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Surgical treatment of intraventricular ependymomas and subependymomas

Leczenie operacyjne wyściółczaków i podwyściółczaków wewnątrzkomorowych

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Abstract

Background and purpose: The aim of the study was to present our experience in the surgical treatment of intraventricular ependymomas and subependymomas with special consideration to the evaluation of the surgical outcome and risk of tumour recurrence.

Material and methods: We report a series of 36 consecutive patients treated surgically for intraventricular ependymoma or subependymoma in the years 1992-2008. There were 26 lateral ventricle and 10 fourth ventricle tumours. Complete resection was achieved in 19 patients while the remaining 17 patients underwent either subtotal or partial resection. Histopathological evaluation revealed ependymoma, subependymoma and anaplastic ependymoma in 20, 11 and 5 cases, respectively.

Results: Eight patients died after surgery due to postoperative brain injury. Five patients were severely disabled postoperatively: one patient developed hemiparesis, three patients presented adynamic syndrome, and one patient developed severe cerebellar ataxia subsequent to vermis injury. All patients with posterior fossa tumours presented with lower cranial nerve deficit. Seventeen patients received radiotherapy postoperatively. There were five recurrent tumours during follow-up; three patients underwent subsequent reoperation. Importantly, five patients with supratentorial tumours and a history of incomplete resection with postoperative radiotherapy had no tumour recurrence in over 10 years' follow-up.

Streszczenie

Wstęp i cel pracy: Celem pracy było przedstawienie własnych doświadczeń w leczeniu operacyjnym wyściółczaków i podwyściółczaków wewnątrzkomorowych, ze szczególnym uwzględnieniem oceny wyników leczenia i ryzyka wznowy guza.

Materiał i metody: Materiał kliniczny obejmuje kolejnych 36 chorych leczonych operacyjnie w latach 1992–2008 z rozpoznaniem wyściółczaka lub podwyściółczaka wewnątrzkomorowego. Wyodrębniono 26 pacjentów z guzami komór bocznych i 10 z wyściółczakami IV komory mózgu. Guz usunięto całkowicie u 19 pacjentów, prawie całkowicie u 6, a częściowo u dalszych 11 osób. W badaniu histopatologicznym wykazano obecność wyściółczaka u 20, podwyściółczaka u 11, a wyściółczaka anaplastycznego u 5 chorych.

Wyniki: Ośmiu chorych zmarło po operacji w przebiegu ciężkiego uszkodzenia mózgu. Pięciu pacjentów zostało wypisanych w stanie ciężkim, w tym trzech z zespołem adynamicznym, jeden z głębokim niedowładem kończyn i jeden z ciężkim zespołem móżdżkowym. U wszystkich pacjentów z guzem IV komory mózgu obserwowano zaburzenia połykania i fonacji. Po operacji 17 pacjentów poddano radioterapii. W okresie dalszej obserwacji u 5 pacjentów zanotowano odrost guza; trzech pacjentów ponownie operowano, wszyscy zmarli z powodu dalszego rozrostu guza. U pacjentów z wyściółczakami nadnamiotowymi usuniętymi niecałkowicie i poddanymi radioterapii zanotowano wieloletnie obserwacje bez dalszego rozrostu guza.

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Conclusions: Intraventricular ependymomas and subependymomas still remain a surgical challenge due to a relatively high incidence of incomplete tumour resections and/or permanent neurological complications associated with their removal. Still, even incomplete tumour removal with subsequent radiotherapy facilitates long-term progression-free survival in some cases.

Key words: ependymoma, subependymoma, brain tumour, operative treatment, radiotherapy.

Wnioski: Leczenie wyściółczaków i podwyściółczaków wewnątrzkomorowych jest związane z dużym ryzykiem operacyjnym i trudnością w całkowitym usunięciu guza. W guzach nadnamiotowych nawet w przypadku ich częściowego usunięcia i poddania pacjenta radioterapii jest możliwe wieloletnie przeżycie bez rozrostu nowotworu.

Słowa kluczowe: wyściółczak, podwyściółczak, guz mózgu, leczenie operacyjne, radioterapia.

Introduction

According to the World Health Organization (WHO) classification, ependymomas (WHO grade II), anaplastic ependymomas (WHO grade III) and subependymomas (WHO grade I) belong to the ependymal tumours that show microscopic features of both epithelial and glial cells. Ependymomas account for 2% of intracranial tumours in adults while in children this proportion approaches 12% [1-3]. At least half of ependymomas occur in the first two decades of life; they localize in the posterior fossa then, particularly in small children. Ependymomas in the adult population are mostly supratentorial; still only a half of them arise from ventricle walls. The remaining half originate within the brain, outside the ventricular system and stem from ependymal cells that arrested within brain parenchyma during embryonic development. Subependymomas, on the other hand, are rare and comprise less than 0.7% of all intracranial tumours [4]. Subependymomas and ependymomas are more common in men; the majority of them relate to the fourth ventricle when compared to subependymomas of the lateral ventricles [5]. In contrast to ependymomas, extraventricular localization of subependymomas is extremely rare [4]. The most common clinical signs include cognitive disturbances and signs of intracranial hypertension that arise from cerebrospinal fluid circulation disturbances and related hydrocephalus [1].

Owing to the specificity of their intraventricular localization and associated, fastidious difficulties in their surgical treatment, we decided to select cases with ventricular system tumours and put them under meticulous analysis. Treatment of ventricular ependymomas is complex and its final outcome is burdened by a high risk of serious neurological complications. It relates to the extent of a slowly growing tumour that expands within the ventricular system and remains clinically silent until it reaches undue dimensions. Accordingly, a successful dissection of the tumour, which usually encompasses critical paraventricular structures, poses a real challenge for a neurosurgeon. On the other hand, the nature of the tumour itself along with frequent partial resections usually necessitates adjuvant oncological treatment. Nonetheless, final outcomes in this group of intracranial tumours remain unsatisfactory and further prognosis uncertain. Accordingly, patients with hemispheric tumours located outside the ventricular system as well as those with pineal region tumours were excluded from our cohort. The objective of our study was to present our experience with surgical treatment of ventricular ependymomas and subependymomas based on a homogeneous, relatively large group that encompasses adult patients treated in a single centre over the last several years. Paramount problems relevant to treatment outcome and risk of recurrence are also discussed. The majority of the studies published so far depict outcomes in the paediatric population owing to the much higher prevalence of these tumours. Accordingly, the presented analysis seems particularly relevant.

Material and methods

Retrospective analysis of 36 patients treated surgically for intraventricular ependymomas or subependymomas between 1992 and 2008 was performed. Two subgroups – one that encompassed 26 patients with lateral ventricle tumours and one that included 10 patients with tumours of the fourth ventricle – were separated. Patient's age varied from 16 to 75 years; the average age was 34 years. Our cohort included 15 women and 21 men (Table 1). The most common primary symptom was headache (Table 2) while duration of symptoms did not exceed a year; in 16 patients it was shorter than 3 months. Clinical symptoms on admission are summarized in Table 3. Most of the patients presented with signs of intracranial hypertension that included papilloedema on fundoscopy. Obstructive hydrocephalus was present in 23 cases; eight patients had a ventriculo-peritoneal shunt implanted prior to definitive surgery. The extent

Table 1. Age and sex of studied patients

Age	Ependymomas in the lateral ventricles		Ependymomas in the fourth ventricle		Overall
	women	men	women	men	
16-30	5	7	2	3	17
31-40	3	5	1	1	10
41-50	–	1	–	2	3
51-60	2	1	–	–	3
> 60	2	–	–	1	3
Overall	12	14	3	7	36

Table 2. First signs of tumour in studied patients

First sign	Ependymomas in the lateral ventricles	Ependymomas in the fourth ventricle	Overall
Headache	14	8	22
Epileptic seizures	5	–	5
Psychoorganic syndrome	3	–	3
Sudden disorders of consciousness	2	–	2
Vertigo	2	2	4

of extraventricular tumour invasion was assessed according to the intraoperative representation and preoperative neuroradiological studies (Table 4). Likewise, the extent of resection was appraised based on the surgeon's intraoperative interpretation as well as an early postoperative computed tomography (CT) scan (7 days after surgery) and late magnetic resonance imaging (MRI) (3 months after surgery), both of which were scheduled in concert with current neuroimaging capabilities. Gross total and partial resections were defined with subtotal resections pointed out in cases when the performing neurosurgeon deliberately left a small portion of the tumour within an eloquent area. The extent of resection in particulate cases is summarized in Table 4. Lack of radicality in selected cases arose from tumour infiltration into the deep brain structures in lateral ventricle tumours, its penetration into the fornix and/or corpus callosum in tumours within the foramen of Monro's vicinity or wide infiltration of the ventricle floor in ependymomas of the fourth ventricle. Histopathological examination revealed ependymomas in 20 patients and subependymomas in 11; five patients harboured anaplastic ependymoma. All subependymoma cases involved tumours of the lateral ventricles. Histopathological diagnoses in correlation to tumour location are summarized in Table 4.

Table 3. Clinical signs on admission

Clinical signs on admission	Ependymomas in the lateral ventricles	Ependymomas in the fourth ventricle
Headache	22	10
Vomiting	12	7
Consciousness disturbances	8	2
Visual disturbances	9	7
Psychoorganic syndrome	5	1
Limb weakness	3	–
Epileptic seizures	4	–

Tumours of the lateral ventricles were removed via the middle frontal gyrus approach; for tumours of the trigonum, the middle temporal gyrus or superior parietal lobule approach was implemented. Ependymomas of the fourth ventricle were accessed either via a telovelar approach or with partial resection of the vermis.

Patients were evaluated on admission, at discharge from the department and in long-term follow-up (either in the department or in the outpatient clinic) based on neurological exam and imaging studies. Radiological dia-

Table 4. Tumour location, extent of resection and histopathology

Location	Extent of resection			Histopathology			Overall
	Gross total	Subtotal	Partial	Subependymoma	Ependymoma	Anaplastic ependymoma	
Lateral ventricle	10	2	1	8	3	2	13
Both lateral ventricles	2	–	2	1	3	–	4
Lateral and third ventricle	2	1	2	1	4	–	5
Lateral ventricle and basal ganglia	–	1	3	1	2	1	4
Fourth ventricle	3	–	1	–	4	–	4
Fourth ventricle and brainstem	–	2	2	–	3	1	4
Fourth ventricle and vermis	2	–	–	–	1	1	2
Overall	19	6	11	11	20	5	

gnostics included CT or MRI; notably, since 1998 all of the patients have had MRI in their preoperative workup. It is worth mentioning, however, that CT has limited value in preoperative diagnostics as it provides inadequate evaluation of infiltration of structures critical for the surgical strategy such as basal ganglia, fornix, corpus callosum or brainstem. Postoperative follow-up varied from 2 to 18 years (mean, 7 years). Catamnesis was available for 24 out of 28 patients in our cohort (86%).

Results

Immediate outcomes assessed with the Glasgow Outcome Scale (GOS) and stratified by tumour location, tumour size and extent of resection are presented in Tables 5 and 6. Four patients died following surgery for tumours of the lateral ventricle. In 3 cases, where large tumours encompassed the lateral ventricles and third ventricle, patients succumbed to injury of the fornix and hypothalamus. The fourth patient, who underwent surgery for an ependymoma within the trigonum approached through the superior parietal lobule, died due to pneumonia. Likewise, four patients operated for fourth ventricle tumours died. In two cases brainstem injury was the immediate cause of the death while the third patient died due to meningitis following ventriculo-peritoneal shunt implantation for hydrocephalus and the fourth one succumbed to postoperative haematoma. High mortality in the group of patients with fourth ventricle tumours is clearly visible (40%) in comparison to the patients with supratentorial tumours (15%). Interestingly, we found a relationship between outcome and the extent of resection. In the group of the patients with fourth ventricle tumours the percentage of gross total or subtotal resections reached 70%. Concurrently, three out of seven patients died. At the same time, out of three patients with

Table 5. Outcome (Glasgow Outcome Scale, GOS) in relation to tumour location

Outcome (GOS)	Tumour localization							Overall
	Lateral ventricle	Both lateral ventricles	Lateral ventricle and third ventricle	Lateral ventricle and basal ganglia	Fourth ventricle	Fourth ventricle and brainstem	Fourth ventricle and vermis	
Good recovery	11	3	2	2	–	–	–	18
Moderate disability	–	–	–	1	2	2	–	5
Severe disability	1	–	1	1	–	1	1	5
Death	1	1	2	–	2	1	1	8

Table 6. Outcome (Glasgow Outcome Scale, GOS) in relation to the extent of resection and the size of the tumour

Outcome (GOS)	Extent of resection			Tumour size		
	Gross total	Subtotal	Partial	≤ 3 cm	> 3 cm < 6 cm	≥ 6 cm
Good recovery	10	1	7	4	11	3
Moderate disability	2	1	2	–	4	1
Severe disability	2	2	1	1	2	2
Death	5	2	1	1	4	3
Overall	19	6	11	6	21	9

fourth ventricle tumours that were partially resected, only one died. In our series of 13 patients with lateral ventricle tumours that encompassed both lateral ventricles, the third ventricle along with tumours that infiltrated the basal ganglia we achieved gross total or subtotal resection in six patients. Still the outcome was unsatisfactory: three patients died and one was discharged in a poor condition. Conversely, all seven patients with large lateral ventricle tumours who underwent partial resection had very good outcomes.

Only one (9%) out of eleven cases of partial tumour resection in our study had an unfavourable outcome while amongst 25 patients with complete or subtotal resection 7 patients died (28%). Based on these data one can argue that in cases where tumours encompass critical brain structures such as the basal ganglia, corpus callosum, tegmentum or brain stem any attempts to achieve radicality should be limited by the very high risk of postoperative neurological sequelae. Likewise, tumour size influenced the outcome. Three out of 9 patients (33%) with massive tumours in which the largest dimension exceeded 6 cm died after surgery while mortality for remaining, smaller tumours was significantly lower at 18.5% (5 out of 27 cases). Differences existed amid histopathologically different tumour types as well. Only one patient (9%) with subependymoma died postoperatively while in the patient groups with ependymoma and anaplastic ependymomas case-fatality averaged 25%.

Five patients were discharged with unfavourable outcomes: three patients with adynamic syndrome, one with severe cerebellar injury and one with profound hemiparesis. In two cases adynamic syndrome was related to postoperative hydrocephalus and significant improvement was achieved with ventriculo-peritoneal shunting; in one case adynamic syndrome arose from fornix injury. Severe cerebellar syndrome subsequent to the dissection of ependymoma that encompassed the fourth ventricle and the vermis developed after dentate nucleus injury in one of the patients. Yet another patient with lateral ventricle ependymoma that infiltrated basal ganglia developed hemiparalysis following complete tumour removal due to injury of the basal ganglia. A patient with preoperative blindness did not improve her vision after tumour removal. All of the patients with a fourth ventricle ependymoma presented swallowing, expectoration and phonation disturbances that gradually diminished during the postoperative period and required phoniatric rehabilitation; on top of that, three patients developed transient sixth nerve paresis. Two patients with lateral ventricle tumours developed epileptic seizures during the late follow-up. One patient with a lateral ventricle tumour and two patients with fourth ventricle ependymomas required shunting for postoperative hydrocephalus.

Seventeen patients underwent conventional radiotherapy following surgery – 14 of them after surgery for supratentorial and three after surgery for fourth ventricle tumours discharged in a good condition. Another 10 patients with ependymomas and three with anaplastic ependymomas along with four patients with subependymomas were qualified for radiotherapy after subtotal resection based on the risk of tumour progression. Three cases of ependymomas (WHO grade II) after gross total resection were not qualified for radiotherapy. The decision was made based on the therapeutic strategy valid during the first years of the analysed period which enforced radiotherapy solely on the basis of the radicality of the surgery. Follow-up revealed tumour recurrence in 5 cases (Table 7). Three supratentorial tumours recurred two years after surgery (one patient with ependymoma and two others with anaplastic ependymomas). One of them underwent reoperation (primarily ependymoma, recurrence progressed to anaplastic ependymoma). All three patients succumbed to the recurrent tumour's progression. Of the two patients with recurrent tumours of the

Table 7. Tumour recurrence

Patient with tumour recurrence	Location	Size	Extent of resection	Histopathology	Radiotherapy
C.S.	Lateral ventricle	> 6 cm	Gross total	Ependymoma	No
I.B.	Lateral ventricle	> 3 cm < 6 cm	Gross total	Anaplastic ependymoma	Yes
K.N.	Lateral ventricle and basal ganglia	> 3 cm < 6 cm	Partial	Anaplastic ependymoma	Yes
J.C.	Fourth ventricle	> 6 cm	Gross total	Ependymoma	No
S.T.	Fourth ventricle	> 3 cm < 6 cm	Partial	Anaplastic ependymoma	Yes

Table 8. Radiotherapy efficacy

Histopathology	Radiotherapy (+)	Radiotherapy (–)	Recurrence
Subependymoma (WHO grade I)	4		0
		6	0
Ependymoma (WHO grade II)	10		0
		3	2
Anaplastic ependymoma (WHO grade III)	3		3
		–	–
Overall	17	9	5

fourth ventricle, the first one presented with recurrence and concomitant tumour dissemination within the spinal canal 1.5 years after the initial surgery. Correspondingly, primary diagnosis was ependymoma while recurrent tumour proved to be anaplastic ependymoma. The other case initially presented as anaplastic ependymoma. It was a 16-year-old patient whose tumour recurred 9 years after initial, partial resection with adjuvant radiotherapy; this patient died after second, subtotal resection of the tumour due to severe brain injury. The efficacy of the radiotherapy is summarized in Table 8. All the three cases of anaplastic ependymomas recurred despite adjuvant radiotherapy while ependymomas (WHO grade II) recurred in two out of three cases that had not any radiotherapy. Of particular importance are the cases with subtotal resections of ependymomas (WHO grade II) who underwent subsequent radiotherapy. Out of seven patients in this group, four have had a follow-up period exceeding 10 years (11, 12, 15 and 18 years) with no clinical or radiological signs of recurrent tumour.

Discussion

Ependymomas (WHO grade II), anaplastic ependymomas (WHO grade III) and subependymomas (WHO grade I), according to the WHO classification, appertain to ependymal tumours that reveal microscopic features of both epithelial and glial cells. Ependymomas account for approximately 2% of intracranial tumours in adults, where they are predominantly located in the supratentorial space, while in children an infratentorial location is much more common and ependymomas make up to 12% of all paediatric brain tumours [1-3]. Subependymomas are much less prevalent and constitute 0.7% of all intracranial tumours; nonetheless this value might be widely underestimated owing to the fact that a significant percentage of these tumours are asymptomatic [4]. Reports exist, however, on rare, pediculate subependymomas of the lateral ventricle [6]. In contrast to ependymomas, subependymomas are extremely rare outside the ventricular system. Despite significant differences in biological activity between various types of

ependymal tumours, a whole group has common characteristics including similarities in the surgical management. Moreover, these tumours are often discussed together [7]. On top of that, although radiological presentation of subependymomas is slightly different from more aggressive ependymal tumours (subependymomas show moderate contrast enhancement in T1-weighted MRI sequences with no surrounding oedema while ependymomas demonstrate intensive, rather homogeneous contrast enhancement and peritumoural oedema) in symptomatic tumours differential diagnosis based on imaging studies is always doubtful and clinically irrelevant. Conversely, asymptomatic tumours necessitate a distinctive approach since a justified suspicion of subependymoma usually imposes conservative treatment and close follow-up of the tumour [5].

Intraventricular ependymomas, in the majority of cases, grow relatively slowly and remain asymptomatic long enough to reach a relatively large size at diagnosis [8]. The most common clinical signs include cognitive decline along with symptoms of intracranial hypertension that arise from cerebrospinal fluid circulation deficiency and subsequent hydrocephalus. Likewise, in our cohort the most often reported signs were those related to intracranial hypertension (headache, papilloedema) while imaging studies revealed obturative hydrocephalus in most of the cases. Less prevalent signs and symptoms in patients with intraventricular tumours included seizures, focal deficits and cerebellar ataxia in posterior fossa cases [1]. Only three patients in our group with tumours localized within the body of the lateral ventricle or trigonum presented with focal deficits. The therapeutic scheme for intracranial ependymomas encompasses surgical dissection and postoperative radiotherapy [3,9,10]. The surgical approach depends on the prospective site of the primary tumour expansion, the degree of intraventricular expansion, transependymal outgrowth into the periventricular zone and the size of the tumour. Yasargil stresses that the essence of intraventricular tumour surgery involves tumour dissection via an approach that avoids critical brain structures and minimizes the risk of perioperative neurological deficits [11]. A piecemeal dissection was implemented in most of the cases owing to the large size of the tumour prior to its final dissection; a similar approach has been stressed by others [12].

In our series of lateral ventricle tumours, we used solely transcortical approaches. Tumours of the anterior part of the body of the lateral ventricle as well as tumours within the foramen of Monro's vicinity, which comprised the majority of our cases, were approached via the middle frontal gyrus. The presence of a large mass of the tumour with transependymal infiltration was the main justification for this approach; moreover, it allowed the dissection of extensive tumours that often comprised both lateral ventricles along with an anterior part of the third ventricle, which represented a significant percentage of the cases. Yasargil advocates for an anterior, transcallosal approach for tumours located within an anterior horn and the body of the lateral ventricle in order to avoid transcortical approaches' complications such as seizures, limb pareses or memory and cognitive deficits [11,13,14]. The transcortical approach has its advantages, though: it is simple, and facilitates a wider surgical manoeuvre within the surgical corridor in the lateral ventricle which, in the era of microsurgery, generates much lower risk of the aforementioned complications than reported previously [15]. This approach was complicated by seizures in two cases; however, the frequency was significantly lower than reported by others [8,12].

In tumours located within the posterior part of the body of the lateral ventricle and trigonum, we applied an approach via the superior temporal lobule and middle temporal gyrus. The middle temporal gyrus approach, which facilitates a shorter surgical corridor, is particularly feasible for either solely intraventricular tumours or tumours with lateral, transependymal extension where it ensures good, early control over the branches of the posterior lateral choroid artery. On the other hand, a potential risk of aphasia in tumours of the dominant hemisphere along with possible visual field deficit has been described [16,17]. A number of authors stress the advantages of a superior temporal lobule approach [11,12,18], particularly in cases with tumour expansion rostrally and within the dominant hemisphere. When compared to the middle, temporal approach it reduces the risk of visual and speech deficits but it does not provide good control over tumour vascularity [19], which conversely increases the risk of limb pareses. One should also remember that transcortical approaches carry higher risk of intracerebral haemorrhage and increase the risk of hemisphere collapse following extensive resection with subsequent pericerebral haematoma or hygroma [19]. In our hands no intracerebral hematoma occurred; however, a few times we found asymptomatic hygromas adjacent to a collapsed hemisphere.

Gross total or subtotal resection was achieved in over 60% of patients with lateral ventricle ependymomas. Schwartz *et al*. [20] reported analogous results in a similar group of patients with supratentorial ependymomas while Majchrzak *et al*. [21] reported 85% radical

dissections of lateral ventricle neoplasm. However, these series are hardly comparable to our cohort as the first one included ependymomas of the lateral ventricle along with pineal region ependymomas and extraventricular tumours as well; the other one presented a plethora of various types of ventricular tumours with only one case of ependymoma.

Four of our patients with lateral ventricle ependymomas (15%) succumbed to severe brain injury after the operation. Three of these patients had tumours that encompassed both lateral ventricles, and two of those had tumour in the third ventricle as well; the last, fourth one had a tumour that filled the trigonum. Similar or slightly lower mortality was reported by others [7,20,21], who confirmed an increased risk of surgery in patients with large and infiltrative tumours of a higher grade. Two other cases of lateral ventricle tumours developed adynamic syndrome that was related to fornix injury in one patient and postoperative hydrocephalus in the other; in this case ventriculo-peritoneal shunt significantly improved agility of the patient and restored his motor independence. Interestingly, in our group of patients we found a well-defined relationship between the outcome and the extent of resection. It is particularly true for extensive tumours of lateral ventricles that involved the fornix, corpus callosum and basal ganglia. Our analysis proved that in cases like that an aspiration for complete resection is futile as it is connected with a very high risk of postoperative neurological deficits.

Fourth ventricle tumours were initially approached via the vermis (five patients), a corridor that ensures a wide view into the fourth ventricle but is burdened by numerous complications. For this reason it was later substituted by the telovelar approach [11]. Two patients after resection via the vermis presented intense cerebellar ataxia possibly related to dentate nucleus injury. In cases where ependymoma extended caudally into the spinal canal (Figs. 1 A-D) (in three cases it reached C2 level and C3 level in a single one), the tumour itself formed the surgical corridor while difficulties were usually related to a displaced posterior inferior cerebellar artery, often encased in tumour [22]. Yasargil and others stress a significant risk of new, postoperative neurological deficits that are related to tumour compression on critical structures within the floor of the fourth ventricle, deep cerebellar nuclei and cerebellar peduncles [11,22]. Moreover, one should emphasize that benign ependymomas do not show infiltrative tendencies apart from their point of origin [23]. The difficulty with radical tumour dissection in this location results in a percentage of gross total resections that varies from 20% to 70% according to various authors [10,22,24]. A crucial part of the operation involves separation of the tumour from the fourth ventricle floor, which is associated with a high risk of injury to the ninth and tenth cranial nerve nuclei. In our experience, the risk of unfavourable outcome is high: as many as four patients succumbed to severe brain injury. All of the patients had postoperative dysphagia and dysarthria. In two cases of fourth ventricle ependymomas, the tumours were located in the roof of the fourth ventricle. In these cases the ependymoma arises from the inferior medullary velum and is feasible for radical dissection, but still it necessitates incision of the vermis [22].

No intraoperative neurophysiological monitoring was implemented during our study. Currently, intraoperative neurophysiological monitoring is an indispensable tool for a neurosurgeon during an intervention within eloquent areas [25]. In our cohort intraoperative monitoring would be particularly applicable in cases with fourth ventricle tumours. Neurophysiological monitoring should then involve brainstem mapping (BSM) and corticobulbar tract motor-evoked potentials (CBT-MEP) [26]. Aforementioned studies provide more information on preserved function of brainstem tracts and nerve centres than previously applied somatosensory evoked potentials (SSEP) and auditory brainstem response (ABR). BSM allows localization of cranial nerves and their motor nuclei within the floor of the fourth ventricle. CBT-MEP allow continuous intraoperative monitoring of the integrity of motor tracts from the cortex via motor nuclei within the brainstem to the supplied muscle. Simultaneous application of both techniques results in a significant reduction of the risk of postoperative neurological deficits.

After surgery, 17 patients received conventional radiotherapy. No prospective, randomized clinical trials exist so far that would compare outcomes of surgical treatment alone versus combined surgery and adjuvant radiotherapy; several series exist, however, that compare the efficacy of these therapeutic schemes and report more favourable results in patients whose treatment included surgery followed by radiotherapy [10,27]. Patients who qualified for radiotherapy included 10 patients with ependymomas, three patients with anaplastic ependymomas and four patients with incomplete resection of subependymoma. Initially, qualification criteria included anaplastic ependymoma diagnosis and incomplete dissection of the tumour. During postoperative follow-up, however, we found recurrent tumours after gross total resection of ependymomas (WHO grade II) without adjuvant radiotherapy. Accordingly, all of the subsequent

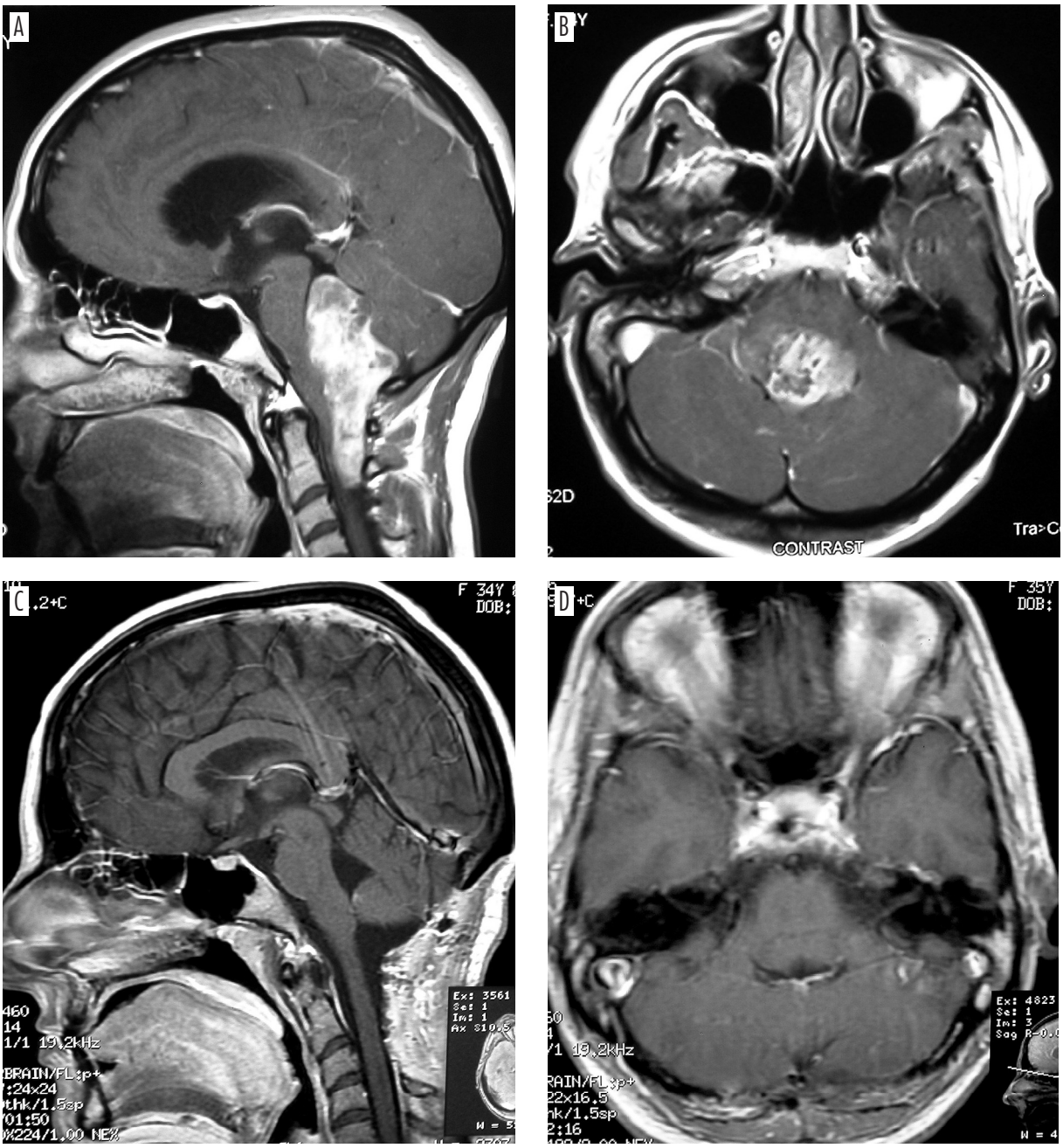

Fig. 1. Ependymoma (WHO grade II) of the fourth ventricle floor. Preoperative (A, B) and postoperative (C, D) magnetic resonance image

patients with ependymomas (WHO grade II) were referred for adjuvant radiotherapy. Still, reports exist that support a conservative approach in the treatment of ependymomas (WHO grade II), i.e. claiming that radiotherapy is unjustified in cases with complete tumour removal [28-31]. The extent of resection is regarded as one of the most important factors that influence survival, recurrence and tumour dissemination. Moreover, it has been pointed out that the tumour should be dissected with a certain margin of white matter [7] and ependymomas adjacent to eloquent areas should be irradiated, whenever radicality of their dissection is uncertain. It is particularly relevant to fourth ventricle tumours. The main aim of radiotherapy is to ensure local control of the tumour at its point of origin for in the vast majority of cases the recurrence takes place at the point of the primary tumour

growth [13]. Thus, irradiation of the whole brain and spinal canal is deemed inefficient in tumour recurrence prevention [31,32]. Posterior fossa ependymomas are an exception; some authors suggest spinal canal irradiation in these cases [33].

Long-term follow-up revealed tumour recurrence in five patients. One of them, an anaplastic ependymoma of the fourth ventricle, presented with tumour dissemination in the spinal canal. Both supra- and infratentorial tumours, primarily or secondarily anaplastic ependymomas, recurred and all of the patients eventually died sovereign of any attempts of reoperation. Some of the authors indicate that even after recurrence ependymomas (WHO grade II) retain their primary biological characteristics [7]. Our data did not confirm this statement, however, for we had had two cases of anaplastic transformation of the tumour. A critical factor that influences overall survival and recurrence is histopathological diagnosis of anaplastic ependymoma. Likewise, tumour dissemination within the central nervous system is unequivocally related to malignant tumour diagnosis and partial dissection of the tumour. It also renders an unfavourable outcome [31,34]. In our group we found one case of anaplastic ependymoma recurrence as late as 9 years after surgery. Similar remarks on long-term survivals of patients with malignant tumours were reported by others [7]. Our findings in the group of patients with ependymomas (WHO grade II) after subtotal resection who underwent radiotherapy are particularly interesting. In four out of seven patients the follow-up period exceeds 10 years (11,12,15 and 18 years, respectively), yet the clinical and radiological examination revealed no recurrence. The only factors that significantly influenced the recurrence in our material were the diagnosis of anaplastic ependymoma (all three patients) and lack of radiotherapy in ependymoma (WHO grade II) cases. Neither age, sex, tumour location nor the radicality of the resection had any influence on tumour recurrence.

Conclusions

1. Surgical treatment of intraventricular ependymomas and subependymomas is burdened by the high operative risk and difficulties with radical dissection of the tumour.
2. Attempts to achieve radical resection in tumours of the ventricular system that encompass critical structures such us the basal ganglia, fornix or brainstem hold a very high risk of neurological deterioration and such a strategy should be thoroughly contemplated. Significantly, the patients with supratentorial tumours even partially resected, who underwent adjuvant radiotherapy, can survive many years without progression.
3. Surgery for fourth ventricle ependymomas carries the highest operative risk.
4. The most important factor that influences the risk of recurrence is the histopathological diagnosis of an anaplastic ependymoma.
5. It seems justified to implement postoperative radiotherapy in all ependymoma (WHO grade II) cases regardless of its location and the extent of resection.

Disclosure

Authors report no conflict of interest.

References

1. Dohrmann G.J. Ependymomas. In: Wilkins R.H., Rengachary S.S. [eds.]. Neurosurgery. Vol. 1. 2nd ed. *McGraw-Hill Companies,* New York 1996, pp. 1195-1200.
2. Robertson P.L., Zeltzer P.M., Boyett J.M., et al. Survival and prognostic factors following radiation therapy and chemotherapy for ependymomas in children: a report of the Children's Cancer Group. *J Neurosurg* 1998; 88: 695-703.
3. Sanford R.A., Gajjar A. Ependymomas. *Clin Neurosurg* 1997; 44: 559-570.
4. Matsumura A., Ahyai A., Hori A., et al. Intracerebral subependymomas. Clinical and neuropathological analyses with special reference to the possible existence of a less benign variant. *Acta Neurochir* (*Wien*) 1989; 96: 15-25.
5. Ragel B.T., Osborn A.G., Whang K., et al. Subependymomas: an analysis of clinical and imaging features. *Neurosurgery* 2006; 58: 881-890.
6. Marchel A., Kroh H., Bojarski P. Pedunculated subependymomas of lateral ventricle. *Folia Neuropathol* 2001; 39: 33-36.
7. Palma L., Celli P., Cantore G. Supratentorial ependymomas of the first two decades of life. Long-term follow-up of 20 cases (including two subependymomas). *Neurosurgery* 1993; 32: 169-175.
8. Piepmeier J.M. Tumors and approaches to the lateral ventricles. Introduction and overview. *J Neurooncol* 1996; 30: 267-274.
9. Donahue B., Steinfeld A. Intracranial ependymoma in the adult patient: successful treatment with surgery and radiotherapy. *J Neurooncol* 1998; 37: 131-133.
10. Rogers L., Pueschel J., Spetzler R., et al. Is gross-total resection sufficient treatment for posterior fossa ependymomas? *J Neurosurg* 2005; 102: 629-636.
11. Yasargil M.G., Abdulrauf S.I. Surgery of intraventricular tumors. *Neurosurgery* 2008; 62: SHC1029-SHC1041.
12. Piepmeier J.M., Spencer D.D., Sass K., et al. Lateral ventricular masses. In: Apuzzo M.L.J. [ed.]. Brain surgery. *Churchill Livingstone*, New York 1993, pp. 581-599.

13. Apuzzo M.L., Chikovani O.K., Gott P.S., et al. Transcallosal, interfornicial approaches for lesions affecting the third ventricle: surgical considerations and consequences. *Neurosurgery* 1982; 10: 547-545.
14. Jeeves M.A., Simpson D.A., Geffen G. Functional consequences in the transcallosal removal of intraventricular tumours. *J Neurol Neurosurg Psychiatry* 1979; 42: 134-142.
15. Ellenbogen R.G. Transcortical surgery for lateral ventricular tumors. *Neurosurgical Focus* 2001; 10: 10-13.
16. D'Angelo V.A., Galarza M., Catapano D., et al. Lateral ventricle tumors: surgical strategies according to tumor origin and development – a series of 72 cases. *Neurosurgery* 2005; 56: 36-45.
17. Rabb C.H., Apuzzo M.L.J. Options in the management of ventricular masses. In: Tindall G.T., Cooper P.R., Barrow D.L. [eds.]. The practice of neurosurgery. *Williams & Wilkins*, Baltimore 1996, pp. 1229-1242.
18. Fornari M., Savoiardo M., Morello G., et al. Meningiomas of the lateral ventricles. *J Neurosurg* 1981; 54: 64-74.
19. Tanaka Y., Sugita K., Kobayashi S., et al. Subdural fluid collections following transcortical approach to intra- or paraventricular tumors. *Acta Neurochir* (*Wien*) 1989; 99: 20-25.
20. Schwartz T.H., Kim S.G., Rachel S., et al. Supratentorial ependymomas in adult patients. *Neurosurgery* 1999; 44: 721-731.
21. Majchrzak H., Majchrzak K., Adamczyk P. Leczenie chirurgiczne guzów komór bocznych. *Neurol Neurochir Pol* 2004; 38: 173-181.
22. Ikezaki K., Matsushima T., Inoue T., et al. Correlation of microanatomical localization with postoperative survival in posterior fossa ependymomas. *Neurosurgery* 1993; 32: 38-44.
23. Rorke L.B., Gilles F.H., Davis R.L., et al. Revision of World Health Organization classification of brain tumors for childhood brain tumors. *Cancer* 1985; 56: 1869-1886.
24. van Veelen-Vincent M., Pierre-Kahn A., Kalifa C., et al. Ependymoma in childhood: prognostic factors, extent of surgery, and adjuvant therapy. *J Neurosurg* 2002; 97: 827-835.
25. Deletis V., Sala F., Morota N. Intraoperative neurophysiological monitoring and mapping during brainstem surgery. A modern approach. *Oper Techn Neurosurg* 2000; 3: 109-113.
26. Morota N., Ihara S., Deletis V. Intraoperative neurophysiology for surgery in and around the brainstem: role of brainstem mapping and corticobulbar tract motor-evoked potential monitoring. *Childs Nerv Syst* 2010; 26: 513-521.
27. Pollack I.F., Gerszten P.C., Martinez A.J., et al. Intracranial ependymomas of childhood: long-term outcome and prognostic factors. *Neurosurgery* 1995; 37: 655-667.
28. Guyotat J., Signorelli F., Desme S., et al. Intracranial ependymomas in adult patients: analyses of prognostic factors. *J Neurooncol* 2002; 60: 255-268.
29. Hukin J., Epstein F., Lefton D., et al. Treatment of intracranial ependymoma by surgery alone. *Pediatr Neurosurg* 1998; 29: 40-45.
30. Awaad Y.M., Allen J.C., Miller D.C., et al. Deferring adjuvant therapy for totally resected intracranial ependymoma. *Pediatr Neurol* 1996; 14: 216-219.
31. Kawabata Y., Takahashi J., Arakawa Y., et al. Long-term outcome in patients harboring intracranial ependymoma. *J Neurosurg* 2005; 103: 31-37.
32. Paulino A.C., Wen B.C. The significance of radiotherapy treatment duration in intracranial ependymoma. *Int J Radiat Oncol Biol Phys* 2000; 47: 585-589.
33. Pierre-Kahn A., Hirsch J.F., Roux F.X., et al. Intracranial ependymomas in childhood. Survival and functional results of 47 cases. *Child Brain* 1979; 10: 145-156.
34. Rezai A.R., Woo H.H., Lee M., et al. Disseminated ependymomas of the central nervous system. *J Neurosurg* 1996; 85: 618-624.