Von Recklinghausen's disease with diencephalic syndrome in an adult

Case report

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The case of a 39-year-old man with von Recklinghausen's disease, presenting with emaciation and a marked increase in serum growth hormone concentration, is presented. Neuroradiological and histological examination confirmed anaplastic astrocytoma in the optic chiasm-hypothalamic region. This is a rare case of diencephalic syndrome and von Recklinghausen's occurring together in an adult.

KEY WORDS • von Recklinghausen's disease • anaplastic astrocytoma • optic chiasm • hypothalamus • diencephalic syndrome • adult

Optic pathway gliomas are the most common type of brain tumor associated with von Recklinghausen's disease. The lesion causing the diencephalic syndrome in childhood is a tumor involving the anterior hypothalamus and optic chiasm. The appearance of both diseases together is extremely rare, and all reported cases have been in patients less than 10 years of age. We report the first such case in an adult.

Case Report

This 39-year-old man presented with emaciation and rapid deterioration of visual acuity and right visual field. His height was 174 cm and weight 45 kg. His body weight had decreased by 20 kg during the 2 years previous to admission, but he was euphoric. There were numerous cafe-au-lait spots and subcutaneous nodules on his trunk. He was diagnosed as having von Recklinghausen's disease while aged in his 20's. His father, sister, two daughters, and son were also affected with the disease.

Examination. Neurological examination was normal except for optic nerve deficits. Visual acuity of both eyes was decreased and the visual field of the right eye was normal. Computerized tomography and magnetic resonance imaging demonstrated a brain tumor in the optic chiasm-hypothalamic region (Fig. 1). Preoperative hormonal examination indicated high levels of growth hormone (GH) (27.5 ng/ml; normal < 5 ng/ml) and adrenocorticotrophic hormone (ACTH) (105.7 pg/ml; normal 4.4–48.0 pg/ml), and both reacted abnormally to intravenous insulin stimulation (Fig. 2). Other endocrinological studies revealed a prolactin (PRL) level of 37.66 ng/ml (normal < 25 ng/ml) and a thyroid-stimulating hormone (TSH) level of 3.41 µU/ml (normal 0.5–4.0 µU/ml), and both showed normal responses to thyrotropin-releasing hormone: PRL, peak value 8.508 ng/ml at 15 minutes; TSH, 6.99 µU/ml at 60 minutes. The level of luteinizing hormone (LH) was 4.2 mIU/ml (normal 1–25 mIU/ml) and follicle-stimulating hormone (FSH) 11.4 mIU/ml (normal 1–15 mIU/ml), and both responded normally to LH-releasing hormone: LH, 18.7 mIU/ml at 30 minutes; FSH, 17.9 mIU/ml at 60 minutes. The preoperative clinical diagnosis was glioma with diencephalic syndrome.

Operation. A craniotomy was performed with partial removal of the tumor. The patient was transferred to another hospital for irradiation after the operation.

Histological Examination. Histological examination of the tumor revealed features of an anaplastic astrocytoma: high cellularity, pleomorphism of each cell, and atypical nuclei without necrosis or vascular proliferation (Fig. 3). Immunostaining for GH, ACTH, and PRL was negative.

Discussion

Although von Recklinghausen's disease is well known to be associated with tumors of the central nervous system such as optic chiasm glioma, its associa-
Von Recklinghausen's disease with diencephalic syndrome

![Image of MRI scans showing pituitary gland separation from optic chiasm and infiltration of tumor toward hypothalamus.]

**FIG. 1.** *Left and Center:* Magnetic resonance images, sagittal (left) and coronal (center) views, demonstrating that the pituitary gland was separated from the optic chiasm lesion. *Right:* Image obtained following administration of gadolinium-diethylenetriamine penta-acetic acid showing infiltration of the tumor toward the hypothalamus.

![Graph showing preoperative endocrine examination with elevated levels of growth hormone (GH) and adrenocorticotropic hormone (ACTH), and abnormal reactions after the intravenous (iv) administration of 5 U insulin.]

**FIG. 2.** Graph of preoperative endocrine examination showing elevated levels of growth hormone (GH) and adrenocorticotropic hormone (ACTH), and abnormal reactions after the intravenous (iv) administration of 5 U insulin.

![Photomicrograph of the tumor showing features of an anaplastic astrocytoma: high cellularity and pleomorphism of each cell. H & E, × 47.]

**FIG. 3.** Photomicrograph of the tumor showing features of an anaplastic astrocytoma: high cellularity and pleomorphism of each cell. H & E, × 47.

The lesion causing this syndrome is a tumor involving the anterior hypothalamus and optic chiasm. Affected patients have endocrine disturbance due to hypothalamic dysfunction. Drop, *et al.*, described a paradoxical decline of GH levels following arginine-insulin infusion in a child. It is unclear whether the hypothalamus is the site of the primary neurofibromatosis defect. The elevated GH level and its paradoxical response to insulin stimulation observed in diencephalic syndrome may be interpreted as a disturbed balance between stimulatory and inhibitory factors. Hisano, *et al.*, reported the case of a child with increased levels of GH and ACTH, and paradoxical response to insulin stimulation.
of both GH and ACTH. Endocrine disturbance seemed to involve not only GH but also ACTH, as reported in our case. DeSousa, et al., suggested that this syndrome was related to the age at onset of hypothalamic compression. We consider emaciation to occur regardless of age.

Most gliomas of the optic nerve, optic chiasm, and hypothalamus in childhood are histologically benign, such as fibrillary and pilocytic astrocytoma. In adults, optic chiasm gliomas may develop in optic pathways and infiltrate the hypothalamus and adjacent structures; these tumors include anaplastic astrocytomas and glioblastomas. Wilson, et al., reported histological changes in a pilocytic astrocytoma of the optic chiasm and hypothalamus after a period of 18 years, which emphasizes the late onset of malignant evolution.

This case of von Recklinghausen’s disease complicated by adult-onset diencephalic syndrome and an anaplastic astrocytoma in the optic chiasm-hypothalamic region may be extremely rare. However, in consideration of the patient’s age and the histological malignancy, the following hypothesis appears plausible. A low-grade glioma may exist without symptoms for years. Malignant change occurs and the tumor invades the hypothalamus, whereupon symptoms resembling those of diencephalic syndrome in children become evident. The diencephalic syndrome may arise as a result of the tumor location and the pattern of invasion.

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References


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