Nevoid Basal Cell Carcinoma Syndrome With Medulloblastoma and Meningioma
—Case Report—

Yutaka FUKUSHIMA, Hidehiro OKA, Satoshi UTSUKI, Kazuhisa IWAMOTO, and Kiyotaka FUJII

Department of Neurosurgery, Kitasato University School of Medicine, Sagamihara, Kanagawa

Abstract

A 35-year-old man presented with a rare case of nevoid basal cell carcinoma syndrome, or Gorlin’s syndrome, associated with both medulloblastoma and meningioma, manifesting as visual field constriction due to multiple parasellar tumors. He had undergone resection of a medulloblastoma at the age of 1 year 9 months, followed by adjunctive irradiation with a total dose of 40 Gy. He presented with multiple subcutaneous nodules on his face and neck. Histological examination of biopsy specimens established the diagnosis of nevoid basal cell carcinoma syndrome. Tuberculum sellae meningioma was removed through a craniotomy, and his symptoms improved. Meningioma is known to occur in the field of therapeutic irradiation, so chemotherapy may be a better option for medulloblastoma associated with nevoid basal cell carcinoma syndrome.

Key words: nevoid basal cell carcinoma syndrome, meningioma, medulloblastoma

Introduction

Nevoid basal cell carcinoma syndrome, also known as Gorlin’s syndrome, is an autosomal dominant disorder characterized by facial peculiarities, skeletal abnormalities, mandibular keratohyalin cysts, and dural calcification. Nevoid basal cell carcinoma syndrome was first reported in 1894, and described and summarized by Gorlin and Goltz. Childhood medulloblastoma is often associated with this syndrome, whereas meningioma is rarely found. We treated a rare case of this syndrome associated with both medulloblastoma and meningioma.

Case Report

A 35-year-old man presented with visual blurring and visual field constriction. He had undergone resection of a cerebellar medulloblastoma at his local hospital at the age of 1 year 9 months. He received 40 Gy of radiotherapy after the craniotomy, and no tumor recurrence was identified in subsequent years. He was monitored by the outpatient department of our hospital. He presented with multiple tumorous lesions of the face and neck at the age of 28 years. Histological examination of biopsy specimens found nevoid basal cell carcinoma syndrome. He visited the ophthalmologist because of visual blurring and visual field limitation in August 2001. Computed tomography (CT) identified suprasellar mass lesions. He was referred to us for further evaluation and treatment. The patient’s family history was negative.

On admission, his body weight was 79.5 kg and his height was 167 cm, suggesting mild obesity. Physical examination found ocular hypertelorism, bulging of the forehead, and multiple 5-mm diameter subcutaneous nodules on the face and neck (Fig. 1). Neurological examination revealed mental retardation, decreased visual acuity on the left (Vs = 0.02), right homonymous hemianopsia with lower 1/4 temporal cut on the left, upward gaze limitation on the left, and impaired performance on the nose-finger-nose test on both sides. Chromosomal analysis showed no abnormality.

Skull radiography disclosed extensive calcification of the falx cerebri and tentorium. CT showed a homogeneously enhanced mass lesion in the suprasellar region. However, no tumor recurrence was found at the cerebellum. The left lateral ventricle was dilated, and a low-density lesion was found...
Fig. 1 Photographs of the patient showing the typical dysmorphic appearance of nevoid basal cell carcinoma syndrome, including bulging forehead, well-developed supraorbital ridges, fused eyebrows, and mild hypertelorism, as well as several operative scars from removed basal cell carcinomas.

Fig. 2 A: Axial computed tomography (CT) scan showing extensive calcification of the tentorium and no tumor recurrence of the cerebellum. B: Axial CT scan with contrast medium showing a suprasellar enhanced mass. The left lateral ventricle is dilated, and a low-density lesion is present in the left temporo-occipital area, which was considered to result from the previous operative procedure.

Fig. 3 Photomicrograph of the tuberculum sellae meningioma showing meningothelial cells with a few meningothelial whorls. HE stain, ×400.

in the left temporo-occipital area, but these lesions were considered to result from the previous operative procedure (Fig. 2). CT also revealed extensive calcification of the tentorium and agenesis of the corpus callosum.

Right frontotemporal craniotomy was performed for tumor removal because of the progression of visual blurring and field defects, and enlargement of the mass lesion. The skull was very thick, and the inner membrane of the dura mater was calcified. Through a trans-sylvian approach, a 2-cm diameter tumor adhering to the tuberculum sellae and three small tumors adhering to the parasellar region were removed. Histological examination identified these tumors as meningothelial meningiomas (Fig. 3).

The patient’s postoperative course was uneventful, and his visual field and visual acuity were improved on the left.

Discussion

Nevoid basal cell carcinoma syndrome is an autosomal dominant disorder linked to chromosome 9q22.3-q31 (40% of new cases are sporadic)\(^1,12\) and may be related to PTCH gene.\(^3,9\) More than 30 different malformations and benign or malignant tumors have been associated with this syndrome. Clinical characteristics include multiple nevoid basal cell carcinomas of the skin, craniofacial anomalies (bulging forehead, ocular hypertelorism, and flat nasal bridge), skeletal anomalies (scoliosis, bifid ribs, and metacarpal dysmorphism), mandibular keratoxyalin cysts, dural calcification, and benign or malignant neoplasms such as cardiac fibroma, rhabdomyoma, and ovarian fibrosarcoma. This syndrome involves the central nervous system, so is reportedly associated with medulloblastoma, meningioma, craniopharyngioma, mental retardation, calcification of the falx cerebri, agenesis of the corpus callosum, and sellar bridging.\(^1,2,6,8,10,11,13\)

More than 40 cases of nevoid basal cell carcinoma syndrome associated with medulloblastoma have been reported. The mean age of the patients was 2 years, whereas patients with only medulloblastoma
Table 1 Summary of cases of meningioma associated with nevoid basal cell carcinoma syndrome

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Age, Sex</th>
<th>Location of tumor; size</th>
<th>Signs and symptoms</th>
<th>Prior radiotherapy</th>
<th>Histology; outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamoney (1969)</td>
<td>64, M</td>
<td>NS</td>
<td>NS</td>
<td>no</td>
<td>meningioma and craniopharyngioma; discovered at autopsy</td>
</tr>
<tr>
<td>Stoelinga et al. (1973)</td>
<td>60, M</td>
<td>olfactory; large (several cm, judging from gross photograph)</td>
<td>NS</td>
<td>no</td>
<td>meningioma; discovered at autopsy</td>
</tr>
<tr>
<td>Southwick and Schwartz (1979)</td>
<td>18, F</td>
<td>multiple</td>
<td>NS</td>
<td>NS</td>
<td>meningioma</td>
</tr>
<tr>
<td>Dawber and Ryan (1980)</td>
<td>44, M</td>
<td>lt parietal; 6.5 cm</td>
<td>aphasia and dysarthria, weakness and numbness of rt hand</td>
<td>yes: for basal cell carcinoma of scalp 4 yrs previously</td>
<td>malignant meningioma; alive 5 yrs postop., NER</td>
</tr>
<tr>
<td>Mortimer et al. (1984)</td>
<td>47, F</td>
<td>rt frontoparietal; 6 cm</td>
<td>lt hemiparesis, partial seizures on lt rt 6th cranial nerve palsy, decreased vision in rt eye</td>
<td>no</td>
<td>meningioma</td>
</tr>
<tr>
<td>Aumaitre et al. (1986)</td>
<td>60, M</td>
<td>rt temporal fossa, greater sphenoid wing; several cm (judging from CT scan)</td>
<td>depression</td>
<td>no</td>
<td>radiological diagnosis; died, no autopsy</td>
</tr>
<tr>
<td>Junes et al. (1988)</td>
<td>24, F</td>
<td>lt temporoparietal; 5 cm</td>
<td>NS</td>
<td>no</td>
<td>meningioma</td>
</tr>
<tr>
<td>Albrecht et al. (1994)</td>
<td>19, F</td>
<td>bifrontal with extracranial extension; 11 cm</td>
<td>mass on forehead</td>
<td>yes: for medulloblastoma 15 yrs previously</td>
<td>malignant meningioma; alive 19 mos postop., NER</td>
</tr>
<tr>
<td>O'Malley et al. (1997)</td>
<td>28, M</td>
<td>bil anterior temporal</td>
<td>depression</td>
<td>yes: for medulloblastoma 26 yrs previously</td>
<td>meningioma</td>
</tr>
<tr>
<td>Present case</td>
<td>35, M</td>
<td>suprasellar multiple</td>
<td>visual field defect, visual loss</td>
<td>yes: for medulloblastoma 34 yrs previously</td>
<td>meningothelial meningioma</td>
</tr>
</tbody>
</table>

CT: computed tomography, NER: no evidence of recurrence, NS: not stated, postop.: postoperatively.

have a mean age of 6 years, but patients with this syndrome tend to survive longer than patients without the syndrome. Our patient developed medulloblastoma at the age of 1 year 9 months, and the tumor had not recurred.

Only 10 cases of nevoid basal cell carcinoma with meningioma, including the present case, have been reported (Table 1). The age of the patients ranged from 18 years to 64 years, with no sex preponderance. Four patients had received irradiation and two had histologically diagnosed malignant tumors. Nevoid basal cell carcinoma syndrome associated with both medulloblastoma and meningioma has been reported in only two patients, in whom the meningioma was probably induced by the radiation. In our case, there was no clear evidence that the meningioma occurred following irradiation of the medulloblastoma or any association with nevoid basal cell carcinoma syndrome. However, meningioma is known to occur within the irradiated field for medulloblastoma.

Nevoid basal cell carcinoma syndrome is frequently associated with medulloblastoma, which is treated by irradiation. Further tumor growth is likely in the area of irradiation, so the radiation dosage and field size should be minimized. Medulloblastoma appears to respond to chemotherapy, and this treatment modality is increasingly favored. Medulloblastoma associated with nevoid basal cell carcinoma syndrome has a better prognosis and an increased survival rate, so we recommend substitution of chemotherapy instead of irradiation therapy, at least in younger patients.

Acknowledgments

This work was supported in part by Grants-in-Aid for Scientific Research from the Ministry of Education (Nos. 08671611, 10877218, and 13671462), an Academic Frontier Project from the Ministry of Education, Science, and Culture, and a Parent’s Association Grant from Kitasato University, School of Medicine, Japan.

References

3) Boutet N, Bignon YJ, Drouin-Garraud V, Sarda P,


Address reprint requests to: H. Oka, M.D., Department of Neurosurgery, Kitasato University School of Medicine, 1–15–1 Kitasato, Sagamihara, Kanagawa 228–8555, Japan.

e-mail: okahiro@med.kitasato-u.ac.jp