Rare disease

Supratentorial neurenteric cyst associated with a intraparenchymal subependymoma

Francesco Natrella,¹ Aldo Mariottini,¹ Raffaele Rocchi,¹ Clelia Miracco²¹Department of Neurology, Neurosurgery and Behavioral Sciences, Section of Neurosurgery, University of Siena, Siena, Italy;²Department of Human Pathology and Oncology, Section of Pathological Anatomy, University of Siena, Siena, Italy**Correspondence to** Dr Francesco Natrella, francesconatrella@gmail.com**Summary**

Neurenteric cyst is a rare developmental lesion that very infrequently is localised supratentorially. Intraparenchymal subependymoma is an even more rare benign tumour. The authors report the case of a 45-year-old gentleman with a background of drug resistant epilepsy. An MRI was performed which showed a left frontal cystic lesion with a solid component. Histopathology confirmed a type C neurenteric cyst associated with an intraparenchymal subependymoma. Following enlargement of the lesion and worsening of symptoms he was referred to our institution for further management. A frontotemporal craniotomy was performed for excision of the lesion but recurrence occurred within 1 year. The lesion was further excised and 19 months post re-excision the patient is seizure free with no evidence of recurrence on MRI.

BACKGROUND

Supratentorial neurenteric cyst is an extremely rare developmental lesion. The aim of our study is to report this unusual case, to review the English literature about supratentorial neurenteric cyst and intraparenchymal subependymoma, to discuss the clinical, radiological and histopathological features of these lesions and to postulate the pathogenesis of their association. Since the lesion caused drug resistant epilepsy, we suggest some hypothesis about its epileptogenicity.

CASE PRESENTATION

Our case refers to an otherwise well 45-year-old man harbouring a neurenteric cyst associated with a subependymoma, a benign tumour very rarely located in the brain parenchyma (five cases previously reported in the English literature – table 1), providing a 19 months follow-up.

A 45-year-old man was suffering from generalised seizures since he was 13. A MRI performed at the age of 30 demonstrated a left frontal extra-axial cystic lesion, which stayed stable through years at further periodic imaging studies. The lesion overlaid the frontal convexity with minimum regional cortical displacement. At the age of 43 the patient underwent to a stereotactic biopsy of the lesion

with an attempt to drain its fluid content at another hospital. As epilepsy did not improve and cyst expanded, the patient came to our institution for further investigations and treatment. Social and family history was non-contributory. No neurologic deficit was elicited on thorough examination. He was on medication with 1200 mg of carbamazepine, 100 mg of phenobarbital and 150 mg of gabapentin daily. Seizures began with a fear sensation and lack of breath. Then the patient was not able to speak, and after a few seconds tonic clonic seizures involving the right half of the face and the right limbs occur. After seizures he had right limbs weakness and aphasia for few minutes to 2 h. Frequency of seizures was one per month.

INVESTIGATIONS

An MRI and a functional MRI (fMRI) were performed. At MRI the cyst had no contrast enhancement and its fluid content was hypo-intense on T1-weighted images and hyper-intense on T2-weighted intense images. In its posterior part there was a solid component, hyperintense on T1-weighted and hypointense on T2-weighted images, with a very slight contrast enhancement (figure 1). A 3-days video EEG monitoring was performed. The procedure showed that seizures originated from an area surrounding

Table 1 Intraparenchymal subependymoma

Pt	Year	Author	S	A	Location	Presentation	Treatment	Outcome
1	1989	Hankey <i>et al</i> ¹	F	21	Right fronto-parietal	Hemiparesis, partial seizures	Craniotomy: complete excision	Good
2	2005	Shuangshoti <i>et al</i> ²	n.i.	n.i.	Parietal	n.i.	Radiotherapy	Death 3.5 years p.o.
3	2005	Shuangshoti <i>et al</i> ²	n.i.	n.i.	n.i.	n.i.	n.i.	Lost follow-up
4	2006	Ragel <i>et al</i> ³	M	34	Right temporal	Partial complex seizures	Craniotomy: complete excision	Excellent
5	2006	Ragel <i>et al</i> ³	M	57	Right parieto-occipital	Headache, left lateral hemianopsia, left hemiparesis	Craniotomy: complete excision	Good
6	2011	Natrella <i>et al</i> (present report)	M	45	Left frontal associated with neurenteric cyst	Generalised seizures	1. Craniotomy: incomplete excision 2. Craniotomy: complete excision	Good

A, age; Pt, patient; S, sex.

Figure 1 MRI showing the cyst before the first surgical procedure, after a stereotactic attempt of biopsy and drainage of cyst content. The cyst was 3.1×3.6×3.7 cm (width × rostro-caudal × anterior-posterior). A and B: coronal and sagittal T1-weighted images. C: axial T1-weighted image after contrast enhancement.

Table 2 Wilkins and Odom's neurenteric cyst classification

Type	Histological features
A	Single-layer or pseudostratified cuboidal or columnar, ciliated or non-ciliated epithelium on a basement membrane
B	The same of type A + components of respiratory or gastrointestinal tract (mucous or serous glands, smooth muscle, elastic tissue, fat tissue, bone, lymphoid tissue, nerve ganglion)
C	The same of type B + ependymal or other glial elements

the cyst. The patient was discussed with neurologists and surgery was advocated.

DIFFERENTIAL DIAGNOSIS

Several other cystic lesions can have the same radiological features of supratentorial neurenteric cysts including arachnoid cyst, true neuroepithelial cyst, dermoid/epidermoid cyst, as well as cysts of parasitic origin. Tumours with large cystic components such as pleomorphic xanthoastrocytoma and metastatic neoplasms can also mimic a neurenteric cyst.

TREATMENT

Under general anaesthesia a frameless image guided left fronto-temporal craniotomy was performed revealing a cystic lesion, located immediately adjacent to the sylvian fissure. This area corresponded to an area between Brocas's area and the motor strip using fMRI. The location of the motor strip was also confirmed localising the central sulcus by the phase reversal of the median nerve cortical somatosensory evoked potentials. Full excision of the lesion was attempted. The solid part of the lesion was apparently totally removed. Neurohistopathology revealed a type C neurenteric cyst (table 2),¹ with a respiratory-like

pluristratified ciliated epithelium associated with ependymal elements (figure 2).

Moreover, a multi-nodular localised glial neoplasm with morphologic features reminding a subependymoma (Grade I WHO) was identified (figure 3).

OUTCOME AND FOLLOW-UP

The postoperative course was complicated by an epidural fluid collection, which required a surgical evacuation. The patient was discharged without neurological deficits. After 1 year the seizures recurred and progressively worsened. An MRI showed the recurrence of the neurenteric cyst (figure 4), which was removed via the previous fronto-temporal approach. Postoperative course was without complications and he was discharged day 9 postop/late. At 19 months follow-up, the patient is seizure free, with no evidence of recurrence on his latest MRI.

DISCUSSION

Neurenteric cyst is a rare developmental lesion that has been recognised for a long time. First described by Puusepp in 1934,² neurenteric cysts have been variably known as gastrocytoma, enterogeneous cyst, teratomatous cyst, endodermal cyst, enteric cyst, intestinoma, bronchogenic cyst, respiratory cyst, epithelial cyst, archenteric cyst, terathoid cyst and split notochord cyst.^{2–13} Nowadays the term neurenteric cyst is the most accepted.¹⁴ Usually found in the posterior abdomen, pelvis and mediastinum, neurenteric cysts occurring in the CNS (central nervous system) are infrequent and mostly located intraspinally as intradural extramedullary cyst, often associated with dysraphic syndromes and located ventrally to the spinal cord in the lower cervical and upper thoracic segments.¹⁵ The intracranial localisation of neurenteric cyst is extremely

rare. Intracranial neurenteric cysts typically arise from the posterior fossa, usually anterior to the brainstem.^{7 16} A review of the current literature showed 29 cases of

supratentorial intracranial neurenteric cysts including the case described in this report (table 3).

Aetiology

Infratentorial neurenteric cyst is thought to originate from an aberrant separation of the notochord during gastrulation, resulting in ectopic endoderm within the ectoderm layer. This theory may also explain the frequent association of infratentorial neurenteric cyst with spinal disraphisms.^{17 18} There are many hypotheses concerning the aetiology of supratentorial neurenteric cyst and all of them try to explain how an endodermal lesion can lie within the CNS. Graziani *et al* suggested that suprasellar neurenteric cysts, Rathke's cleft cysts and colloid cysts share a common origin from migrant

Figure 2 Histological section showing the pluristratified ciliated epithelium that lined the cyst (H&E, x400).

Figure 3 Clustered nuclei and fibrillary stroma reminding a subependymoma (H&E, x400).

Figure 4 MRI at time of recurrence: T1-weighted images after gadolinium administration. The cyst was slightly enlarged to 3×3.9×4 cm (width × rostro-caudal × anterior-posterior).

Table 3 Supratentorial neurenteric cysts: review

Pt	Year	Author	S	A	Location	Presentation	Treatment	Outcome
1	1961	List and Williams ²⁴	F	40	Interhemispheric fissure, extra-axial	Motor deficit, paresthesia, partial seizures	Craniotomy: incomplete excision Craniotomy: incomplete excision Fluid drainage	Good
2	1991	Campbell and Varma ²⁵	F	33	Right fronto-parietal, extra-axial	Focal seizures	Craniotomy: incomplete excision	Good
3	1992	Scaravilli <i>et al</i> ²⁶	M	36	Left optic nerve	Reduced visual acuity	Craniotomy: complete excision	Good
4	1994	Leventer <i>et al</i> ²⁷	F	23	Left orbital apex, superior orbital fissure	Visual loss, opthalmoplegia in left eye	1. Biopsy 2. Fluid drainage 3. Fluid drainage 4. Craniotomy: incomplete excision 5. Craniotomy: complete excision	Good
5	1996	Bavetta <i>et al</i> ²⁸	M	28	Right frontal, extra-axial	Generalised seizures	Craniotomy: complete excision	Excellent
6	1998	Ho <i>et al</i> ²⁹	F	45	Right parietal, extra-axial	Partial seizures, paresthesia	1. Craniotomy: complete excision 2. Cyst fenestration	Good
7	1999	Sampath <i>et al</i> ³⁰	M	27	Parasellar	Raised ICP, left-sided ptosis	Craniotomy: complete excision	Good
8	2000	Mishra <i>et al</i> ³¹	F	19	Septum pellucidum	Hydrocephalus	Craniotomy: complete excision	Excellent
9	2001	Morgan <i>et al</i> ¹	F	30	Oculomotor nerve	Opthalmoplegia	Craniotomy: biopsy, fluid drainage	Good
10	2002	Cheng <i>et al</i> ¹⁸	M	49	Right frontal, extra-axial	Memory deficits	Craniotomy: complete excision	Excellent
11	2004	Christov <i>et al</i> ³²	F	31	Right fronto-parietal	Raised ICP	1. Fluid drainage 2. Craniotomy: complete excision	Good
12	2004	Kachur <i>et al</i> ³³	F	35	Right frontal, intra-axial	Partial seizures, headache	Craniotomy: complete excision	Excellent
13	2004	Tan <i>et al</i> ³⁴	F	68	Left frontal, extra-axial	Hemiparesis, seizures	Craniotomy: complete excision	Excellent
14	2006	Neckrysh <i>et al</i> ³⁵	F	72	Frontal midline, extra-axial	Personality change, anosmia	Craniotomy: complete excision	Excellent
15	2006	Preece <i>et al</i> ¹⁶	F	72	Left frontal, intra-axial	Psychosis	Craniotomy	Unknown
16	2006	Preece <i>et al</i> ¹⁶	M	34	Left frontal, extra-axial	Seizures	Craniotomy	Unknown
17	2006	Preece <i>et al</i> ¹⁶	F	78	Right frontal, extra-axial	Seizures	Craniotomy	Unknown
18	2006	Preece <i>et al</i> ¹⁶	M	48	Left intra/periventricular	Tremor, right arm numbness, facial droop	Craniotomy	Unknown
19	2006	Preece <i>et al</i> ¹⁶	M	78	Frontal lobe, extra-axial	Seizures	Craniotomy	Unknown
20	2006	Stubenvoll ³⁶	M	25	Right frontal lobe, extra-axial	Generalised seizures	Craniotomy: cyst fenestration	Good
21	2007	Myagi and Katayama ³⁷	M	63	Right parietal, extra-axial	Headache, dizziness	Craniotomy: complete excision	Excellent
22	2008	Marchionni <i>et al</i> ³⁸	F	20	Left temporal, peri-insula and cerebello-pontine	Headache, hemiparesis, left deafness and blurred vision	Craniotomy: incomplete excision Craniotomy: complete excision	Good
23	2008	Takumi <i>et al</i> ³⁹	M	32	Left frontal convexity	Headache, status epilepticus	Craniotomy: complete excision	Excellent
24	2009	Dunham <i>et al</i> ⁴⁰	F	58	Right parietal	Headache, memory deficits	Craniotomy: complete excision	Excellent
25	2010	Basheer <i>et al</i> ³⁴	M	54	Right parieto-occipital, extra-axial	Raised ICP	Craniotomy: complete excision	Excellent
26	2010	Mittal <i>et al</i> ¹⁹	F	76	Right fronto-parietal, extra-axial	Partial seizures, motor deficit	Craniotomy: complete excision	Excellent
27	2010	Reddy <i>et al</i> ⁴¹	M	20	Left posterior and middle fossa across the tentorium	Raised ICP, reduced visual acuity	Craniotomy: incomplete excision	Good
28	2011	Little <i>et al</i> ⁴²	M	70	Frontal lobe, extra-axial	Gait disturbance	Craniotomy: complete excision	Excellent
29	2011	Natrella <i>et al</i> (present report)	M	45	Left frontal lobe, extra-axial	Generalised seizures	Stereotactic biopsy + fluid drainage Craniotomy: incomplete excision Craniotomy: complete excision	Good

A, age; ICP, intracranial pressure; Pt, patient; S, sex.

Outcome: excellent – no postoperative complications; no postoperative deficits. Good – slight postoperative complications or not permanent postoperative deficits.

remnants of Seessel's pocket, depending on the final location of the latter: Rathke's cleft cysts originate from intrasellar location, colloid cysts from intraventricular remnants, neurenteric cysts from presellar or retrosellar remnants.¹⁹ This hypothesis, however, cannot explain the fact that Rathke's cleft cysts seem to have the same ectodermal origin of pituitary adenomas and craniopharyngiomas^{20–22} and cannot account for paramedian and lateral supratentorial neurenteric cysts. Recently Mittal *et al* proposed an anomalous endodermal cell migration dorsally through the primitive neurenteric canal into ectoderm.¹⁸ These cells can then freely travel in both cephalad and more lateral localisation.¹⁸

Clinical presentation

Clinical signs seem to be dependent on cyst's localisation, being secondary to compression or irritation of

surrounding neural structures. Seizures are the most frequent clinical presentation of supratentorial neurenteric cysts. Epileptogenicity of brain cystic lesion is probably independent to the composition of cyst fluid, as stated by Weiser *et al*.²³ Nevertheless they did not analyse the amino acid composition of any neurenteric cyst. Unfortunately the amino acid composition of the neurenteric cyst of our patient was not analysed because of technical problems. Nevertheless, we think that neurenteric cyst may behave like a brain tumour, leading to seizures through a perilesional cortical inflammatory reaction, which causes a dysplastic reorganization of the adjacent cortical areas.^{24–25} Since in the case we report the lesion was much smaller than it was before surgery when seizures recurred, we also think that the fluid content of neurenteric cyst may play a role in epileptogenicity. The other main clinical features

included sensory and motor deficits and signs of raised intracranial pressure.

Neuroradiology

MRI is the ideal imaging technique. Neurenteric cyst has well-defined borders and no contrast enhancement, and its content is usually hypo-intense on T1-weighted and hyperintense on T2-weighted images.^{7 16 26} CT scan can detect calcification in the cyst wall and shows the neurenteric cyst as a low-density area with lack of contrast enhancement.²⁶

Histopathology

Neurenteric cysts have usually a thin wall and a fluid content, which can appear clear or creamy.¹⁴ Microscopically, they are often lined with a gastrointestinal-type epithelium (about 50% of the cases); less commonly with ciliated, respiratory epithelium (17%) and with mixed types (about 30%).^{14 18} A malignant transformation after total resection has been reported.²⁷ We report the first case of neurenteric cyst associated with a subependymoma.

Management

Surgery is the therapy of choice for neurenteric cyst. A conservative management should be advocated for slow growing lesions harboured in eloquent areas, that is, when surgery is somehow risky and symptoms can be pharmacologically controlled. The surgical removal of the supratentorial neurenteric cyst should be total, as the recurrence of the lesion seems to be strictly related to an incomplete resection. Indeed, the patients who had an incomplete resection had a poorer outcome than those who had a total removal of the cyst: all seven cases of incomplete resection had a good outcome versus 12 out of 16 cases of complete resection with an excellent outcome (75%). Six cases (17.4%) required a multi-stage surgery (two to five procedures). Since extensive craniospinal dissemination has been reported,²⁸ patients harbouring a neurenteric cyst should avoid shunt surgery.

Subependymoma

Subependymoma is a rare (0.2%–0.7% of intracranial tumours), benign tumour that arises most frequently in the fourth ventricle (50%–60%), lateral ventricles (30%–40%) and rarely in the spinal cord.^{29 30} An intraparenchymal location of subependymoma is extremely rare (five cases previously reported in the English literature – table 3).^{1 31 32} The clinical presentations of intraparenchymal subependymomas are summarised in table 3. This lesion usually appears well defined and lobulated on MRI, hypo- to hyperintense on T1 and T2-weighted imaging, with little to no contrast enhancement.³¹ There are several theories about the cell of origin of subependymomas: a precursor cell, which can differentiate into either ependymal cell or astrocyte; subependymal glia or a mixture of astrocytes and ependymal cells.³³ Others suggested that subependymomas could arise from a hamartomatous lesion or as a reaction to chronic ependymitis.³⁴ We postulate that in the case reported the subependymoma arose from the ependymal elements or from the subependymal glia included in the type C neurenteric cyst. Subependymomas have a benign course and a propensity for expansive and not infiltrative growth.

Complete surgical excision is usually curative. Two cases of aggressive subependymomas with local invasion and metastasis have been described.³⁴

Learning points

- ▶ A supratentorial neurenteric cyst in association with a subependymoma has never been reported before.
- ▶ The fluid content of the neurenteric cysts may play a role in the epileptogenicity of them.
- ▶ As the cyst we described is a type C neurenteric cyst we suggest that the subependymoma arose from the ependymal elements or from the subependymal glia included in the cyst.
- ▶ An incomplete removal of the lesion seems to predict a high risk of recurrence, so a complete resection is mandatory.

Competing interests None.

Patient consent Obtained.

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