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CLINICAL OVERVIEW

# Atypical cystic meningioma overexpressing AQP1 in early infancy: case report with literature review

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**Abstract**

Meningiomas in early infancy are rare lesions, worth to be reported for their exceptional occurrence. The authors report a case of an 11-month-old female child with asymmetric macrocephaly due to the presence of a cystic atypical meningioma associated to bilateral subdural collections.

**Conclusion: This unusual and unique case of atypical cystic meningioma in early infancy showed a high positivity to immunostaining of aquaporin 1, and this pattern could correlate with the coexistence both of cysts and subdural collections.**

## INTRODUCTION

Childhood and infancy meningiomas are quite rare lesions, representing 0.4–4% of all intracranial tumours in this age group (1). Absence of dural attachment and male predominance are typical of paediatric patients; the intraventricular location is higher than in adults, respectively, 15–22% versus 0.2–4% (2,3). These lesions are frequently associated with neurofibromatosis (23–41%) (4). Paediatric meningiomas under 12 months of age are rare and even rarer if we consider the cystic lesions and the atypical variant. We were able to find only 14 cases of cystic meningiomas under 12 months of age in the literature. Among these, only two cases are referred to be malignant and none is referred to be atypical. The case reported is peculiar for the age of the patient, the cystic aspect, the atypical variant at pathology examination and also for the association with asymmetric macrocephaly and bilateral subdural collections.

## CASE PRESENTATION

We report a case of an 11-month-old female child who was referred to our Centre with the diagnosis of plagiocephalia detected by the family paediatrician. The baby was born after full-term pregnancy without any complication.

Neurological examination revealed asymmetric macrocephaly without tension in the anterior fontanel, bilateral exophthalmos, without deficit in the ocular movements and without papilledema. The MRI revealed the presence of right frontal cysts contiguous to a solid frontal midline mass, adherent to the cerebral falx, with calcifications, inhomogeneous enhancement after gadolinium injection, necrosis and slight alterations in the cerebral blood flow at perfusion imaging (Fig. 1). The cysts were peritumoural, but their wall did not enhance and they were separated from the ventricular spaces. Bilateral subdural fluid collections were also present: the bigger, on the right side, was posteriorly and superiorly located; the left one, smaller, was visible only up to the vertex.

Neuroimaging was completed with MRI with multivoxel 1.5T $^{1}$H-MR spectroscopy, which showed low levels of Myoinositol and Creatinin, and slight increase of Cholin peak (Fig. 2).

The child underwent major surgery with a bifrontotemporal craniotomy. The lesion was extremely adherent to the surrounding brain tissue and hard in consistency, and sometimes also drilling was necessary. The complete removal of the lesion was achieved, but the bilateral subdural collections grew, probably due to the debridement of the thin arachnoid network forming intraparenchymal cyst, requiring a temporary external drainage (Fig. 3).

Pathology examination revealed the morphologic pattern of a meningothelial and transitional type meningioma. The tumour was adherent and infiltrating the surrounding parenchyma. Mitoses (5 mitoses for 10 HPF), necrosis and atypical cells with prominent nucleoli were present.

Immunohistochemical stains were performed on paraffin embedded tissue using antibodies antiepithelial membrane antigen EMA (clone E29, prediluted, Dako, Glostrup, Denmark), GFAP (clone 6F2, 1:1000, Dako), S100 protein (polyclonal, prediluted, Dako), Synaptophysin (clone SP11, 1:1000, NeoMarkers, Fremont, CA, USA), Neurofilaments (clone 2F11, 1:1000, Diagnostic Biosystems, Pleasanton, CA, USA), CD34 (clone QBend-10, 1:50, Dako), AQP1 (clone 1/22, 1:100, Abcam, Abcam PLC, Cambridge, UK) and AQP4 (polyclonal, 1:400, MW pH6, Santa Cruz Biotechnology, Santa Cruz, CA, USA). A polymer-based, sensitive detection system was used (Envision+, Dako). All immunostains were performed on an automated stainer (Autostainer, Lab Vision, Fremont, USA).

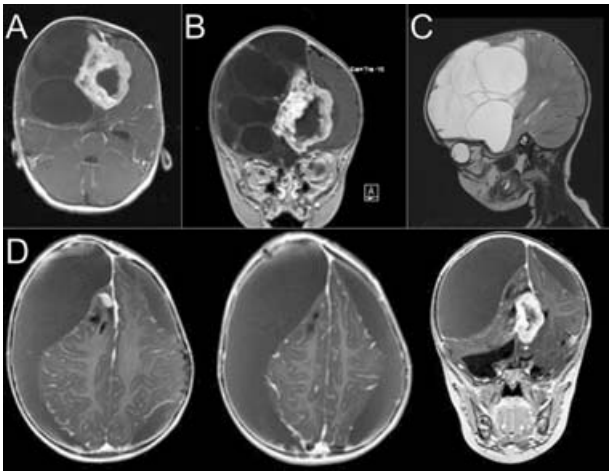


**Figure 1** Preoperative MRI images showing a frontal cystic enhancing lesion with associated subdural fluid collections. The right one is bigger and posterior–superior compared with the cysts. The left one, smaller, is present only towards the vertex. A = axial T1-weighted scan with gadolinium; B = coronal T1-weighted scan with gadolinium; C = sagittal T2-weighted scan; D = axial and coronal T1-weighted scans with gadolinium.

EMA was strongly positive in neoplastic cells, as in meningiomas. GFAP, S100 (astrocytic markers), Synaptophysin and Neurofilaments (neuronal markers) were negative in the neoplasia and positive in the infiltrated parenchyma. The CD34 (marker of endothelial cells) and AQP1 were positive in vessels (Fig. 4). The AQP4 was positive in the parenchyma surrounding the neoplasm (Fig. 5).

These findings supported the diagnosis of atypical meningioma (WHO, grade II) with superficial parenchymal invasion. The postoperative MRI showed the complete removal of the lesion with residual wide cerebrospinal fluid (CSF) collection in the right frontal region and bilateral hemispheric subdural collections. The postoperative course was uneventful. Neurofibromatosis was ruled out also in the family screening.

## DISCUSSION

Primary tumours of the meninges in childhood are rare lesions, accounting for 0.4–4.1% of published series of intracranial neoplasms (1). Male predominance and absence of dural attachment are typical of paediatric age, occurring

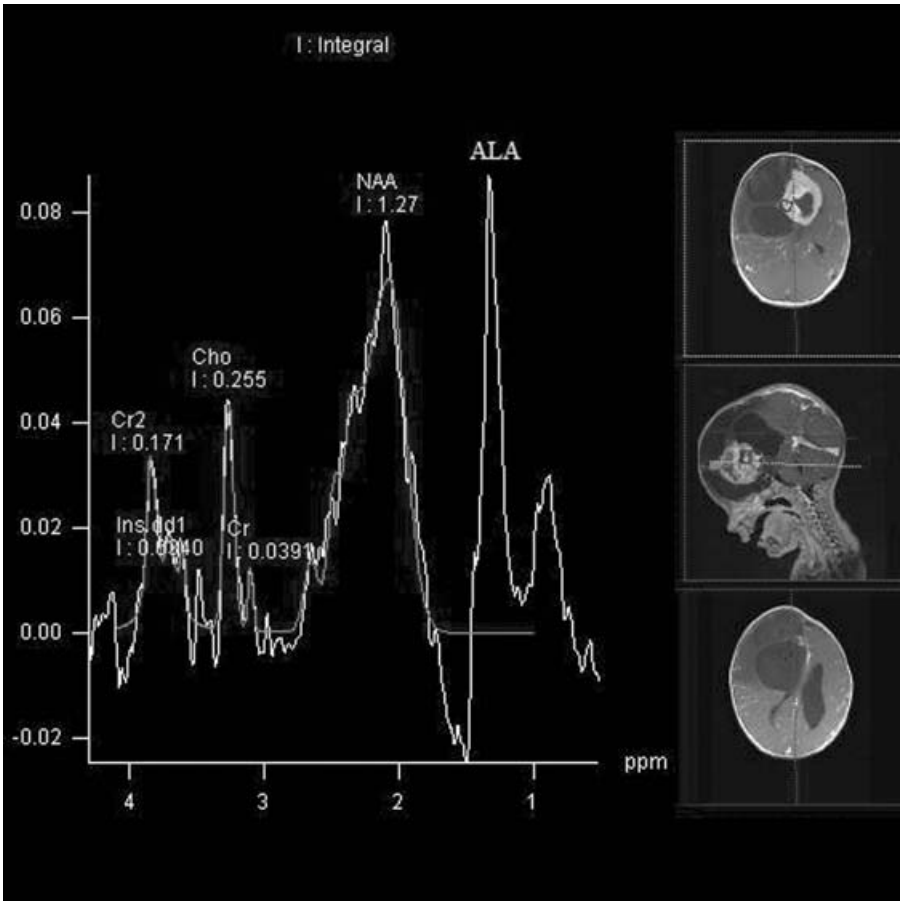


**Figure 2** MRI with multivoxel 1.5T $^{1}$H-MR spectroscopy, which shows low levels of Myoinositol and Creatinin, slight increasing of Cholin peak and the presence of a high Alanin peak, suggestive for extra-axial tumours.

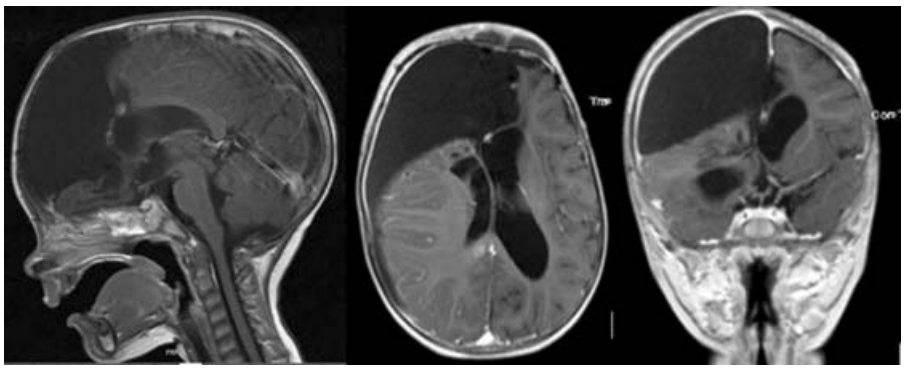

**Figure 3** Postoperative MRI with gadolinium: gross total removal of the lesion with residual right subdural collection.

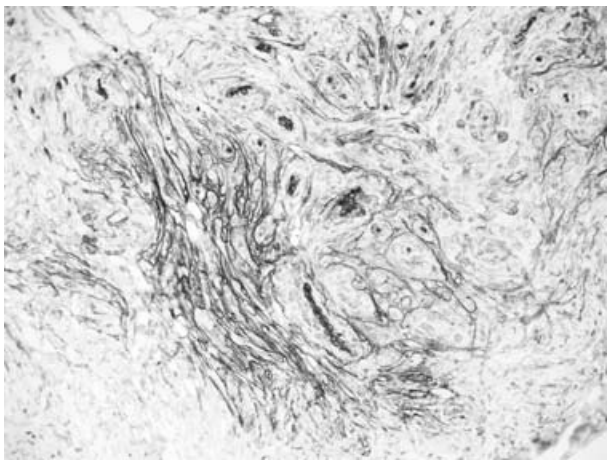

**Figure 4** Histopathology specimen (400×) after immunohistochemical stain for AQP1 is suggestive for a strong membranous immunostaining focally present in neoplastic cells of meningioma. Endothelium was positive too.

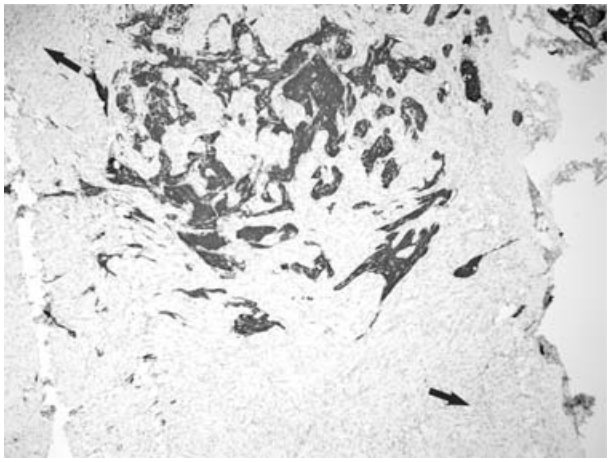

**Figure 5** Histopathology specimen (400×) after immunohistochemical stain for AQP4: the surrounding cerebral parenchyma showed immunoreactivity for AQP4. The neoplastic cells were negative (black arrows). Endothelium was positive.

**Table 1** Cystic meningiomas in patients aged less than 12 months

| Author | Months/sex | Pathology | Follow-up |
|---|---|---|---|
| 1. French, 1959 | | Sarcomatous | |
| 2. Taptas, 1961 | 4/M | Fibroblastic | 1 month |
| 3. Florin and Reid, 1961 | 2/M | Angioblastic | 2 months |
| 4. Mendiratta, 1967 | 4/M | Malignant | |
| 5. Suematsu, 1974 | 5/M | Fibroblastic | 2 years |
| 6. Satyanarayana, 1975 | 6/M | Fibroblastic | 12 days |
| 7. Endo, 1978 | | Fibroblastic | |
| 8. Numagachi, 1978 | 6/M | Fibroblastic | 2 years |
| 9. Dong, 1980 | 6/M | Fibroblastic | Dead 14 days after |
| 10. Amano, 1980 | 10/M | Fibroblastic | 2 months |
| 11. Katayama, 1985 | 5/M | Fibroblastic | 4 months |
| 12. Sakaki, 1987 | 8/M | Hemangiopericytic | 2 years |
| 13. Sharma, 1991 | 6/M | Fibroblastic | 10 days |
| 14. Molleston, 1994 | 6/M | Malignant | 4 years |
| 15. Present case, 2007 | 12/F | Atypical | 3 months |

in 27.7% of cases (5). The intraventricular and the intraparenchymal are both possible locations, being the intraparenchymal quite rare (5). Histological features of these tumours are similar to those in adults with a relatively low tendency for malignant behaviour; they have a low recurrence rate, and the outcome and survival rate are excellent. Almost 40% of meningiomas in children have associated neurofibromatosis.

In the literature we were able to find out only 15 cases of cystic meningiomas under 12 months of age, including our own case: among these, nine were fibroblastic meningiomas, two were malignant and the only atypical meningioma was the present case (Table 1; 6–19). Besides, all but our patient were male, and the follow-up, ranging from 10 days to 4 years, reports only one death.

Another aspect of concern is the differential diagnosis. The case described above presented all the radiological, clinical and morphological features of a desmoplastic infantile ganglioglioma (DIG) and was at the beginning misdiagnosed as DIG.

DIGs are rare intracranial supratentorial cystic tumours usually occurring in the first 2 years of life, characterized

 

by desmoplasia and different neuronal and astrocytic differentiation. So far, less than 60 well-documented cases are reported in the literature (20), also with atypical features, such as calcifications (20) or high Ki-67 proliferation index (21). DIGs are classified as benign WHO grade I tumours of infancy, generally associated with epilepsy and with good prognosis, with reports of recurrence-free intervals of up to 14 years (22).

In our case, the MRI with multivoxel 1.5T $^{1}$H-MR spectroscopy (CSI-MRI-30) was useful in the differential diagnosis with a cystic meningioma, for the presence of a high Alanin peak, suggestive for extra-axial tumours.

Considering the peculiarity of this patient, two aspects need to be analyzed: the growth of chronic bilateral subdural collections and the asymmetric macrocephaly. These two clinical findings should be considered to be an expression of the same unexplained phenomenon regarding the mechanism leading to fluid collections formation. According to Amano et al. (15), the congenital meningioma has the potential of producing interstitial fluid to form cysts, while for Pinna et al. (23), peritumoural cysts may be the final stage of peritumoural vasogenic oedema with fluid collections around the tumour. In the present case, we analyzed the presence of AQP1 in the meningioma specimens, as AQP1 is known to be expressed in blood vessels. The heavy expression of AQP1 in tumour vessels could be linked to the tendency to form cysts and to collect overproduced fluid in subdural collections, as in choroid plexus tumours (24). The AQP4 expression was not significantly expressed in neoplastic cells as well as AQP1. The AQP4 is reported to be linked with peritumoural oedema (25), but in this case the produced fluid was not interstitial and the lesion had no oedema. The described tumour presented an overexpression of AQP1 in blood vessels and an overproduction of fluid as some choroid plexus tumours do. The awareness that such an explanation is not suitable for all cystic and fluid collections-associated meningiomas should be taken into account, but it could be interesting to analyze aquaporins in other similar lesions trying to find a possible relationship between protein overexpression and oedema or peritumoural fluid collections (26–31).

Regarding the asymmetric macrocephaly, in the present case, cysts volume and growth pattern influenced cranial vault shape and volume. Macrocephaly is typical of intracranial lesions or conditions developing in the first year of life. In particular, Sharma and Newton showed in 1991 that 92% of infants with cystic meningiomas presented macrocephaly as the first sign (18). In our patient, the rapid increase of the frontal right cysts had probably influenced the head size and shape more locally, giving the aspect of the plagiocephalia.

## CONCLUSIONS

Meningiomas in early infancy are rare lesions, and cystic meningiomas are even rarer. The differential diagnosis with DIG is mandatory. Both lesions have a good prognosis, although the possibility of an atypical variant exists, as in our patient. This is the first reported case of cystic atypical meningioma under 12 months of age and the first with the analysis of AQP1.

## References


1. Tufan K, Dogulu F, Kurt G, Emmez H, Ceviker N, Baykaner MK. Intracranial meningiomas of childhood and adolescence. *Pediatr Neurosurg* 2005; 41: 1–7.
2. Marrero CL, Dominiguez J, Ramos R, Gomez J, Lurido JA. Intraventricular meningioma: case report in infancy. *Neurocirugia (Astur)* 2005; 16: 523–7 (Spanish).
3. Pau A, Dorcaratto A, Pisani R. Third ventricular meningiomas of infancy. A case report. *Pathologica* 1996; 88: 204–6.
4. Turgut M, Ozcan OE, Bertan V. Meningiomas in childhood and adolescence: a report of 13 cases and review of the literature. *Br J Neurosurg* 1997; 11: 501–7.
5. Kohama I, Sohma T, Nunomura K, Igarashi K, Ishikawa A. Intraparenchymal meningioma in an infant – case report. *Neurol Med Chir (Tokyo)* 1996; 36: 598–601.
6. French L. Tumors – intracranial and cranial. In: Lackson IJ, Thompson RK, editors. *Pediatric Neurosurgery*. Oxford: Blackwell Scientific, 1959: 290–4.
7. Taptas JN. Intracranial meningioma in a four-month-old infant simulating subdural ematoma. *J Neurosurg* 1961; 18: 120–1.
8. Florin RE, Reid ND. Congenital angioblastic meningioma: review of the literature and report of case. *Bull Los Angeles Neurol Sci* 1961; 26: 151–6.
9. Mendiratta SS, Rosenblum JA, Strobos RJ. Congenital meningioma. *Neurology* 1967; 17: 914–8.
10. Suematsu K, Tokuda S, Miyazaki Y: Intracranial meningiomas in a five-year-old infant: a case report and review of the literature. *Brain Nerve* 1974; 26: 453–64.
11. Satyanarayana K, Chandy SM, Rao TS, Chandy MJ, Abraham J. Congenital meningioma with subdural hygroma and poroencephaly: a case report. *Neurol India* 1975; 23: 57–8.
12. Endo S, Aihara H. Intracranial meningioma of the newborn: a case report. *No To Hattatsu* 1978; 10: 248–51.
13. Numaguchi Y, Hoffman JC, O' Brien MS, Fukui M, Matsuura K, Kitamura K. Meningiomas in childhood and adolescence. *Neurol Med Chir* 1978; 18: 119–27.
14. Dong H, Huang S, Huang C. Congenital meningioma. *Chin Med J* 1980; 93: 159–63.
15. Amano K, Miura N, Tajika Y, Matsumori K, Kubo O, Kobayashi N, et al. Cystic meningioma in a 10-month-old infant. *J Neurosurg* 1980; 52: 829–33.
16. Katayama Y, Tsubokawa T, Yoshida K. Cystic meningioma in infancy. *Surg Neurol* 1986; 25: 43–8.
17. Sakaki S, Nakagawa K, Rimura H, Ohue S. Intracranial meningiomas in infancy. *Surg Neurol* 1987; 28: 51–7.
18. Sharma V, Newton G. Cystic meningioma in infancy. *Yon Med J* 1991; 32: 370–3.
19. Molleston MC, Moran CJ, Roth KA, Rich KM. Infantile meningioma. *Pediatr Neurosurg* 1994; 21: 195–200.
20. Bhardwaj M, Sharma A, Pal HK. Desmoplastic infantile ganglioglioma with calcification. *Neuropathology* 2006; 26: 318–22.
21. Tantbirojin P, Sanpavat A, Bunyaratavej K, Desudchit T, Shuangshoti S. Desmoplastic infantile ganglioglioma with high proliferation index: report of a case. *J Med Assoc Thai* 2005; 88: 1962–5.
22. Tamburrini G, Colosimo C Jr, Giangaspero F, Riccardi R, Di Rocco C. Desmoplastic infentile ganglioglioma. *Childs Nerv Syst* 2003; 19: 292–7.
23. Pinna G, Beltramello A, Buffatti P, Signorini G, Colombari R, Bricolo A, et al. Cystic meningiomas – an update. *Surg Neurol* 1986; 26: 441–52.


 

24. Longatti P, Basaldella L, Orvieto E, Dei Tos A, Martinuzzi A. Aquaporins expression in choroid plexus tumours. *Pediatr Neurosurg* 2006; 42: 228–33.
25. Tan WL, Wong JH, Liew D, Ng IH. Aquaporin-4 is correlated with peri-tumoural edema in meningiomas. *Ann Acad Med Singapore* 2004; 33: S87–9.
26. Badaut J, Lasbennes F, Magistretti PJ, Regli L. Aquaporins in brain: distribution, physiology, and pathophysiology. *J Cereb Blood Flow Metab* 2002; 22: 367–78.
27. Dolman D, Drndarski S, Abbott NJ, Rattray M. Induction of aquaporin 1 but not aquaporin 4 messenger RNA in rat primary brain microvessel endothelial cells in culture. *J Neurochem* 2005; 93: 825–33.
28. Kobayashi H, Minami S, Itoh S, Shiraishi S, Yokoo H, Yanagita T, et al. Aquaporin subtypes in rat cerebral microvessels. *Neurosci Lett* 2001; 297: 163–6.
29. Kobayashi H, Yokoo H, Yanagita T, Satoh S, Kis B, Deli M, et al. Induction of aquaporin 1 by dexamethasone in lipid rafts in immortalized brain microvascular endothelial cells. *Brain Res* 2006; 1123: 12–9.
30. Saadoun S, Papadopoulos MC, Davies DC, Bell BA, Krishna S. Increased aquaporin 1 water channel expression in human brain tumours. *Br J Cancer* 2002; 87: 621–3.
31. Verkman AS. Aquaporin water channels and endothelial cell function. *J Anat* 2002; 200: 617–27.

 