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Pilocytic Astrocytomas of the Posterior Fossa
A Follow-up Study in 33 Patients

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Summary

The extent of resection in pilocytic astrocytoma of the posterior fossa often remains undefined and the indications for further treatment in incompletely resected tumours are a matter of debate. It has been also realized that the problem of hydrocephalus in patients with pilocytic astrocytoma of the posterior fossa has not yet been solved and the diagnostic impact of postoperative CT findings remains questionable.

We retrospectively reviewed the data from 33 patients harbouring a pilocytic astrocytoma of the posterior fossa to evaluate the impact of surgical technique in terms of radicality and of postoperative imaging results upon prognosis and adjunctive treatment. In addition, the issue of hydrocephalus was considered and related to different treatment modalities.

Thirty patients underwent surgical treatment whereas 3 had open biopsy of the tumour. Macroscopically gross total resection of the tumour was performed in 20 patients, whereas resection was partial in 10.

Follow-up was obtained in 29 patients for a period which ranged between 2 and 184 months (85 months ± 56 months). Outcome was good in 24 patients who had only slight neurological deficit and poor in 3 patients, who were severly disabled. Two patients died during the follow-up period. Recurrent tumour growth occurred in 2 cases with incompletely resected tumours.

From the series presented, it was concluded that long-term follow-up with CT seems mandatory in cases with contrast-enhancing residual tumour. Recurrent tumour growth should be assumed in postsurgical patients with an enlarging area of enhancement shown in follow-up CT studies. Permanent ventriculoperitoneal shunting is required in certain patients with pre- or postoperative hydrocephalus. While percutaneous irradiation treatment is not curative, the role of radiosurgery has to be defined in the future.

Keywords: Pilocytic astrocytoma; posterior fossa; operative procedure; neuro-imaging techniques.

Introduction

Cranial pilocytic astrocytomas, initially described by H. Cushing in 1931[5], are grouped together with low-grade glial neoplasms because of their benign biological behaviour[4]. They represent slowly growing tumours in whom malignant transformation occurs very rarely[18]. Histologically, these neoplasms are well defined by the occurrence of elongated and slender hair-like cells containing stout neuroglial fibrils[10, 24].

As a consequence of improved neuro-imaging and surgical techniques as well as postoperative intensive care, morbidity and mortality of patients with pilocytic astrocytomas of the posterior fossa has decreased in recent years[16]. Nevertheless, this entity accounts for considerable morbidity and mortality mainly in young patients.

We evaluated the findings of 33 patients with pilocytic astrocytoma of the posterior fossa in order to elucidate the peculiarities in the management of this lesion such as: surgical technique, pre- and postoperative treatment of hydrocephalus, the influence of residual tumour considering long-term survival and the impact of imaging results upon further treatment.

Methods

The retrospective analysis included the historical, clinical, neuro-imaging and intra-operative data of 33 patients presenting with pilocytic astrocytoma of the posterior fossa. The patients were treated at the Neurosurgical Department of the University of Cologne from

1978 to 1993. The series consisted of 19 male and 14 female patients with a mean age of 19 years (range: 1–55 years). Eight patients were less than 10 years old, one of them had microcephalus and was serverely handicapped.

In each patient, a pre-operative computerized tomography (CT) was performed, in 9 patients magnetic resonance imaging (MRI) was obtained.

Tumour resection was performed with the patient in the sitting position, using the operating microscope and micro-instrumentation. In recent cases, an ultrasonic aspirator was utilized for tumour resection. When technically feasable, the resection was halted only when normal surrounding brain became visible. Intravenous anaesthesia was given using fentanyl, midazolam and dehydrobenzperidol in most cases. Artifical respiration included a positive endexpiratory airway pressure of 5 cm H_2O. Peri-operative monitoring of evoked potentials (BAEP) was used only in the most recent cases. The diagnosis was based on histological findings according to the the criteria of Kleihues[18].

Postoperatively, 30 patients underwent serial CT examinations being regularly performed once a year. All but 3 patients received dexamethasone with an iv-regime of 4 × 4 mg/day over 5 days.

Results

Clinical Findings

The patients presented with a mean duration of symptoms and signs of 21 months (range: 3 wks–12.7 ys). They predominantly reported cephalgia, recurrent vomiting or (Table 1) unsteadiness of gait. Neurological examination revealed cerebellar symptoms in 32 patients with clinical evidence of brainstem involvement in 11 (Table 2). Papilloedema was found in 13 patients. No neurological abnormalities were seen in one. A coincidence of pilocytic astrocytoma and neurofibromatosis (Type I)[30] was observed in one case.

Pre-operative Neuro-imaging

CT regularly revealed a hypodense lesion in the posterior fossa. Solid tumour parts were associated with a cystic component in 20 patients. Calcified areas were identified in 4. In 26 out of 29 cases intravenous contrast medium induced a moderate enhancement of the tumour. In 19 patients the astrocytoma was primarily located within the cerebellar vermis, in 11 patients the cerebellar lobes were affected. Four patients presented with brainstem involvement. In one patient the astrocytoma was confined to the brainstem. In 17 cases the space-occupying effect of the tumour caused a triventricular hydrocephalus.

MRI performed in 9 patients confirmed the CT findings. In 4 cases compression of the IVth ventricle was confirmed (Fig. 1). In one patient brainstem infiltration was identified, which was not previously recognized on CT-examination (Fig. 2). The pilocytic astrocytoma appeared hypo- or isointense on T1- and hyperintense on T2-weighted MR images. Gadolinium-DTPA was injected in 7 patients, leading to a homogeneous tumour enhancement (Fig. 3).

As a consequence of the space-occupying effect of the tumour in the posterior fossa angiography of the vertebrobasilar system revealed a dislocation of blood vessels in 11 cases.

Table 1. *Signs and Symptoms of 33 Patients with Pilocytic Astrocytoma of the Posterior Fossa*

	n = 33	% (100)
Headache	25	76
Vomiting	20	61
Imbalance	12	36
Vertigo	10	30
Gait disturbance	6	18
Blurred vision	2	6
Diplopia	2	6
Hypacusis	1	3
None	1	3

Table 2. *Neurological Findings in 33 Patients with Pilocytic Astrocytoma of the Posterior Fossa*

	n = 33	n% (100)
Ataxia	27	82
Papilloedema	13	39
Nystagmus	12	36
Dysmetria	8	24
Tremor	7	21
Cranial nerve palsy	5	15
Tetraparesis	4	27
Hemiparesis	2	6
Dysarthria	3	9
Gaze palsy	2	6

Histological Findings

Histological examination revealed tumour tissue of piloid cells with dense fibrilformation, scanty cells, partly of loose cell arrangement with microcystic degeneration (Table 3). Rosenthal fibers and granular bodies were common. Calcification was also seen. The stroma consisted of blood vessels showing hyalinosis, irregular loops or endothelial proliferation. Significant mitotic activity was absent. Expression of glial fibrillary acidic protein (GFAP), tested in some cases, was positive.

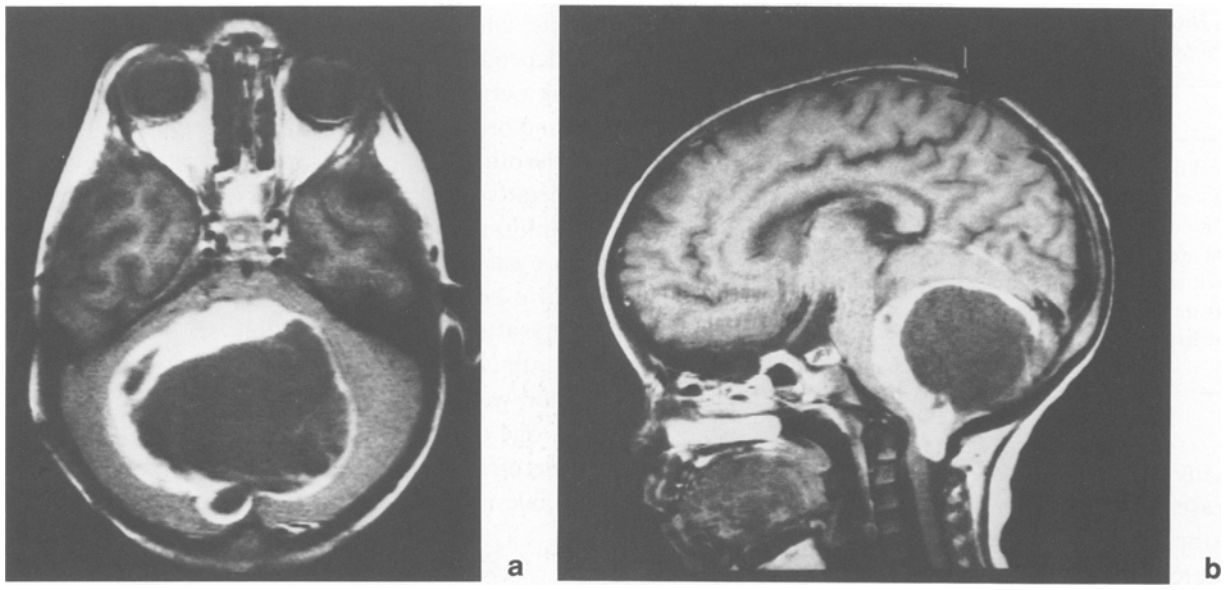

Fig. 1. 3.5-year old girl with progressive ataxia. Enormous smoothly delineated tumour in the posterior fossa (max. diameter 7 cm). The central cyst is surrounded by contrast-enhancing tumourous tissue of variable thickness. Note the herniation of tumour components through the foramen magnum. Elevation of the tentorium and compression of pons and medulla oblongata are caused by the tumour. (a) Axial and (b) sagittal T1-weighted SE (TR: 500 ms, TE: 30 ms)

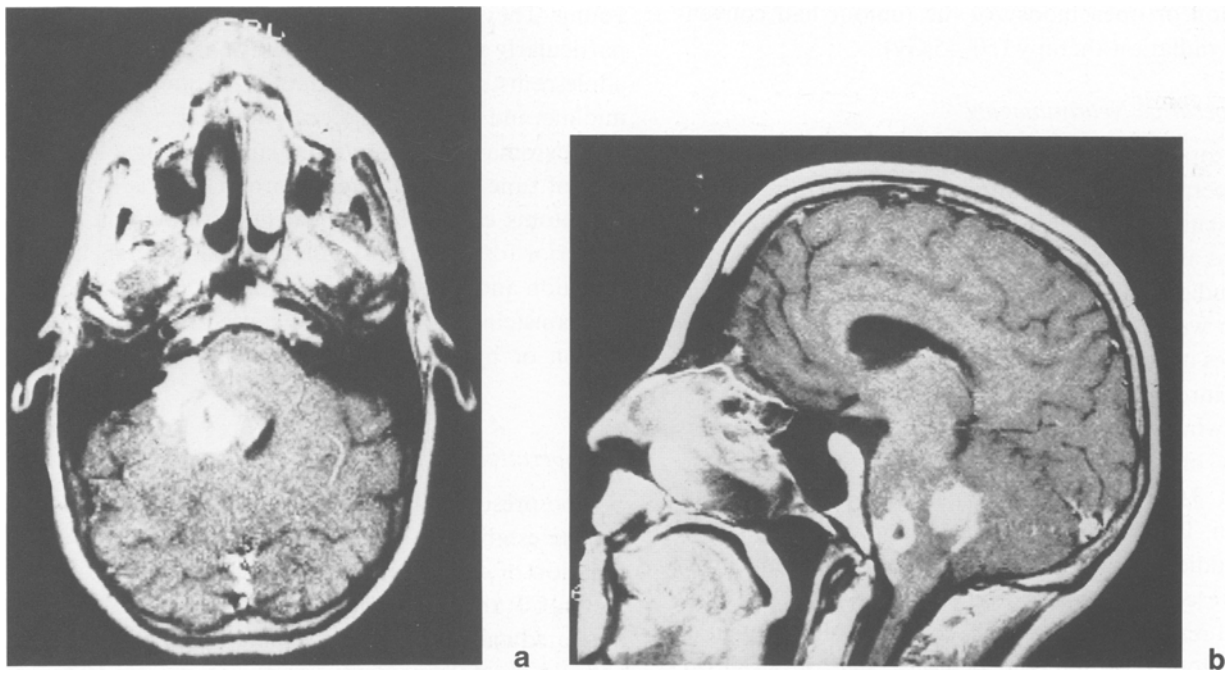

Fig. 2. 17-year-old girl with v. Recklinghausen disease (Typ I) and advanced tetraparesis. Inhomogeneously enhancing tumour with an irregular shape especially in the left cerebellar peduncle and left pons. Compression of the 4th ventricle and tumour extension into the cerebellopontine angle. There is a small area of pontine oedema detectable on the sagittal slice. (a) Axial and (b) sagittal SE (TR: 560 ms, TE: 17 ms)

Surgery and Adjuvant

Therapy

While 30 patients were treated surgically, 3 patients with brainstem infiltration had open biopsy of the tumour and CSF shunting. Pre-operatively, 15 patients with hydrocephalus received external CSF drainage. In 20 cases the tumour cysts were opened, in 11 the roof of the IVth ventricle was perforated. In 20 out of 30 cases the surgeon felt he had carried out a macro-

Table 3. *Histologic Findings in 33 Patients with Pilocytic Astrocytoma of the Posterior Fossa*

	n = 33	% (100)
Rosenthal fibers	23	70
Microcystic degeneration	18	55
Proliferation of glial fibers	17	52
Calcified areas	11	33
Encreased vascularization	15	45
Vascular thrombosis	4	12
Vascular hyalinosis	3	9
Mitoses	0	0

scopically total resection. Resection was deamed partial in 10 cases.

Postoperatively, subdural hygroma was observed in 5 and cerebellar haematoma in 3 patients. Six patients, three of whom underwent incomplete resection, developed obstructive hydrocephalus postoperatively, requiring external or ventriculo-peritoneal CSF-drainage in 3 cases, respectively. Four patients with incomplete resection or open biopsy of the tumour had conventional radiation therapy (50–55 Gy).

Postoperative Neuro-imaging

A total of 91 CT examinations were undertaken postoperatively and during the follow-up period. 28 patients had at least one CT check-up days to months after operation. In 21 cases, contrast enhanced CT-studies were obtained. In one patient, the examination was performed within 72 h postoperatively, in 20 cases it was carried out 3 months after the operative procedure. There was no enhancement in 12 patients, 10 of whom underwent gross total resection, whereas 2 only had partial removal (Fig. 4). On first examination 3 CTs disclosed enhancement at the tumour margin. These enhancing areas disappeared on CT control studies during follow-up. In 2 of the patients gross total resection was performed, whereas only one had partial removal. In 6 patients contrast enhancement of the tumour residuum was demonstrated on serial CT examinations (Fig. 5). Three of the patients had a gross total resection, the other three underwent only partial removal.

Outcome

Follow-up data were obtained in 29 patients (94%) for a mean period of 85 months (range = 2–184 months). Outcome was excellent in 14 patients, who remained without neurological deficit and fair in 10 patients, who were slightly handicapped, but leading an independent life. Outcome was poor in 3 cases, requiring permanent nursing. Two patients with poor outcome originally presented with brainstem infiltration, the other developed a supratentorial stroke during the operative procedure. Another 2 patients with brainstem infiltration died 18 and 27 months after the diagnosis was established. There was recurrent tumour growth in 2 patients, who underwent re-operation 3 and 10 years after the first operation. In one case gross tumour resection was possible, in the other only partial resection was achieved. Two patients died postoperatively, one due to an epidural haematoma, the other because of severe brain oedema. Neither sex nor age had a relevant impact on outcome.

Discussion

Clinical Findings

Pilocytic astrocytomas are supposed to derive from the subependymal glia and occur predominantly in the young. They are most frequent in the cerebellum and particularly within the optic pathways of children and adolescents. Most of the tumours are located near the midline and commonly occur unifocal[18, 30]. Pilocytic astrocytomas may remain undiagnosed for a long period of time because tumour progression is slow[12, 18]. Symptoms caused by a pilocytic astrocytoma of the posterior fossa are most often related to cerebellar infiltration and occlusive hydrocephalus (Table 2). Signs of brainstem involvement are caused by tumour infiltration or by brainstem compression by the tumour mass.

Pre-operative Neuro-imaging

The presurgical diagnosis of pilocytic astrocytoma can be established with high confidence by the combination of clinical and radiological findings[19].

On CT and MRI images the tumour is sharply demarcated and smoothly marginated with only discrete oedema. In CT-examinations the lesion tends to be round or oval, the tumour matrix generally is hypo- or isodense. In our patients a marked homogeneous contrast-enhancement of the tumour was found in 26 out of 29 cases. Cyst formation, observed in 20 of our patients, and tumour calcification, seen in four cases, are regarded as characteristic features. In this series MRI was superior compared to CT-studies in delineating brainstem involvement. Delineation of the relationship between tumour and IVth ventricle was seen

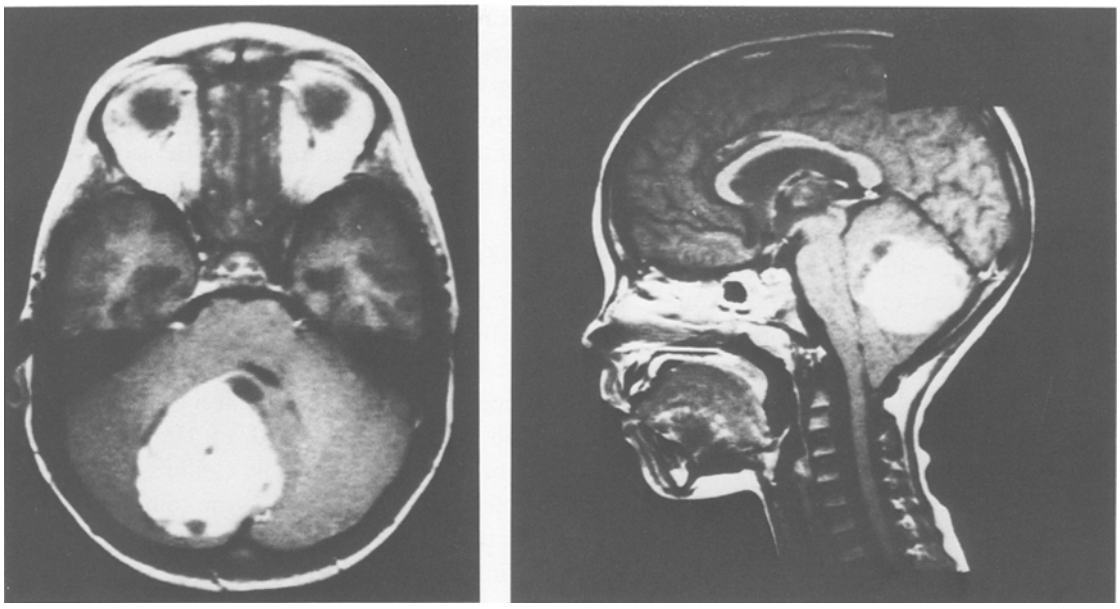

Fig. 3. 6.5-year-old boy with left-sided hemiparesis, progressive headache, and vomiting. Well confined tumour with striking Gd-enhancement in the right cerebellum and vermis. Multiple small cysts with a diameter of up to 1.5 cm are detectable at the rim of the tumour. (a) Axial, T1-weighted SE (TR: 400 ms, TE: 30 ms); (b) sagittal, T1-weighted SE (TR: 400 ms, TE: 30 ms)

better on MRI. Pre-operative angiography, performed in 11 cases, was helpful in identifying dislocated vessels and for differentiating pilocytic astrocytoma from haemangioblastoma, in which neovascularization was expected.

Operative Peculiarities

Pilocytic astrocytomas of the posterior fossa should be removed as radically as possible, because the infiltrating tumour growth takes a progressive course[2, 9, 27, 29]. Gjerris and Klinken[11] determined a 25 year cumulative survival rate of 94% in patients with complete tumour resection, whereas 3 out of 9 patients, who underwent incomplete resection in the series of Geissinger and Bucy[9] had died after a mean follow-up period of 12 years. Intra-operatively, cerebellar tissue may be removed without causing cerebellar dysfunction, when central cerebellar nuclei, the superior cerebellar peduncle or the long tract pathways or nuclei in the brainstem related to cerebellar function are left intact[2].

In patients with extensive tumour growth and infiltration of brainstem structures or of cerebellar nuclei incomplete tumour resection is advocated[9]. Regression and even complete resolution of residual tumour tissue may be observed in these cases[1].

Intra-operatively, it was difficult to say in the series presented, whether a total radical or subtotal resection had been performed, because the cleavage plane between tumour and surrounding brain remained undefined in most cases. Because of these difficulties others report tumour recurrence in so-called completely resected pilocytic astrocytomas in up to 15% of the cases[1, 21, 23].

There has been some discussion whether a solid or cystic appearance of the tumour has a prognostic impact with the solid tumours indicating poor prognosis[1, 12, 27]. Although longterm survival rates have not been determined in our series, we felt that the prognosis of the solid tumour type was poorer because of the more pronounced diffuse tumour growth. In our series, 4 patients with a fatal course of the disease all had solid tumours.

A matter of debate is the operative procedure in patients with cystic degeneration of the tumour. Some authors[16, 29] think that tumour growth derives from a mural nodule in these cases. In consequence, resection of the nodule is advocated whereas the wall of the cystic process should hardly contain any tumour and therefore may be left in situ. Others[25] favour complete resection of the cystic process, when there is enhancement

of the wall of the tumour cyst on CT. In our series complete resection of the wall was performed whenever possible because identification of the mural nodule was difficult on CT.

Postoperative Neuro-imaging

Schneider *et al.*[25] performed postoperative CT studies with contrast in 23 patients with benign cerebellar astrocytoma to clarify the extent of tumour resection. The examination was performed within 72 hours postoperatively. Based on the postoperative CT scan 12 patients had residual tumours. According to the intra-operative findings the surgeon believed that a macroscopically total resection had been carried out in 9 of these patients, so that considerable discrepancies were noted between the radiological findings and the judgement of the surgeon based on his intra-operative observations. Our study supports this view. We performed our CT studies after an intervall of 3 months postoperatively because the postoperative damage to the bloodbrain barrier was supposed to have subsided. Based on these data an indication for early re-operation was not seen. Residual tumour enhancement was observed in 5 of our 15 patients with gross total resection. On the other hand, there was no contrast-enhancement in 2 out of 6 patients with incomplete tumour resection. Although intra-operative findings and postoperative CT studies did not show a close correlation in the present study, the 2 patients with recurrent tumour growth were correctly identified according to CT criteria. Both showed an increasing tumour enhancement over the years. Therefore, in our view, annual CT contrast studies should be performed in all the patients who underwent surgery for pilocytic astrocytoma of the posterior fossa and show a residual tumour enhancement on CT in order to identify these individuals who run a high risk of recurrent tumour growth.

Recurrent Tumour Growth

In a combined series including data of 393 inhomogeneously treated patients with pilocytic astrocytoma of the posterior fossa documented from 1931 to 1988, the incidence of tumour recurrence was 23%[1]. The authors observed 76 early and 15 late recurrences. These 2 groups were seperated by Collin's law, defined by a follow-up interval free of symptoms in months divided by the patient's age at diagnosis plus 9 months. No specific histological features of the tumour were related to recurrence rate[1]. Others[6] had found 3 subtypes of tumour recurrence, including 1) early recurrence within 4 years postoperatively, 2) late recurrence which is unrelated to the radicality of surgery and histological features and 3) malignant transformation of a pilocytic astrocytoma also with leptomeningeal dissemination[3, 9, 21, 23]. Whereas radiation therapy is suggested in these cases as primary treatment, patients with recurrent tumour growth should have operation in order to improve long-term prognosis[16]. In the present series recurrent tumour growth was not observed in the 17 patients with gross total resection, in whom a follow-up examination could be obtained. Tumour resection was incomplete in 10 cases. At follow-up ex-

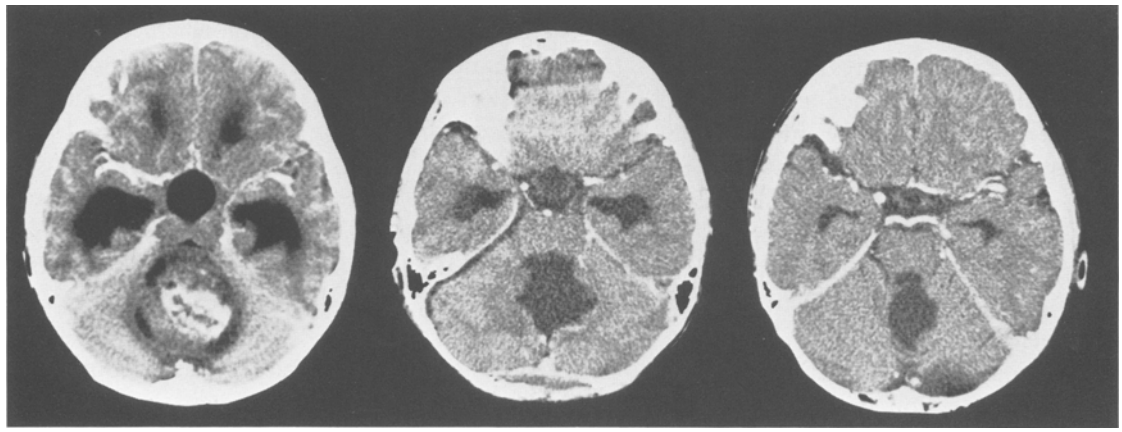

Fig. 4. 6-year-old girl with progressive headache and ataxia. Left: The pre-operative CT-scan shows a well delineated tumour with inhomogenous and weak contrast enhancement in the vermis and the 4th ventricle (max. diameter: 5 cm); multiple small cysts can be detected in the center and the rim of the tumour. There is also a hydrocephalic dilatation of the lateral ventricles and the 3rd ventricle. Middle: Two days after resection of the tumour a slight enhancement is visible along the left dorsal wall of the dilated 4th ventricle. Right: 6 months later there is no suspicious contrast enhancement, indicating complete resection of the pilocytic astrocytoma

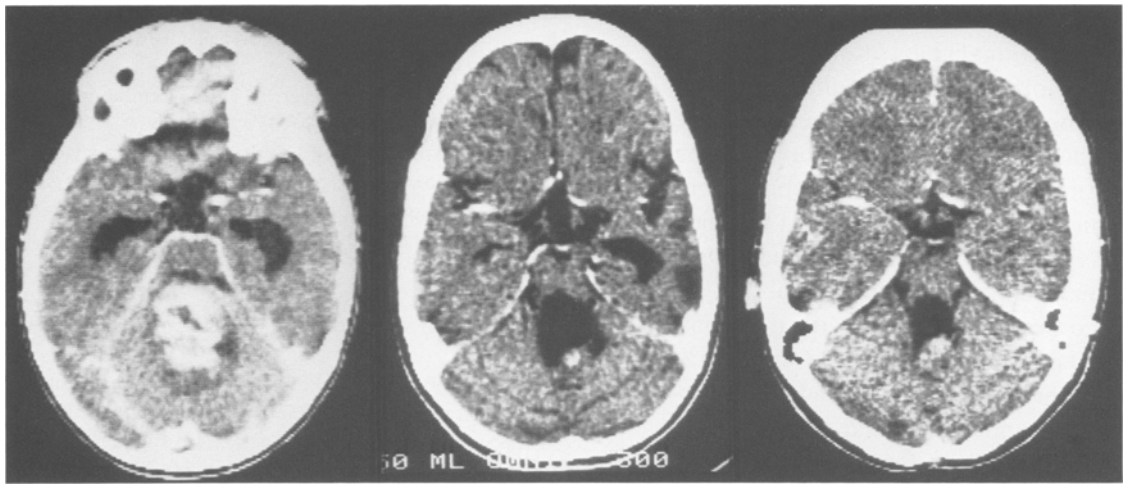

Fig. 5. 4.5-year-old boy with ataxia, headache, and progressive clouding of consciousness. A lobulated contrast enhancing tumour is depicted in the vermis and 4th ventricle. Left: Small cysts are shown in the center and the rim of the tumour. Furthermore, dilatation of the lateral ventricles can be noted. Middle: 14 months after resection of the pilocytic astrocytoma a small enhancement on the posterior wall of the dilated 4th ventricle is visible after administration of contrast media (max. diameter: 6 mm). Right: 5 years later a contrast enhancing mass with a maximum diameter of 1.5 cm is visible in the same position, indicating recurrent tumour growth

amination 6 had no or only a slight neurological deficit, one remained severly disabled, another one died. Two patients suffered tumour recurrence 3 and 10 years after the first operation. The re-operation consisted of a gross total resection in one and partial removal in the other. Both patients remained severely handicapped and required permanent help. In our study malignant transformation was not observed during follow-up.

Hydrocephalus

Hydrocephalus is a frequent complication of pilocytic astrocytoma of the posterior fossa[26]. In recent years the indication for pre-operative CSF-shunting has been discussed[13, 26]. Some authors think that pre-operative ventricular CSF shunting may result in upward herniation, bleeding into the tumour and shunt dependency. There may be a displacement of the tumour and cerebellum towards the brainstem, thus making an operative procedure in this region more difficult. Peri-operative CSF-drainage is advocated as an alternative[13].

We submitted 15 of our patients with pilocytic astrocytoma and hydrocephalus to pre-operative CSF-drainage. 8 patients were treated with external CSF drainage, 7 underwent permanent ventriculoperitoneal shunting. Serious complications have not been observed in this subgroup. In 6 cases the postoperative course of the disease was complicated by a triventricular enlargement, requiring external CSF drainage or ventriculoperitoneal shunting in 3 patients each. Swelling of the remaining brain tissue or subarachnoid adhesions are discussed as possible mechanisms in the literature[26]. In the present series the development of postoperative hydrocephalus did not show a correlation to the extent of tumour resection.

Irridation and Chemotherapy

The value of postoperative irridation and chemotherapy in patients with pilocytic astrocytoma has also been discussed. Postoperative irridation or chemotherapy is not indicated in patients following a gross total resection[1, 7, 8, 29]. Patients with incomplete resection might benefit from irridation therapy using doses of 45–60 Gy[7, 20, 29], whereas the experience with stereotactic treatment modalities in incompletely resected tumours are limited[17]. Some believe that irridation causes malignant transformation of a pilocytic astrocytoma in rare cases[8, 28]. In the present series 4 patients with pilocytic astrocytoma of the posterior fossa and extensive brainstem involvement were submitted to irridation therapy [50–55 Gy]. Two of them underwent incomplete tumour resection. One patient remained without permanent deficit, the second one suffered severe impairment. Another 2 patients, who had open

biopsy of the tumour, died because of progressive tumour growth. Although malignant transformation of the tumour was not observed, we felt that irridation therapy failed to show a significant influence on the clinical course of disease in these cases. Mainly in the two patients with incomplete tumour resection spontaneous resolution of the tumour could not be ruled out. Mundinger *et al.*[22] reported on the treatment results of radiation therapy with interstitial ^{125}I in 19 patients with nonresectable, circumscribed gliomas of the brainstem. The actual survival rate was 54.8% at 5 years after diagnosis. So stereotactic radiation therapy may offer a more appropriate and effective alternative in the treatment of these tumours.

Chemotherapy has not been given in our series. To the best of our knowledge no larger series with chemotherapy of pilocytic cerebellar astrocytoma have been published. With regard to its biological and histological properties it seems unlikely that chemotherapy could be useful in cases of incomplete tumour resection and for regrowth.

Conclusion

Our study illustrates that the extent of tumour resection in pilocytic astrocytoma of the posterior fossa cannot be defined by early postoperative CT-criteria. Long-term follow-up with CT seems mandatory in cases with contrastenhanced tumour residue. On follow-up examination these contrast-enhancing residues may disappear or remain unchanged. Recurrent tumour growth should only be suspected in those surgically patients with a growing CT-enhancement over the years. In these patients re-operation should be performed.

Although hydrocephalus is a common finding in patients with a pilocytic astrocytoma of the posterior fossa, permanent ventriculoperitoneal shunting is required only in some patients with pre- or postoperative hydrocephalus.

An indication for percutaneous irridation is no longer given. The precise role of radiotherapy in cases with incomplete tumour resection or recurrence remains to be defined in the coming years.

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