Multiple meningiomas in a patient with Rubinstein–Taybi syndrome

Case report

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The authors report a case of multiple meningiomas in a 37-year-old woman with Rubinstein–Taybi syndrome. The patient harbored a bifrontal ossifying meningioma and multiple intracranial meningiomas. She underwent surgery for the frontal ossifying meningioma and a right frontoparietal meningioma.

KEY WORDS • meningioma • Rubinstein–Taybi syndrome • tumor

Rubinstein–Taybi syndrome is a congenital malformation disease characterized by facial anomalies, broad thumbs, big toes, short stature, and mental retardation.6 It is inherited in an autosomal-dominant manner, and recently chromosomal rearrangements, microdeletions, and point mutations in one copy of the gene encoding the CREBBP were shown to be the underlying causes of RTS.5 The CREBBP plays a role as coactivator in the regulation of gene transcription.3 Approximately 5% of patients with RTS harbor neural or developmental neoplasms, especially those of the head.4 Among the reported tumors in the central nervous system were two oligodendrogliomas, two medulloblastomas, and two meningiomas. In the present case we report on multiple meningiomas in a patient with RTS.

Case Report

First Admission. This 37-year-old woman with previously diagnosed RTS presented with a progressive bone-like swelling of the forehead. Computerized tomography scanning revealed bifrontal hyperostosis of the skull (Fig. 1), with no other intracranial lesion. A biopsy specimen of the lesion showed an ossifying meningioma. The swelling gradually increased during the next year and the lesion was partially resected for cosmetic reasons. Subsequently, the patient underwent adjuvant local radiotherapy. Preoperative magnetic resonance imaging results had demonstrated multiple de novo Gd-enhanced intracranial masses with the aspect of meningiomas (Fig. 2). These studies were expectantly followed with serial CT scanning.

Second Admission. Four years later the patient exhibited a change in her character, progressive bradyphrenia, proptosis, and a mild left-sided hemiparesis. A CT scan revealed significant enlargement of the right frontoparietal mass together with peritumoral edema, compression of the lateral ventricle, and midline shift (Fig. 3). She underwent decompressive surgery. Intraoperatively, the tumor had a clear cutting plane with the cortex and could be resected relatively easily, although the most frontal portion turned out to be continuous with an en plaque growing, meningioma-like sphenoid wing tumor. Histological analysis showed chordoid-type meningioma (Fig. 4). Postoperatively, the patient suffered slowly progressive intubation-related laryngeal swelling and died of respiratory complications 6 weeks later.

Discussion

There are two previously reported cases of solitary meningioma in a patient with RTS.1,7 These cases involved two adult women 39 and 41 years old. To our knowledge, the present case is the first report of multiple meningiomas in a patient with RTS.
At the molecular level, RTS is caused by disruption of one copy of the CREBBP gene.\(^5\) Note that CREBBP is an essential coactivator of many transcription factors. In addition, it has the ability to acetylate histones, which is also regarded as an important step in the regulation of gene transcription.\(^2\) Genetic disturbances in the regulation of gene transcription often result in developmental disorders and uncontrolled cell growth. Indeed, chromosomal translocations affecting the CREBBP gene have been found in hematological malignancies.\(^7\) Given that patients with RTS are haploinsufficient for CREBBP, it is tempting to hypothesize that functional allelic loss puts them at risk for tumorigenesis. Thus far, the role of CREBBP in the origin of meningiomas has not been analyzed. In addition, it remains to be elucidated why RTS mutations of this ubiquitously expressed gene preferentially cause developmental and neural tumors of the head.

References


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