Disseminating histologically benign multiple papilloma of the choroid plexus: case report

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A rare case of extensively disseminating multiple benign choroid plexus papilloma is shown. The patient first reported with high-grade hydrocephalus and two tumours in the 3rd and 4th ventricle was treated by atrioventricular shunt insertion, subtotal resection of the 4th ventricle tumour, and adjuvant ⁶⁰Co irradiation of the posterior fossa. The dissemination that followed was revealed by computerised tomography and magnetic resonance imaging, and involved both the supra- and infratentorial ventricular systems, spinal canal, and brain parenchyma. Three years after the resection of the 4th ventricle tumour, the patient underwent excision of a temporal lobe lesion for relief of neurological symptoms, but showed no improvement and died 5 years after the primary diagnosis of CNS tumour. An autopsy was not performed. Analysis of the primarily resected mass showed distinct papillary pattern with no anaplasia, mitoses, multinucleation or giant cell formation, and cytokeratin positivity at the absence of vimentin and glial fibrillary acidic protein. Analysis of the temporal lobe tumour again showed definite papillary formation with no signs of malignisation and virtually no mitotic figures, and the presence of cytokeratin, but not vimentin or glial fibrillary acidic protein. On both occasions, the diagnosis was choroid plexus papilloma (WHO grade I).

key words: choroid plexus papilloma, cytokeratin, ventricular system, metastasis

INTRODUCTION

Choroid plexus papillomas (CPP) are rare, usually slow growing benign neoplasms arising from either ventricular choroid tissue or ependyma [13, 17]. However, cases of primary CPP showing no connection with either the choroid plexus or the ventricular system, including one arising directly from the brain parenchyma, had also been reported [8, 11, 20]. CPP constitute less than 3% and 1% of all intracranial tumours in children and adults, respectively, and their reports in adults are relatively scarce in the literature (for reviews see [12, 17]; see also [6, 9, 21, 22] for the most recent case reports). The histopathological structure of CPP usually mimics that of normal choroid plexus [17], and some of the early reports of CPP may have actually presented no true tumours, but a villous hypertrophy of the choroid plexus (for a discussion of this issue see [22]). Metastases from CPP are extremely rare and are mostly diagnosed in adults, may comprise one or more secondary foci and show no histological signs of malignisation, and usually involve subarachnoid space [3, 5, 6, 13, 19]. Below, an unusual case is presented of a histologically benign multiple CPP with secondary lesions spreading postoperatively into multiple locations in the supra- and infratentorial ventricular ependyma, spinal canal, and brain parenchyma.
CASE HISTORY

Preoperative history and examination. A 50-year-old man with a 3-month history of progressive headaches and movement disorders reported to neurology ward in July, 1992. Neurological examination disclosed abnormal stance and gait with a tendency to drop to the left side, left-sided dysdiadochokinesia, and bilateral dysmetria and horizontal nystagmus. CT scan (not shown) revealed a $2.8 \times 2.0$ cm size tumour in the parasellar cisterns' region and lower part of the 3rd ventricle, another tumour sized $3.0 \times 2.0$ cm in the vicinity of the 4th ventricle, and a high-grade hydrocephalus with cerebrospinal fluid (CSF) leakage into the periventricular white matter. The patient had first declined the surgery suggested, but further aggravation of the somatic symptoms resulted in his readmission for the treatment 10 months later.

Treatment and postoperative course. First stage intervention consisted of atrioventricular shunt insertion that resolved the signs of elevated intracranial pressure (ICP). Tumour resection had been scheduled after the next 3 months. However, the patient reported over one month early with a relapse of unsteadiness and strong headaches suggesting re-emergence of elevated ICP. A renewed uropolinum-enhanced CT scan (Fig. 1) showed slight enlargement of the tumour of the 3rd ventricle ($3.0 \times 2.0$ cm), marked expansion of the 4th ventricle tumour ($4.0 \times 3.0$ cm), and hydrocephalus of increased grade that indicated shunt malfunctioning. The latter was corrected by replacing blocked distal catheter; concurrently, the drainage modality was changed for intraperitoneal one. One-week later, occipital craniotomy to the foramen magnum followed by C1 laminectomy and incision of the dura revealed tonsillar cerebellar herniation down to the C2 level. Intertonsillar approach exposed a heavily bleeding grey-rose tumour covering and invading the fundus of the 4th ventricle; the penetrating growth pattern rendered total resection impossible. The surgery was completed leaving a small part of the tumour in the ventricle fundus and the aqueduct obstructed by the tumour of the 3rd ventricle. The patient next underwent fractionated adjuvant $^{60}$Co irradiation of the posterior fossa with a total dose of 25 Gy over nine weeks. The treatment was gratified by a marked clinical improvement of the patient’s condition. Yet, a follow-up CT scan done in January 1994 showed regrowth of the 4th ventricle tumour. Examinations performed regularly during the next two years confirmed the tumour bad in the 3rd and 4th ventricles, but no enlargement of the ventricular system. The man remained neurologically stable until the beginning of 1996, at which time his complaints indicated recurrence of elevated ICP. Functioning of the shunt was not disturbed. Gadolinium contrast-enhanced magnetic resonance imaging revealed many new lesions (of intermediate intensity on T1-weighted images and hypointense on T2-weighted images) at the following locations: 1) right temporal lobe (a cystic tumour), 2) base of the left temporal lobe pole, 3) the right pontocerebellar angle and posterior fossa anteriorly to the medulla oblongata (multiple tiny foci), 4) periphery of the left cerebellar hemisphere, and 5) spinal canal at the C1-C2 level (Fig. 2). The main objective of further surgical treatment was alleviation of the neurological symptoms by mass effect. The man underwent total resection of the right temporal lobe tumour in June 1996, but showed no improvement and died at his home 5 years after the primary diagnosis of CPP. The family did not agree to an autopsy.

Histopathological findings. The formalin-fixed surgery specimens were embedded in paraffin and stained with haematoxylin-eosin. Immunohistochemical analyses
were done with PAP method and DAB chromogen using the following antibodies: anti-GFAP (Serva), anti-vimentin and anti-cytokeratin (Immunotech).

The tumour of the 4th ventricle (Fig. 3, upper panels) showed an intricate arborising pattern of papillae covered by a single layer of pseudostratified cuboidal or columnar epithelium, and occasional lamellar microcalcification. The nuclei were oval and basally located. No anaplasia, mitotic figures, multinucleation or giant cell formation were found. Immunohistochemistry showed cytokeratin positivity, but no presence of vimentin and glial fibrillary acidic protein. The diagnosis was CPP (WHO grade I).

The right temporal lobe metastatic tumour, removed three years later (Fig. 3, lower panels), again showed delicate papillary formation composed mostly of single layers of fairly uniform columnar epithelial cells of regular shape and pattern, with sporadic piling of the epithelium. Mitotic figures were virtually absent, and there were no necrotic foci. Immunohistochemistry once more showed the presence of cytokeratin and the absence of vimentin and glial fibrillary acidic protein in the tumour. The diagnosis was CPP (WHO grade I) again.

DISCUSSION

Although CPPs are most common in the first decade of life, they may occur at any age. Their preponderate localisation is the lateral ventricles in children and the 4th ventricle in adults; the 3rd ventricle is rarely involved [12, 13, 17]. The CPP-related hydrocephalus is assumed to result from cerebrospinal fluid overproduction, drainage system obstruction, and subarachnoidal space obliteration after recurrent haemorrhages [9, 12, 22].

The etiopathogenesis of CPPs is unclear. The telomerase status of choroid plexus tumours is not known. An increased occurrence of choroid plexus tumours was reported in patients with Aicardi syndrome, that is a chromosome X-linked disorder (see [18]). Reports of CPP cases associated with von Hippel-Lindau disease showed loss of an allele on chromosome 3 [1, 7]. CPP karyotypic data showed the presence of extra hybridisation signals with a chromosome 7 probe in two thirds of these tumours, and a number of less consistent aberrations [4]. Some authors postulated viral involvement [16, 19], and there is a growing body of evidence showing a role for simian virus 40 antigens in both human ependymomas and choroid plexus tumours (see [2] for a review, and [23] for the most recent developments).

The treatment of choice for benign choroid plexus tumours remains radical surgery, which is curative in most cases that allow total excision; the hydrocephalus is to be treated only if persistent [12, 17]. However, a few cases of local CPP recurrence with or without signs of malignisation were reported even following apparently total excision (for reviews see [6]). Nevertheless, adjuvant treatment, such as radiotherapy and chemotherapy, is only recommended for special cases, which may include disseminated tumours, but remains questionable in the absence of any indication of malignancy [12, 14, 17, 21]. The long-term survival is remarkable even in patients with subtotal removal [20]. Yet, the biological behaviour of CPP cannot be predicted in an individual case; few percent of these tumours show histologic features of malignancy or behave in a clinically malignant way and disseminate via the CSF [3, 5, 12, 13; 17]. Interestingly, a case of distant CPP seeding (which

Figure 2. Gadolinium diethylenetriaminepentaacetic acid-enhanced T1-weighted magnetic resonance images taken in April 1996. Left panel: Sagittal scan showing the tumours located in the 3rd and 4th ventricles, ventral part of the brain stem and dorsal part of the spinal cord (white arrowheads). Middle panel: Coronal scan showing the presence of multiple lesions in the right pontocerebellar angle. Right panel: Axial scan showing the presence of tumour foci in the left and right temporal lobes.
may occur months or years postoperatively) was also reported, showing no connection between the secondary lesion and the ventricular system [6].

As indicated by the asymmetric distribution of the primary tumour foci (see [22]) and the dissemination process, the present case represents true multiple CPP, and not a villous hypertrophy of the choroid plexus. CPP metastasis usually occurs at a single implantation site. Other reports of multiple benign CPP and of extensive dissemination of histologically benign primary CPP in adults have only been published most recently [9, 14].

Interestingly, the extensive CPP dissemination we report here occurred in the absence of any histopathological signs of anaplasia or increased occurrence of mitoses. Another case of extensive craniospinal seeding from a well-differentiated CPP of the 4th ventricle that showed complete absence of anaplasia has been reported recently [9]. CPP dissemination through the CSF drainage system resembles that of ependymoma [10, 19] and probably results from the tumour’s contiguity with cerebrospinal fluid. Localisation of metastatic lesions in the case presented here is at least partly consistent with this mechanism. An important factor in the case presented could be intra- and/or postoperative seeding from the subtotal resected tumour of the 4th ventricle. However, according to some authors, shunt insertion for the relief of hydrocephalus decreases CSF pressure and by the way can accelerate tumour growth or regrowth [15], which mechanism might also be active in the present case. Because autopsy had not been performed, we can only speculate that the cause of death was either further dissemination of the CPP, or expansion of the primary tumours located in the 3rd and 4th ventricles.

This case proves the possibility of massive dissemination of a histologically benign CPP throughout the CNS, and indicates that benign phenotype does not preclude the presumably genetically conditioned aggressiveness of this tumour.

Figure 3. Photomicrographs showing cellular patterns (left panels: H & E staining, original magnification × 40) and cytokeratin immunohistochemistry (upper right panel original magnification × 40, lower right panel original magnification × 100) in the choroid plexus papilloma of the 4th ventricle (upper panels) and in the choroid plexus papilloma metastasis removed from the right temporal lobe (lower panels).
REFERENCES