begun. Treatment was planned in a single stage, with a combined removal of the frontal lesion and subsequent transcranial removal of the suprasellar tumor.

Supratentorial tumor removal was performed through a right fronto-temporo-sphenoidal (modified pterional) craniotomy. The tumor consisted of hard nodular and cystic components and gross total tumor removal was achieved. The suprasellar tumor was subsequently removed through the same approach. The fibrous yellowish tumor could be removed totally. Postoperatively, the patient was cooperative and oriented with no new neurological deficit.

* Corresponding author at: Department of Neurosurgery, Jena University Hospital, Friedrich Schiller University Jena, Erlanger Allee 101, D-07747 Jena, Germany. Tel.: +49 3641 9323011; fax: +49 3641 9323012.
E-mail addresses: haciyakupoglu@gmail.com (E. Haciyakupoglu), aydinsav@gmail.com (A. Sav), drsebahattin@superonline.com (S. Haciyakupoglu), jan.walter@med.uni-jena.de (J. Walter).

http://dx.doi.org/10.1016/j.clineuro.2014.03.002

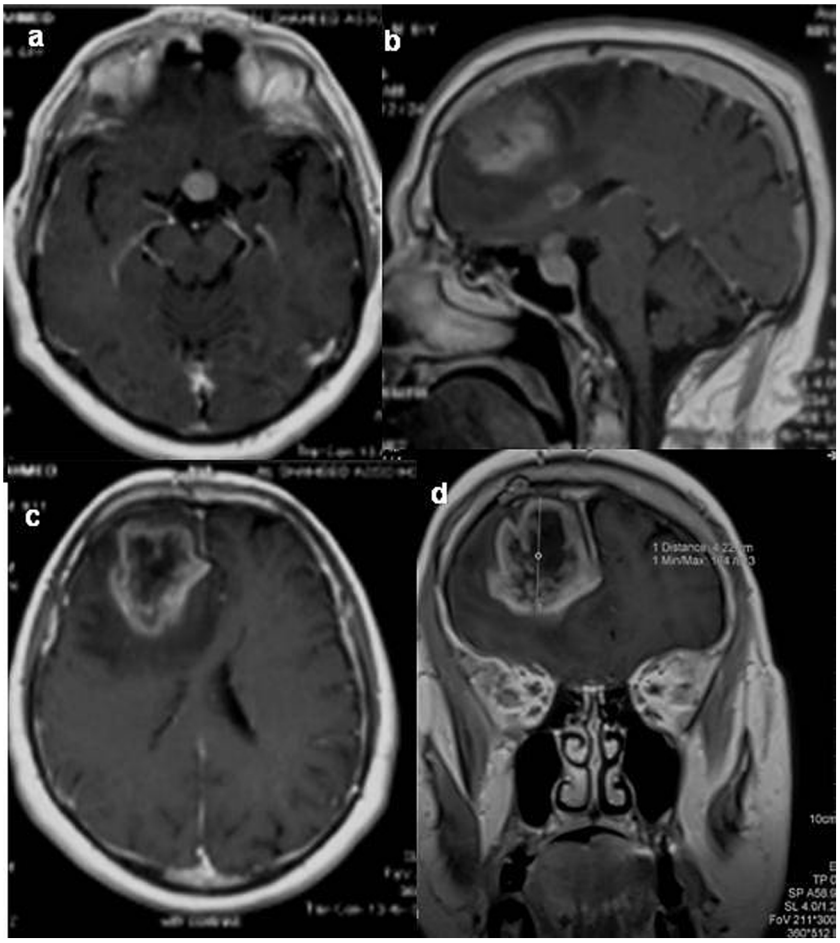

Fig. 1. (a) Preoperative axial magnetic resonance imaging (MRI) of the brain showing a well defined sellar tumor with homogeneous contrast enhancement after gadolinium (Gd) administration. (b) Sagittal contrast-enhanced T1-weighted MRI scan demonstrates a suprasellar extension of the pituitary adenoma and revealing a further mass lesion in the right frontal lobe. (c and d) Axial and coronal Gd-MR images demonstrating the supratentorial mass lesion with ring-like enhancement, heterogeneous necrotic appearance and dense vasogenic peritumoral edema, well compatible with a GBM.

Histological examination of the right frontal tumor revealed an infiltration of the cerebral cortex and white matter. The tumor was found to be highly cellular, composed of atypical astrocytic cells with numerous mitoses (mitotic index: 0–1/high power field), necroses and microvascular and endothelial proliferation (Fig. 2). Primary antibodies were positive for EGFR, p53 (group 3), Ki-67 (10–15%), Olig2, and GFAP but negative for P16, VEGF, PTEN and mutated IDH1. The histologic diagnosis was glioblastoma (GBM), grade IV (WHO, 2007). The MGMT promoter was methylated in 80–100%.

The suprasellar tumor consisted of monotonous and chromophobe cells with eccentric, hyperchromatic nuclei and polygonal cytoplasm. There were numerous PAS positive glycoprotein particles. The markers for the primary antibodies were positive for GFAP, synaptophysin, Ki-67 (%0–2), S-100, and LH but negative for EGFR, p53 (group 0), GH, PRL, TSH, ACTH, FSH and Pan-Ck. Histopathological diagnosis was null cell pituitary adenoma (FSH−; LH+; TSH−).

Dexamethasone therapy was tapered and the patient was referred to endocrinological consultation for hormone replacement therapy. The patient was discharged on day 8 with recommendation of adjuvant radio-chemotherapy.

3. Discussion

Coexistences of endodermal and neuroectodermal tumors, as in our patient, are quite uncommon. In phacomatosis syndromes disease like neurofibromatosis type 1, mesodermal and neuroectodermal tumors are reported to occur in the same patient simultaneously. In this disease, there are common characters in chromosome 1, 6, 16, 22 mutations, which play an important role in tumorigenesis. Comparably, a p53 gene mutation is frequent in pituitary adenomas but also plays a crucial role in the pathogenesis of all brain tumors. Although the glioblastoma was p53 positive in our case, immunohistochemical staining of the pituitary tumor specimen revealed negative reaction with this nuclear oncoprotein. Glioblastomas are divided into two groups: primary GBM originate from neural stem cells, whereas secondary GBM occur by malignant transformation of astrocytomas. In GBMs p53 gene mutations, hypermethylations of the MGMT gene promoter, loss of 1p/19q chromosome heterozygosity, overexpression of the MDM2 proto-oncogene, deletion of chromosome 10, and mutations of isocitrate dehydrogenases 1/2 are common. In our case the immune markers for the nuclear p53 oncoprotein were positive. Besides overexpression and amplification, in GBM there are also mutations at the signal transduction pathways of platelet derived growth factor, vascular endothelial growth factor, transforming growth factor α/β, hepatocyte growth factor and epidermal growth factor. In our case, immune markers for VEGF were negative, but EGFR markers were positive. Activation of the intracellular PI3K/Akt/mTOR signaling pathway, which may be overactive because of a PTEN deficiency, leads to reduced apoptosis and increased tumor proliferation. Gene mutations or deletions of the tumor suppressor CDKN