

CLINICAL STUDY

Neurenteric cysts, incidence and surgical treatment

Kozak J, Bizik I, Surkala J, Steno J, Steno A

Department of Neurosurgery, Faculty of Medicine Comenius University and University Hospital Bratislava, Slovakia. kozakjan@hotmail.com

ABSTRACT

OBJECTIVES: Neurenteric cysts (NCs) of the central nervous system (CNS) are cystic congenital lesions that may occur anywhere along the neural tube. They are most common in the spinal region, in the lower part of the cervical and upper thoracic spine. Intracranial NCs occur rarely and there are only small series of patients published in literature worldwide. Microsurgical resection is the treatment of choice. We present our experience in treatment of NCs and review of literature.

METHODS: Seven patients with NC of CNS who were operated at the Department of Neurosurgery of Comenius University at University Hospital Bratislava within nine years (2010–2018) were included in the study. The series was retrospectively evaluated with an emphasis on symptomatology, surgery and postoperative course.

RESULTS: In three of the seven patients, NC was localized intracranially, in the other four, NC was in the spinal canal. In three patients, a complete removal of NC was achieved (2 intracranial NC, 1 spinal NC). In other patients, a portion of the cyst wall was left to prevent the development of a postoperative neurological deficit. After surgery, the neurological symptoms were completely resolved in six patients, while in one patient, they were alleviated. In one patient, a complication occurred during the postoperative course. There was no recurrence during the follow-up (3–111 months, mean duration 39 months).

CONCLUSION: In our series of patients with intracranial and intraspinal tumors, the incidence of NC was higher than presented in the published data. Our own surgical experience has shown that complete tumor resection is not always possible for intimate adherence to the surrounding structures. Leaving a tiny portion of the cyst wall allowed us to achieve good clinical results with no recurrence. Long-term follow-up of patients is required due to the risk of recurrence. However, it can already be stated that an adequate extent of resection leads to good clinical results (*Tab. 1, Fig. 4, Ref. 33*). Text in PDF www.elis.sk.

KEY WORDS: neurenteric cyst, endodermal cyst, microsurgical resection, recurrence, prognosis.

Introduction

NC of CNS is a congenital cystic lesion that is composed of basal membrane epithelium resembling the gastrointestinal tract (GIT) or respiratory epithelium (1–5). It is assumed that NC originates in abnormal ectoderm-endoderm separation due to the persistence of neurenteric canal during the third week of gestation. However, the exact mechanism of development is not currently known (2, 6). NCs are most commonly found to be intradural extramedullary in the lower cervical and upper thoracic segments of spine (6–8). These spinal NCs may be associated with other developmental anomalies of the spine (10, 11). Intracranial NCs are less common and mostly occur in the midline region of posterior fossa (1, 6, 12). Overall, NCs form a narrow group of neoplasms and are mentioned only in a small patient series in the literature (1, 8, 14). The incidence of NC of CNS is reported at

0.01 % in the literature (6). Microsurgical removal is the treatment of choice (1, 6, 14). Incomplete resection is accompanied by a higher rate of recurrence, nevertheless the prognosis is very good (1, 6, 15). Despite its generally benign nature, relatively dramatic manifestations of NC are described in the literature, such as rapid deterioration of clinical status, or malignant transformation of NC (6, 17–19). The aim of the study is to present our surgical experience with the treatment of NC and their correlation with literature data.

Material and methods

Seven patients (four women and three men) with histologically verified NC of CNS underwent surgery at the Department of Neurosurgery of Comenius University in Bratislava in the period between 2010 and 2018 (nine years). Of these, two were children (< 18 years). The age of the patients ranged from 8 to 67 years. Intraoperative electrophysiological neuromonitoring was used to maintain the integrity of neurological functions during surgery. All patients underwent post-operative magnetic resonance imaging (MRI), another MRI examination three months and six months apart followed by yearly intervals. Clinical status assessment was evaluated by the neurosurgeon.

Department of Neurosurgery, Faculty of Medicine Comenius University and University Hospital Bratislava, Slovakia

Address for correspondence: J. Kozak, MD, Department of Neurosurgery, Faculty of Medicine Comenius University and University Hospital Bratislava, Limbova 5, SK-833 05 Bratislava, Slovakia.
Phone: +421.2.59542532, Fax: +421.2.59543532

Tab. 1. Series of patients with NC operated during the period 2010–2018.

Case No.	Age and sex	Symptomatology and duration of symptomatology	Localization of NC	Extent of resection	Recurrence	Follow-up (months)
1	42, F	Cephalaea, 2 months	IV. ventricle	GTR	–	111 months
2	67, F	Mild paraparesis of lower extremities, myoclonus of lower extremities; 6 months	C7/Th1	STR	–	84 months
3	34, M	CC sy, 18 months	C1–C3	STR	–	42 months
4	17, M	CC sy, vomitus, 3 weeks	Cervicocranial junction	STR	–	14 months
5	61, F	Quadruparesis, 6 months	C6/C7	GTR	–	12 months
6	8, M	Severe quadraparesis; < 24 h	C6/7	STR	–	6 months
7	67, F	Cephalaea, 2 months	Convexity, frontal lobe left hemisphere.	GTR	–	3 months

F – female, M – male, GTR – gross total resection, STR – subtotal resection, CC– sy cervicocranial syndrome

Results

NC was localized in the spinal canal in four patients and intracranially in three patients (Tab. 1). All spinal NCs were localized intradurally extramedullary and ventral to spinal cord, which makes surgery more complex. No spinal anomalies have been reported with spinal NC. Clinical symptoms of intracranial NC (Tab. 1) were headache (in two patients) and cervicocranial syndrome (in one patient). Spinal NCs are most commonly manifested by paretic symptoms and rarely by pain syndrome. In one patient with spinal NC (patient No. 6), the disease manifested as a rapid development of quadraparesis. The surgical approach to intracranial NC was via craniotomy. Brain convexity NC and NC localized in the fourth ventricle were removed completely. A small portion of the NC localized in the craniocervical junction was left in order not to damage the surface of medulla and its pial vessels. In a patient with NC in the fourth ventricle, a swelling of cerebellum with acute obstructive hydrocephalus has developed after surgery. There was a need of revision surgery with external decompression by removing the bone flap and introducing a temporary external ventricular drainage. The removal of spinal NCs was achieved via laminectomy. NCs have always been accessible from one side of the spinal cord. After evacuating the cyst content the cyst wall was resected in order to secure the integrity of the spinal cord. This was also

aided by intraoperative registration of motor-evoked potentials (MEP). An insignificant decrease in amplitude of MEP in one patient led to a change in surgical tactics leaving a small portion of the tumor capsule. Neurological status has improved in all patients including a patient with postoperative complication requiring

surgical revision. During the follow-up period, the neurological deficit was completely resolved in six out of seven patients; in one patient the severe quadriparesis regressed to mild, and after a few months the patient was left with just a slight disturbance of fine finger motor skills.

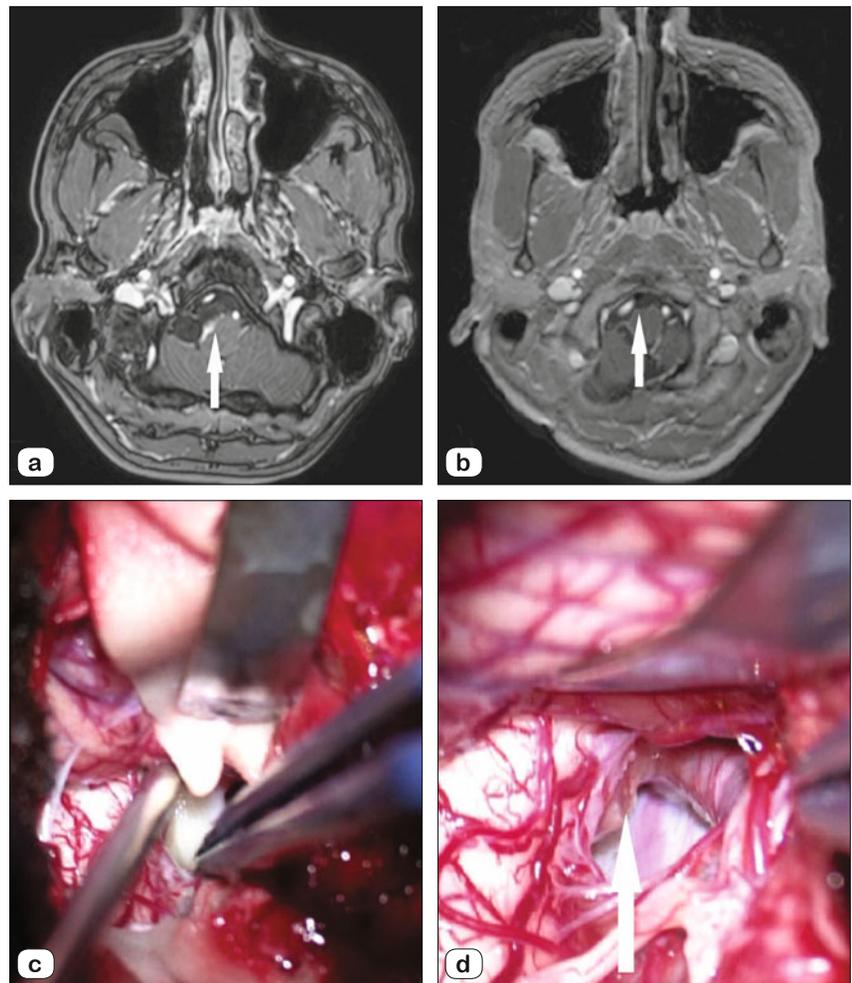


Fig. 1. Patient No. 4; MRI T1W sequence with contrast agent of the cervicocranial junction before the surgery. (a) Yellow arrow shows postcontrast enhancement of the cyst wall on the surface of medulla; MRI 9 months after STR (b) Red arrow points to a residual cyst wall that was left during the surgery due to strong adherence. View from operative microscope during the surgery; (c, d) NC (in blue forceps) is white milky with liquid content. Green arrow shows the residual cyst wall that was left on the surface of the medulla.

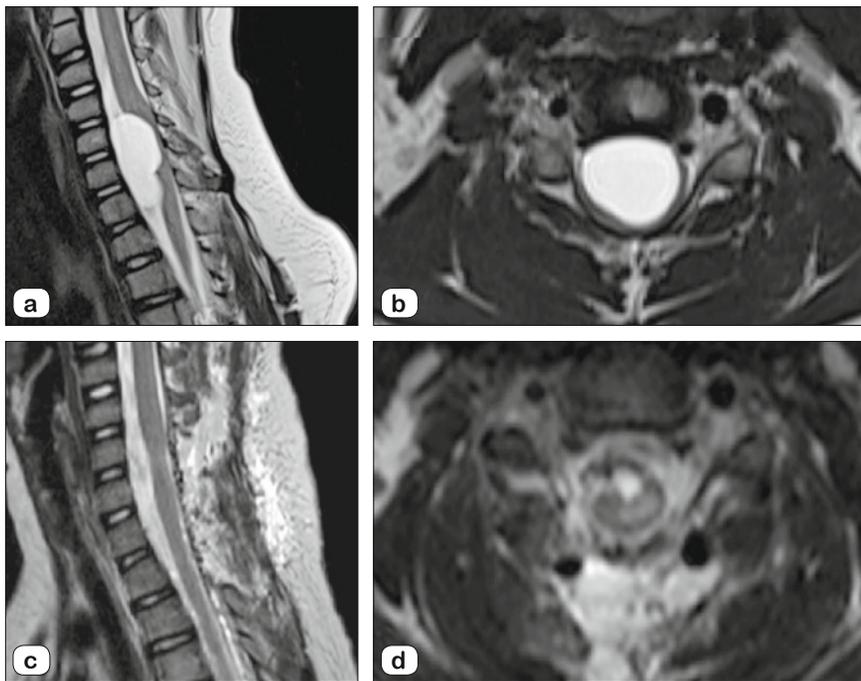


Fig. 2. Patient No. 6. MRI T2W sequence in sagittal (a) and axial (b) planes shows a ventrally located cyst compressing the spinal cord. MRI T2W sequence in sagittal (c) and axial (d) planes shows the spinal cord after subtotal resection of NC.

Illustrative case No. 1 (Patient No. 4)

A 17-year old patient was admitted for a three-week history of cervical pain and paravertebral spasm. MRI showed an extraxial cyst in the craniocervical junction with mild compression of the medulla. A portion of the cyst near the medulla was enhanced after administering a contrast agent (Fig. 1a). The surgery was performed under general anesthesia in a semi-sitting position with intraoperative monitoring of MEP and the approach was via lateral suboccipital craniectomy and partial hemilaminectomy of C1. After durotomy, cystic expansion of the lactic stain was deposited anterolaterally before the brain stem. After cutting the cyst wall, its dairy-rocked contents containing small crystals was aspirated. The cyst wall was separated from the cranial nerves and vessels. In the area of post-contrast enhancement on MRI, the wall of the cyst adhered tightly to the medulla and therefore, it was necessary to keep this part (Figs 1c, 1d). During the procedure, we registered a non-significant decrease in MEP of the right leg. The postoperative period was without complications and deterioration. The patient's complaints ceased in the early postoperative period. MRI after nine months showed subtotal resection of NC. After administering a contrast agent only small area was discretely enhanced at the site of the retained part of the NC wall (Fig. 1b). Histological examination determined the final diagnosis of NC.

Illustrative case No. 2 (Patient No. 6)

An eight-year old patient was admitted for a rapid onset of severe progressive quadraparesis. MRI revealed an intradural extramedullary cyst with compression of the spinal cord at the C5-7 level (Figs 2a, 2b). Surgery was performed in a prone position and

with dorsal approach via laminectomy. A partial release of the strongly arched spinal cord was achieved by dissecting the denticulate ligament. The cyst wall at the caudal pole was transparent. After cutting the cyst wall, and aspirating its content, the cyst wall was resected. A small part of the cyst wall was left in the ventral part of the spinal cord due to strong adherence (Fig. 3). Postoperative MRI showed resection of the cyst with decompression of the spinal cord (Figs 2c, 2d). The postoperative period was without any complications with rapid alleviation of neurological symptomatology (the patient was able to walk on the fourth postoperative day). Histological examination revealed a cyst wall lined with a columnar ciliated epithelium with hypocellular gliotic tissue, by which the final diagnosis of NC was established.

Illustrative case No. 3 (Patient No. 7)

A 67-year old patient was examined for cephalgia persisting for two months and arterial hypertension. MRI revealed an intracranial extraxial cyst at the convexity in the left frontal region. In the dorsal part of the cyst, there was a heterogenous signal interpreted as a hemorrhage in the late subacute stage (Figs 4a, 4b). The skull vault over the cyst was thin. A radical resection was done via standard craniotomy. The cyst content was rocky and dense and slightly green in the dorsal part (at the site of presumed bleeding in the MRI) (Figs 4c, 4d). The immediate postoperative period was without any complications and cephalic pain retreated. The histological examination determined the final diagnosis of NC. On the ninth postoperative day, an epileptic seizure occurred which was not repeated after adjusting the anticonvulsive therapy. The patient is under neurological follow-up; the anticonvulsive treatment has not yet been completed.

Discussion

NCs of CNS are rare congenital and mostly benign lesions (6, 14). The first report of NC of CNS was published by Kuba and Fulton in 1928 and was first described in detail in the spinal region by Puusepp in 1934 (3, 5). Due to the histological picture of the cyst wall, which is formed by epithelium resembling the epithelium of GIT, or respiratory tract, Puusepp named this lesion "intestinoma". Holcomb and Matson introduced the term neuroenteric cyst in 1954 (20). Intracranial NC has been described approximately 30 years later as spinal NC in 1962 by Small et al (9). In the current literature, several synonyms are cited for NC, namely enterogenic cyst, endodermal cyst, neuroendodermal cyst, enteric cyst, archenteric cyst, bronchiogenic cyst and gastrocytoma

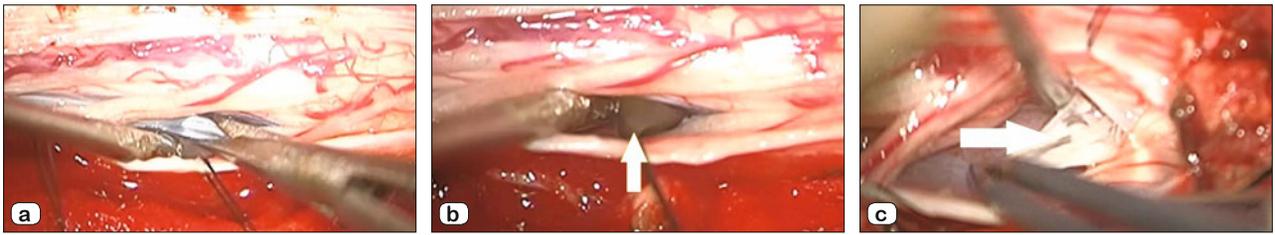


Fig. 3. Patient No. 6. View from operative microscope. Mobilization of the spinal cord is possible by dissecting the denticulate ligament (a). White arrow (b) points to the caudal pole of NC. Cyst wall is transparent. Aspiration of cyst content was followed by resection of cyst. Other parts of cyst wall (arrow) were milky-colored (c)

(2, 6, 21). Neurenteric cyst is used most frequently.

NCs originate in cells of the endodermal germ line. Currently, there are several theories of NC, but none of them explains each and every occurrence of NC in the CNS (2, 7, 10–12, 25). The origin of spinal NC is believed to migrate into the ectoderm through an unclosed neurenteric canal during the third week of embryonic development (neurenteric canal represents a transient communication of amniotic cavity and yolk sac, i.e. primitive gut and respiratory tract with notochord) (6). The origin of supratentorial NC is assumed to form the Seessel's pouch, which represents the transient diverticle of the oropharyngeal membrane of the cranial end of the foregut. This is the basis for the emergence of Rathke's cleft cyst and colloid cyst, as evidenced by their common immunohistochemical parameters (2, 26).

Our patient series consists of only seven patients. However, if we take into account the rare occurrence of NC, it has a number of specificities. In the given period of nine years, at our department, we carried out 3006 surgical procedures for intracranial and intraspinal tumors. Thus, this rare diagnosis accounted for 0.23 % of all surgical procedures for CNS neoplasms and tumors. The incidence of NC is approximately 0.01 % (6). For example, Chen et al published 12 cases of NC in 17 years and only 11 cases in 30 years were published as being treated at The Hospital for Sick Children in Toronto (14, 16). Our patient series thus shows a more frequent incidence. In our series, the intraspinal and intracranial NC ratio was the same, with approximately a three-fold greater frequency of occurrence of spinal NC in the published literature (1, 6, 7, 16). In our group, we also recorded rare regions of NC (fourth ventricle and supratentorial NC). Typically, the spinal NCs are localized intradurally extra-medullary and ventral to the spinal cord. Rarely (approximately in

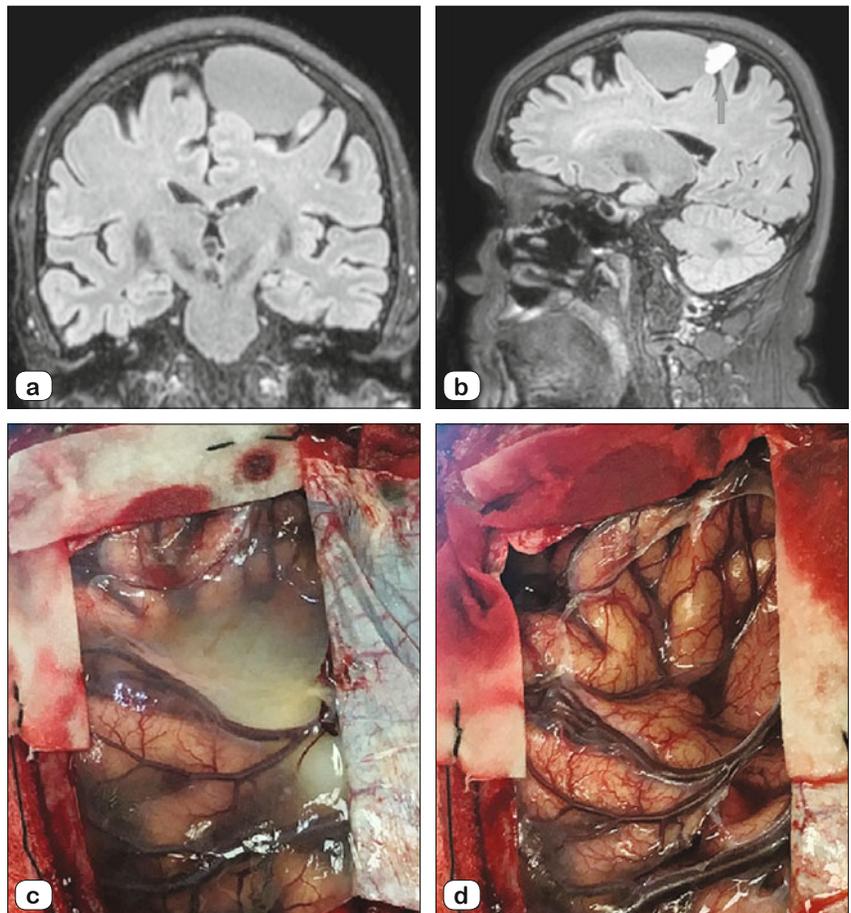


Fig. 4. Patient No. 7; MRI FLAIR sequence of supratentorial NC located on the convexity in left frontal region in coronal (a) and sagittal (b) planes. Dorsal aspect of cyst shows signal heterogeneity (red arrow) interpreted as a hemorrhage in late subacute stage. View from operative microscope before the resection (c) and after the complete removal (d).

5 %), NCs may occur intramedullary (1). Spinal NCs belong to the occult spinal dysraphism group and nearly half of the cases are associated with spina bifida, kyphoscoliosis, Klippel-Feil syndrome, lipomyelomeningocele and diastematomyelia (6, 7, 27). Intracranial NCs are rare and only about 100 cases have been reported in the literature (15, 28). Unlike spinal NCs, intracranial NCs do not occur with spinal anomalies (7, 15). Most of the intracranial NCs are localized infratentorially in the prepontine region, pontocerebellar angle, craniocervical junction, and in the great cistern or

the fourth ventricle (1, 6, 7, 12, 22–25). Supratentorial NCs are larger in size and their overall incidence is very low (15, 29). In their review article, Chakraborty et al reported only 35 cases (13, 15). Intraparenchymal NC is extremely rare (18, 29).

Common manifestations of intracranial NC include headache, epileptic seizure and focal symptomatology with cranial nerve palsies (1, 15, 21, 25). In most spinal NC patients, the symptomatology often results from spinal cord compression often with progressive symptoms (6–8). The symptoms may also be fluctuating in nature as a result of the periodic rupture of the cyst with the evacuation of its contents and the re-filling of the cyst (6, 28). The evacuation of cyst content to subarachnoid space may lead to aseptic meningitis and hydrocephalus (11, 29). In some cases, NCs are responsible for rapid deterioration due to intracystic bleeding or osmotic absorption of cerebrospinal fluid inside the cyst (18, 19, 25). Repeated intracystic bleeding may imitate a brain abscess (19). In our series, cephalgia was the most common symptom of intracranial NC. Spinal NC corresponded to the typical intraspinal neoplasm symptomatology. In one case, however, spinal NC manifested acutely by rapid deterioration (Illustrative case No. 2). The surgical procedure led to fast alleviation of neurologic symptomatology.

Imaging, treatment and prognosis

MRI is a method of choice in the diagnostic algorithm of NC. In both T1W and T2W sequences, NCs are isointense, or slightly hyperintense relative to the cerebrospinal fluid signal (6, 32). The MRI signal intensity depends on the protein concentration inside the NC and on the range of reactive inflammatory changes in the surrounding structures (1, 6, 16). The administration of contrast agent does not enhance NC conspicuously, however, a slight enhancement of peripheral content may be present. Preece et al have described such postcontrast enhancement and believe that it results from chronic inflammatory changes due to repeated cyst ruptures (27). In our series, a similar postcontrast enhancement was observed in one patient (Illustrative case No. 1). The diffusion-weighted imaging (DWI) sequence shows only partial diffusion restriction. There is no perifocal edema present around the cyst on imaging exams (6). Epidermoid cyst, dermoid cyst, arachnoid cyst, cystic schwannoma, craniopharyngeoma, Rathke's cleft cyst, colloid cyst and neurocysticercosis need to be distinguished (1, 6, 27, 33).

Histologically, NC is a cystic lesion with a lining composed of cuboid-to-columnar epithelium with a basal membrane resembling the GIT epithelium or respiratory epithelium. The epithelium may contain apically present cilia and often contains mucin-producing goblet cells (27). NC is very similar to colloid cyst and the Rathke's cleft cyst (2, 26). Rare, but even more serious is the malignant transformation of NC into adenocarcinoma. Only 6 cases were reported and all of them were intracranial NC (15, 29, 30). When trying to identify risk parameters for recurrence, there was no correlation of relapse with either MIB1 index or number of mitoses in the examined pathological samples (25). However, a more frequent recurrence was observed in NCs containing a greater proportion of mucin-producing goblet cells in the cyst wall (16).

In our series, there was no such recurrence during the follow-up period (39 months on average).

Microsurgical resection is the optimal treatment of NC. Intraoperatively, NCs are most often extra-axial milky lesions (1, 14, 16, 25, 29). They are filled with gelatinous, xanthochromic-to-oily liquid and may contain small crystals and calcifications. NCs have a predominantly clear boundary between the cyst wall and surrounding neural structures. However, strong adherence can be present. In this case, it is necessary to leave a part of the cyst wall in order not to harm the surrounding neural structures (1, 6, 14–16, 25). Our experience confirms these features. All NCs in our group were observed to have a milky cyst wall, but such cyst wall staining does not have to be homogenous. The cyst content varied from a muddy mass to transparent oily fluid. A complete removal of NC was done in nearly half of the patient (gross total resection in three patients, subtotal resection in four patients). Strong adherence of cyst wall to the surrounding neural structures was the rationale behind all subtotal resections. Despite the incomplete removal, a good control of disease was achieved and no recurrence of NC was recorded. The postoperative course was also favorable. A transient deterioration was reported in one patient (Patient No.1). Based on our results, subtotal resection appears to be justified if the radical resection is accompanied even by a small risk of neurological deterioration.

Although most spinal NCs are located ventral to spinal cord, the surgical procedure is almost always feasible from the dorsal approach. Microsurgical resection of intracranial NCs is carried out exploiting standard infratentorial and supratentorial approaches. During intracranial NCs resection, it is important to prevent cyst content from spreading to subarachnoid space as it may lead to epileptic seizures and chemical meningitis (1, 15, 29). The incidence of epileptic seizures is reported in up to 22 % of patients following supratentorial NC surgery (15).

Long-term follow-up of patients with NC shows that recurrence can occur long time after surgery (1, 6, 14, 29, 32). Nevertheless, the rarity of NC is the reason, why it is difficult to estimate the recurrence rate (7, 32). A study of eight patients by Chavd et al with the longest reported follow-up (up to 30 years) after partial resection showed recurrence in 37 % of patients. The interval between primary surgery and relapse ranged from four months to 14 years with a median of 36 months (32). Biopsy and cyst aspiration lead to an early relapse; therefore, these procedures are not recommended (1). Long-term follow-up by MRI is required and reoperation is indicated in case of symptomatic relapse of NC (6, 14, 32).

Conclusion

NCs are rarely occurring neoplasms with an overall good prognosis. There are distinctive pathologies that need to be considered during the diagnostic process and when planning a surgical procedure. The incidence in our series is higher than previously published. We even report NCs in rare regions of occurrence, such as supratentorial NC and NC in fourth ventricle. Since acute deterioration may be the first symptom of NC, we recommend early surgery. Based on our experience with the surgical treatment of

NC, we believe that not only radical but also subtotal resection can lead to good control of disease opening on to good postoperative course and outcome. Recurrence may occur several years after surgery; therefore, a long-term follow-up lasting even more than ten years after surgery is recommended.

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