Neuroradiology
DOI 10.1007/s00234-014-1356-9

PAEDIATRIC NEURORADIOLOGY

Magnetic resonance imaging of anterior temporal lobe cysts in children: discriminating special imaging features in a particular group of diseases

Renato Hoffmann Nunes · Felipe Torres Pacheco · Antonio Jose da Rocha

Received: 6 January 2014 / Accepted: 19 March 2014

Abstract
Introduction We hypothesised that disorders with anterior temporal lobe (ATL) cysts might exhibit common peculiarities and distinguishable imaging features that could be useful for diagnosis. We reviewed a series of patients for neuroimaging contributions to specific diagnoses.
Methods A literature search was conducted, and institutional imaging files were reviewed to identify MR examinations with ATL cysts in children. Patients were divided according to head size, calcifications, white matter and cortical abnormalities. Unsupervised hierarchical clustering of patients on the basis of their MR and CT items was performed.
Results We identified 23 patients in our database in whom MR revealed ATL cysts. Our series included five patients with congenital muscular dystrophy (05/23=21.7 %), six with megalencephalic leukoencephalopathy with subcortical cysts (06/23=26.1 %), three with non-megalencephalic leukoencephalopathy with subcortical cysts (03/23=13.1 %), seven with congenital cytomegalovirus disease (07/23=30.4 %) and two with Aicardi–Goutières syndrome (02/23=8.7 %). After analysis, 11 clusters resulted in the highest discriminative indices. Thereafter, patients' clusters were linked to their underlying diseases. The features that best discriminated between clusters included brainstem abnormalities, cerebral calcifications and some peculiar grey and white matter abnormalities. A flow chart was drafted to guide the radiologist in these diagnoses.
Conclusions The authors encourage the combined interpretation of these features in the herein proposed approach that confidently predicted the final diagnosis in this particular group of disorders associated with ATL cysts.

Keywords Cystic lesions · Infectious disease · Neuromuscular disease · White matter diseases · Neurodevelopmental disorders

Introduction

Intracranial cysts have been reported in many disorders [1], including several inherited and metabolic diseases [2–4]. Anterior temporal lobe (ATL) T2/fluid attenuated inversion recovery (FLAIR) hyperintensities have also been described as an additional and useful imaging feature for diagnosis in the appropriate clinical setting [5]. Recently, ATL cysts have also been reported as a characteristic presentation of dilated perivascular spaces in this particular location [6]. Moreover, ATL cysts are a distinguishable feature for specific MR-based approaches for the diagnosis of white matter (WM) disorders [7–9]. However, to the best of our knowledge, the contribution of this peculiar MR feature to aid in the differentiation between particular diagnoses has not been completely investigated in the current literature.

Our aim was to evaluate the most frequently reported diseases associated with ATL cysts. We hypothesise that these disorders might exhibit common peculiarities and distinguishable features that could be useful for diagnosis. We reviewed a series of patients to test MR contributions to specific diagnoses.

Electronic supplementary material The online version of this article (doi:10.1007/s00234-014-1356-9) contains supplementary material, which is available to authorized users.

R. H. Nunes · F. T. Pacheco · A. J. da Rocha
Division of Neuroradiology, Fleury Medicina e Saúde, São Paulo, Brazil

R. H. Nunes (✉) · F. T. Pacheco · A. J. da Rocha
Division of Neuroradiology, Santa Casa de Misericórdia de São Paulo Paulo, Serviço de Diagnóstico por Imagem, Rua Dr. Cesário Motta Junior 112, Vila Buarque, São Paulo 01221-020, Brazil
e-mail: renatohn@hotmail.com

Published online: 23 April 2014

Methods

Literature search

This research was conducted using the PubMed database to find the most common paediatric diseases related to ATL cysts. All types of publications and medical subsets were included, but the search was restricted to human studies written in English that were published before June 1st, 2013. The search keywords were limited to 'children' and 'imaging' to obtain a homogenous and more comparable list, and the results were crossed with the terms 'anterior temporal cysts' and 'temporal lobe cysts'. Additional textbooks were accessed to obtain complementary information [10–12].

Image acquisition and patient selection

Institutional imaging files were reviewed after the institutional review board approval to identify MR examinations with ATL cysts in children. The following MR scans were available to us and were included in the study: (1) from a paediatric patient (2) demonstrating ATL cysts (3) with a known cause for the disease. Extra-axial cysts, lesions with associated susceptibility artefacts, enhancement or restricted diffusion, such as cystic neoplasms, abscess, granulomas or hematomas, were excluded. Cysts with different signal intensities from the cerebrospinal fluid (CSF) were also excluded. Cystic encephalopathies not related to the typical appearance of ATL cysts, such as vanishing white matter disease, leukoencephalopathy with cysts and calcifications and progressive cavitating leukoencephalopathy, were not considered for this current purpose. Isolated ATL cysts not related to any disease or neurological syndrome, including glioependymal, neuroglial cysts and dilated perivascular spaces, were not considered. No other patients were excluded in this study.

We included data from multiplanar MR examinations obtained at 1.0 and 1.5 T, which covered the whole brain with appropriated field-of-view, 5-mm thick slices with an additional 0.5-mm gap and a minimum matrix of 224×512. Included examinations were required to include T1- and T2-weighted images and FLAIR sequences with appropriated parameters. CT scans in the axial plane were also evaluated to confirm the presence of calcifications. All MR and CT scans had been obtained for regular patient care without any influence from this study.

Imaging analysis

Three neuroradiologists blinded to the diagnoses and clinical data retrospectively reviewed all individual cross-sectional images in a consensus analysis.

Patients were later divided according to head size in clinical assessments and the presence of any abnormal imaging findings, such as calcifications, WM and cortical abnormalities. Microcephaly or macrocephaly was considered when the clinical examination measurements were at least two standard deviations below or above the mean for age and gender, respectively [13]. The medical records of all patients were also reviewed to define the final diagnosis based on current criteria proposed for all studied disorders.

Statistical analysis

Thereafter, unsupervised hierarchical clustering of the patients on the basis of their MR item profile, disregarding the head size, was performed to assess possible differences in MR abnormalities between disorders. We omitted fortuitous MR abnormalities that exhibited a low distinguishing value in our experience to reduce the number of variables for statistical analysis due to the relatively small numbers of patients. The dendrogram was built using the distance based on the chi-square test of equality for two sets of frequencies (measure for frequency count data) and average linkage between groups. The latter analysis resulted in compact, well-separated clusters. Two external validation measures (adjusted Rand index and normalised mutual information) were calculated for 1–23 (the largest number considered reasonable) clusters to determine the optimal number of clusters from the resulting dendrogram. The number of clusters that resulted in the highest indices was chosen to be optimal. The maximum pair-wise symmetrised Kullback–Leibler divergence was calculated per item to determine the items that discriminated best between the clusters. Items with the highest divergence are the most discriminative.

Results

Literature review

A list of 98 articles matched the search criteria of our literature review. After analysing the abstracts, 19 articles describing ATL cysts as part of the disease were selected [9, 14–31]. The other articles were excluded because they were not clearly related to the current issue, or ATL cysts were only a fortuitous finding.

Case series

In our database, we retrospectively identified 23 patients (13 female—13/23=53.5 %) ranging in age from 3 months to 14 years, with a mean postnatal age of 4.5 years and a median age of 4 years at the time of the first MR imaging in whom MR revealed ATL cysts (Fig. 1). Our series included five patients with congenital muscular dystrophy (CMD—05/23=21.7 %), six with megalencephalic leukoencephalopathy

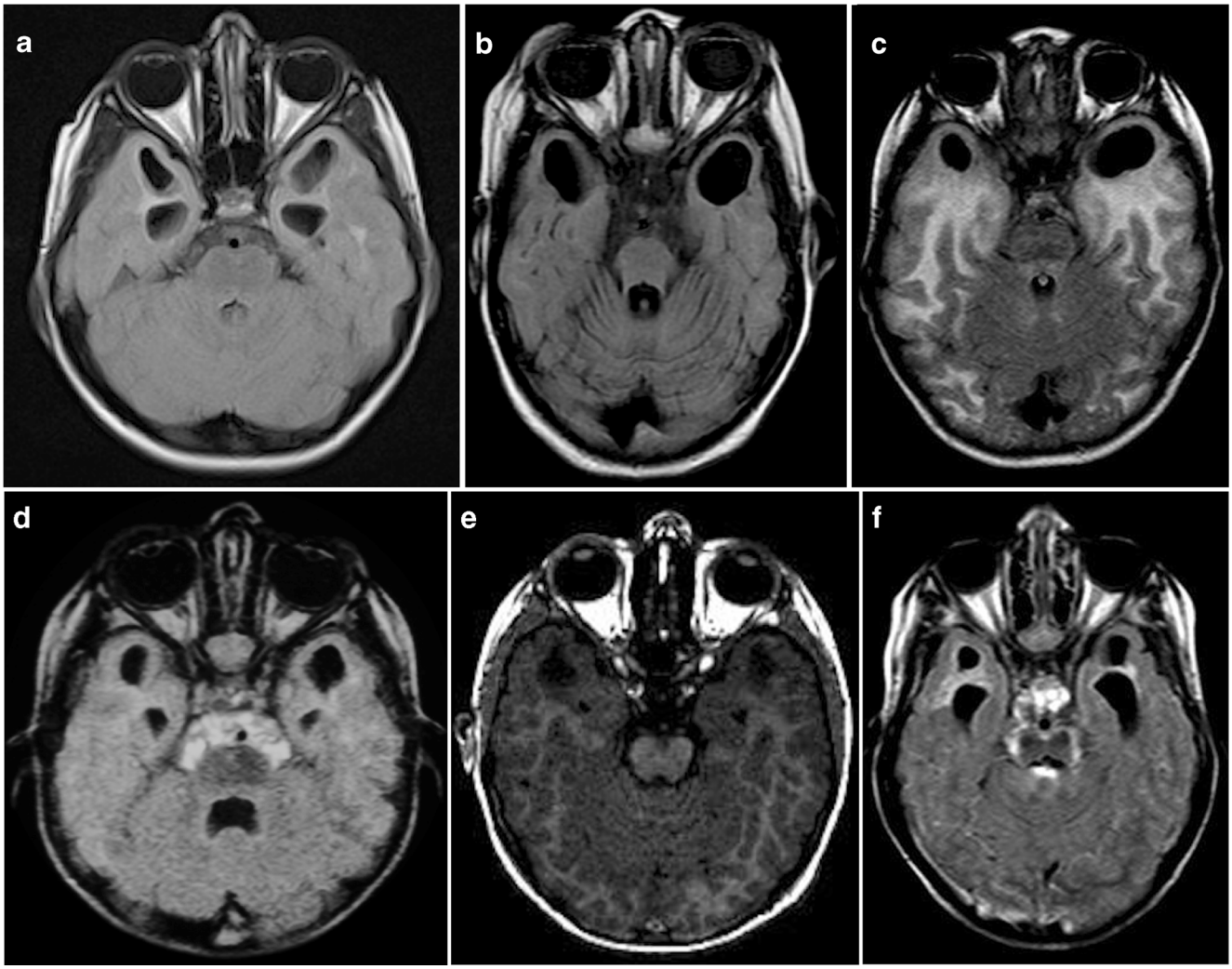

Fig. 1 MR images demonstrate patterns of ATL; **a** An 8-year-old boy with congenital CMV; axial FLAIR image. **b** A 7-year-old girl with AGS; axial FLAIR image. **c** A 2-year-old boy with MLSC; axial FLAIR image. **d** A 1-year-old boy with NMLSC; axial FLAIR image. **e** A 6-year-old boy with CMD; axial non-enhanced T1-weighted image. **f** A 4-year-old girl with CMD; axial FLAIR image

with subcortical cysts (MLSC—06/23=26.1 %), three with non-megalencephalic leukoencephalopathy with subcortical cysts (NMLSC—03/23=13.1 %), seven with congenital cytomegalovirus disease (congenital CMV disease—07/23=30.4 %) and two with Aicardi–Goutières syndrome (AGS—02/23=8.7 %). The clinical features and the location and distribution of additional imaging abnormalities are summarised in the supplementary online Table.

Head size

Macrocephaly was clinically confirmed in 10 of 23 (10/23=43.5 %) patients. Macrocephaly was diagnosed in four patients with CMD (04/05=80.0 %) and in all of the included MLSC patients (06/06=100.0 %). Conversely, microcephaly was documented in five of 23 patients (5/23=21.7 %), including three with congenital CMV disease (03/07=42.8 %) and two AGS patients (02/02=100.0 %). Normocephaly was present in the remaining patients (08/23=34.8 %).

Intraparenchymal calcifications

The presence of calcifications was analysed in the CT scans, which were performed in all included patients. Brain calcifications were observed in seven of 23 (07/23=30.4 %) patients in our series. All of these patients exhibited periventricular calcifications, whereas basal ganglia distribution was only observed in the AGS patients in our study cohort (02/02=100.0 %). The remaining subjects with brain calcifications were diagnosed with congenital CMV disease (05/07=71.4 %) (Fig. 2), including three normocephalic and two microcephalic individuals.

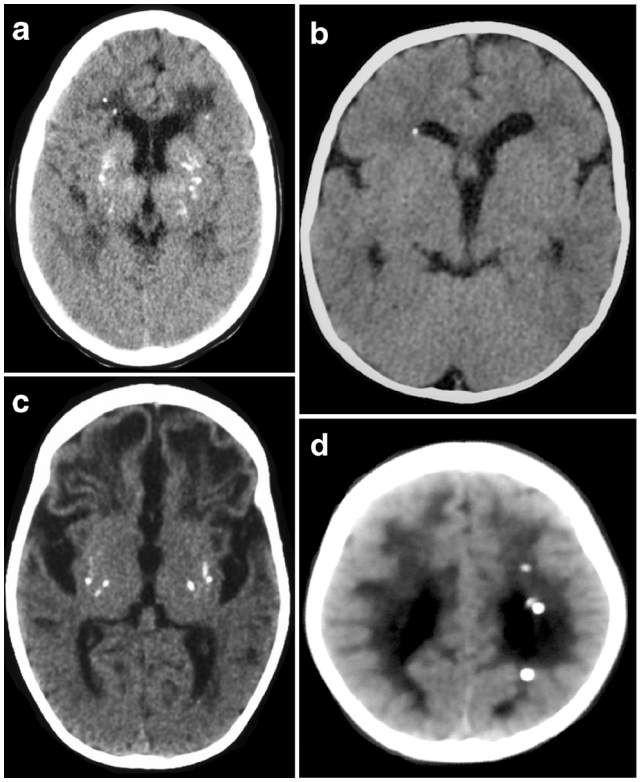

Fig. 2 Axial CT images demonstrate patterns of calcification. **a** A 7-year-old girl with AGS. Axial CT image shows periventricular and basal ganglia calcifications. **b** A 2-year-old girl with congenital CMV. Axial CT image reveals a periventricular calcification focus adjacent to the right frontal horn of the lateral ventricles. **c** An 18–month-old girl with AGS. Axial CT image demonstrates basal ganglia calcification. **d** A 4-year-old boy with congenital CMV. Axial CT image demonstrates periventricular calcification foci adjacent to the body of the left lateral ventricle

White matter abnormalities

All of the subjects included in our series exhibited a bilateral hypersignal on T2/FLAIR from the periventricular regions through the subcortical WM in the tip of the temporal lobes around the cystic formations. However, most of the patients exhibited a more extensive WM impairment, with the exception of two patients (02/23=8.7 %) who exhibited an isolated pattern of WM lesions. One of these two patients was diagnosed with CMD (01/05=20.0 %), and the other was diagnosed with congenital CMV disease (01/07=15.3 %). Furthermore, two CMD patients (02/05=40.0 %) and all of the six MLSC subjects (06/06=100.0 %) exhibited a more diffuse pattern characterised by a more intense and homogeneous extension of WM involvement. Another prevalent pattern identified was the extension of the abnormality in the subcortical temporal pole in which parietal deep WM distribution predominated. This pattern was observed in the three NMLSC patients (03/03=66.7 %) and four congenital CMV disease (04/07=57.1 %) subjects. Moreover, a predominantly frontal involvement was demonstrated in two CMD patients (02/05=40.0 %), one congenital CMV disease patient (01/07=15.3 %) and all AGS (02/02=100.0 %) patients, who were differentiated by an anteroposterior gradient. The remaining patients were characterised by more subtle patterns distinguished by temporal tip impairment and scattered foci in the periventricular and subcortical WM, specifically of the parietal lobes, and included one patient with NMLSC (01/03=33.3 %) and two patients with congenital CMV disease (02/07=30.6 %) (Fig. 3).

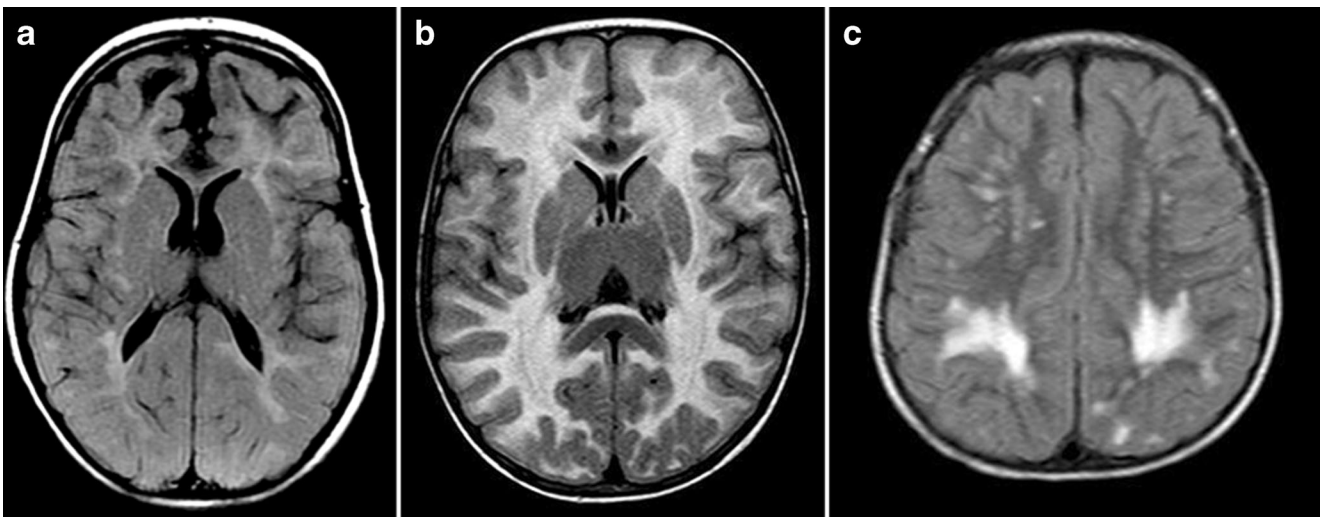

Fig. 3 MR images reveal patterns of white matter abnormalities. **a** A 7-year-old girl with AGS. Axial FLAIR image demonstrates hyperintensity in the periventricular and subcortical white matter with an anteroposterior gradient. There are also cystic formations in the frontal lobes. **b** A 2-year-old boy with MLSC. Axial FLAIR image demonstrates diffuse white matter hyperintensity. **c** A 3-year-old girl with congenital CMV. Axial FLAIR image demonstrates scattered foci in the periventricular and subcortical white matter, predominantly in the parietal lobes

Cortical abnormalities

Cortical malformations were also documented in eight of 23 (08/23=34.8 %) patients from our series, including all CMD patients (05/05=100.0 %). The most common finding in CMD patients was focal polymicrogyria/pachygyria, which was observed in four subjects (04/05=80.0 %). The remaining patient exhibited complete lissencephaly and periventricular nodular heterotopia (01/05=20.0 %). In addition, three subjects with congenital CMV disease (03/07=42.9 %), one of whom exhibited microcephaly, were diagnosed with focal polymicrogyria/pachygyria (Fig. 4).

Posterior fossa abnormalities

Posterior fossa abnormalities were a remarkable finding in CMD patients. All of these patients (05/05=100.0 %) exhibited brainstem and cerebellar abnormalities, which were not found in any other patients in our series (Fig. 5).

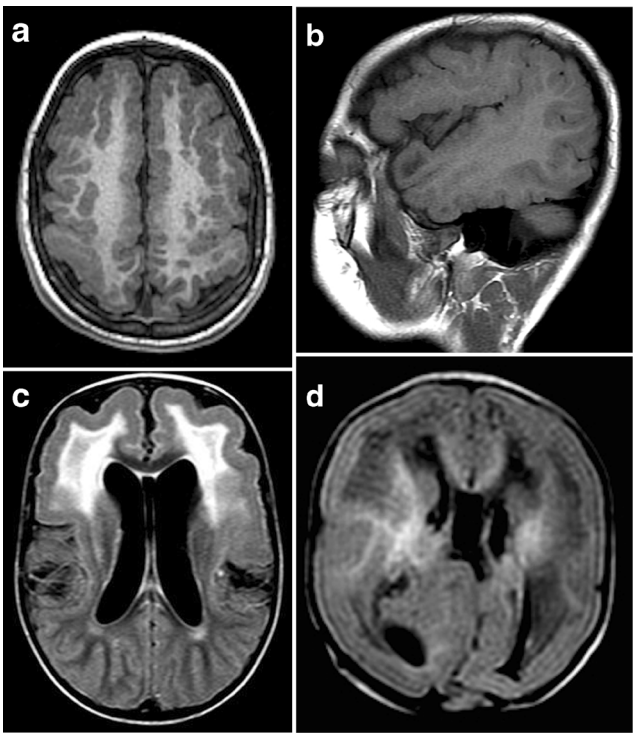

Fig. 4 MR images reveal patterns of cortical abnormalities. **a**–**b** A 7-year-old boy with congenital CMV. Axial and sagittal pre-gadolinium-enhanced T1-weighted images demonstrate frontal and perisylvian polymicrogyria. **c** A 4-year-old girl with MCD. An axial FLAIR image demonstrates frontal pachygyria and bilateral frontal white matter hyperintensity. **d** A 3-month-old boy with MCD (Walker–Warburg syndrome). Axial FLAIR images demonstrate lissencephaly and a diffuse white matter impairment

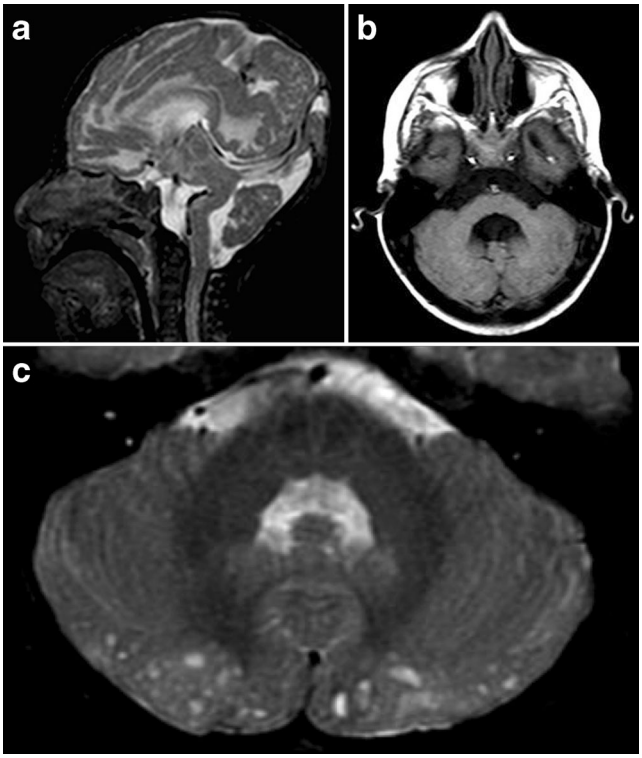

Fig. 5 MR images demonstrate patterns of infratentorial abnormalities. **a** A 6-month-old boy with MCD (Walker–Warburg Syndrome). Sagittal T2-weighted image demonstrates occipital encephalocele (after partial surgical correction) and hypoplastic brainstem, particularly in the pons. There was also posterior kinking, resulting in a broad inverted S-shaped brainstem. **b** A 4-year-old girl with CMD. Sagittal and axial pre-gadolinium-enhanced T1-weighted images reveal flattening of the ventral portion of the pons, enlargement of the midbrain tectum, subtle mid-pons kink and vermian hypoplasia. **c** A 6-year-old boy with MCD. Axial T2-weighted image demonstrates dysmorphic hemispheric cerebellar cortex with small cyst-like structures

Cluster analysis

In the cluster analysis, 11 clusters resulted in the highest discriminative indices (supplementary online figure). Thereafter, the patients in the clusters were linked to their underlying diseases. Clusters 1, 2, 3 and 4 comprised patients with CMD. Cluster 5 contained patients with MLSC, and cluster 11 contained patients with AGS. NMLSC and one CMV patient formed cluster 6. The remaining CMV patients were grouped in clusters 7, 8, 9 and 10.

Flow chart

The features that best discriminated between clusters for the final diagnosis were brainstem abnormalities, cerebral calcifications and some peculiar grey matter and WM abnormalities. A flow chart (Fig. 6) was drafted on the basis of these results to validate MR and CT scan imaging features and to reach the diagnoses of the diseases associated with ATL cysts.

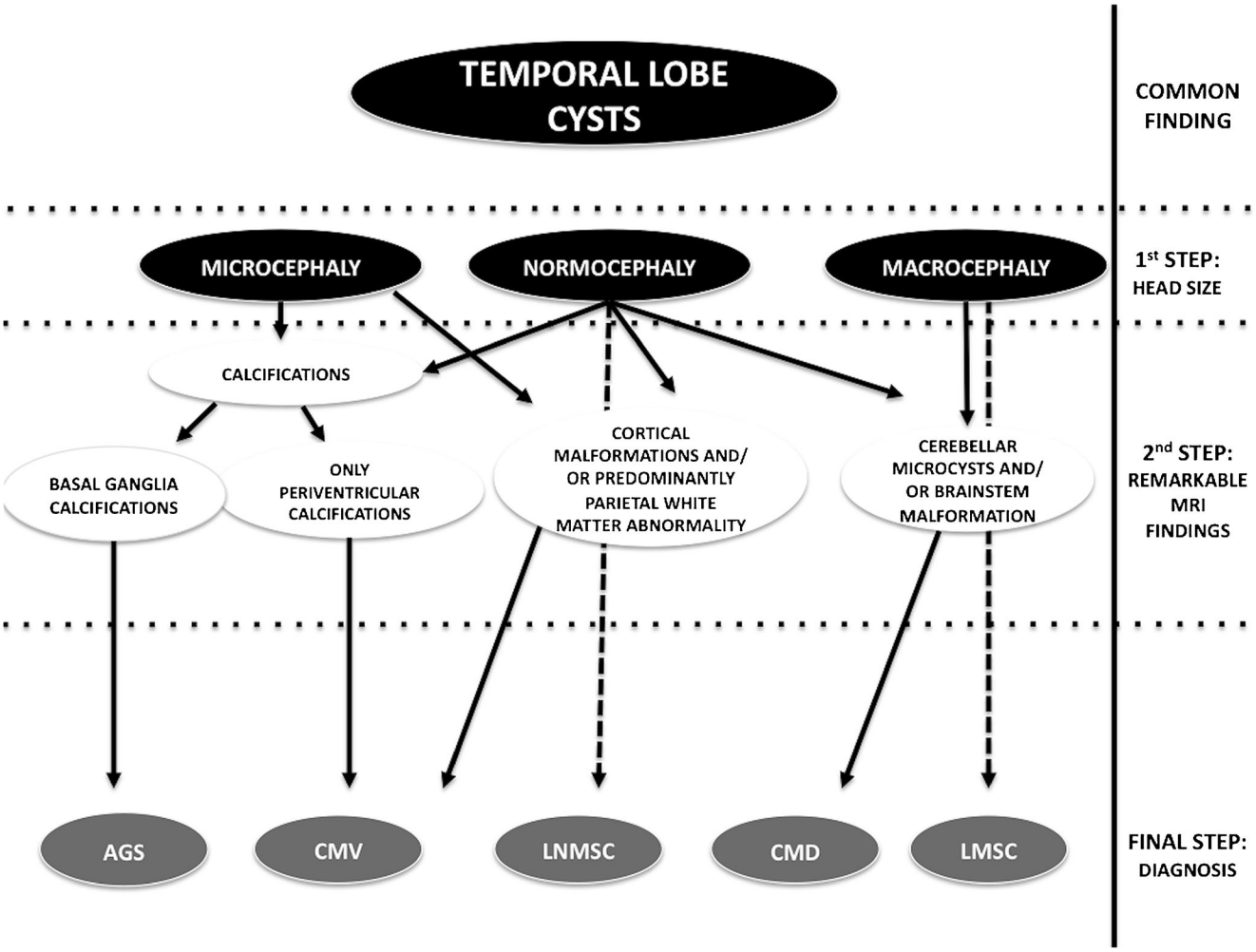

Fig. 6 A clinical and neuroimaging-based flow chart for evaluating patients with ATL

Discussion

The identification of several brain disorders has emerged from the union of metabolic characteristics with genetic research and imaging advances. Many typical patterns of diseases, including their structural and metabolic abnormalities, have been increasingly recognised in vivo after MR merging in clinical practice [10].

Special MR features have been reported as the key points for diagnostic imaging approaches [7]. Imaging interpretation is based on common peculiarities and distinguishable features that add to the correct diagnosis. Despite the great range of known MR patterns, which allows for the recognition of several paediatric diseases, we did not find any report that focused on ATL cysts and congenital diseases. This uncommon finding has been associated with a short list of brain disorders in the current literature [1, 29]. Our review included a representative number of cases of these rare disorders, which allowed us to propose this MR-based approach considering ATL cyst as a special imaging feature.

Brain circumference could be used in many different diagnostic settings, especially when parenchymal abnormalities are observed in early life. Previous reports have used head circumference size to discriminate brain disorders and affected patients [30]. Microcephaly has proven to be an important discriminating feature when used in conjunction with ATL cysts and restricting the diagnoses to only two possibilities, namely, congenital CMV disease and AGS [9, 32].

CMV is the most common viral infection among newborns, affecting approximately 0.5–2.4 % [26] and promoting cerebral and cerebellar cortex abnormalities, periventricular calcifications and lenticulostriate vasculopathy [33]. Aicardi and Goutières [34] first described a rare autosomal recessive disorder characterised by acquired microcephaly, chronic CNS lymphocytosis and elevated levels of CSF interferon-alpha, which result in severe neurological and cognitive impairment usually characterised as an early progressive encephalopathy with reduced amounts of brain WM [35, 36].

Our proposed approach emphasised another discriminating feature, independent of clinical background, characterised by

intraparenchymal calcifications that were only observed in congenital CMV disease and AGS. Congenital CMV infection calcifications occur in 34–70 % of patients, predominantly in periventricular regions, but they also occur as faint and punctate scattered foci within the basal ganglia and the brain parenchyma [8]. Brain calcifications in AGS patients predominate in the basal ganglia [34]. Our approach confirmed that the distribution of the calcifications may contribute to a correct diagnosis.

A variety of WM hyperintensities patterns on T2/FLAIR in microcephalic patients were another important discriminating MR feature [8, 9]. Similar to Van der Knaap et al. [9], we observed that all congenital CMV disease patients exhibited a pattern of random bilateral and multifocal involvement of the WM, predominantly the deep WM of the cerebral hemispheres, with the largest foci in the parietal lobe with a sparing of the subcortical and periventricular WM. Conversely, our AGS patients exhibited an anteroposterior gradient of WM involvement in agreement with a previous report [36], and this gradient tended to be symmetric and regular with more marked involvement of the tips of the frontal and temporal lobes. Large cavities or cyst-like formations in the WM have been rarely reported in AGS patients [32]. The relevance of this feature for a specific diagnosis remains uncertain and needs further analysis in a larger series of patients.

Macrocephaly was a remarkable feature that distinguished MLSC patients in our series. MLSC is a rare leukodystrophy characterised by an increased brain size, and it appears during the first year of life with a swelling of the cerebral WM and the presence of subcortical cysts, mainly in the ATL regions in patients with a little neurological impairment, including difficulty walking and epilepsy [37]. Diffuse WM involvement in the absence of a cortical abnormality was also documented in our series in agreement with previous literature [14, 38].

In addition to MLSC, macrocephaly was also found in 40 % (02/05) of the patients from our series with CMD [39]. Patients with CMD exhibit subcortical ATL cysts, and its pathogenesis is not fully understood [10, 39–41]. Macrocephaly is more prevalent in Walker–Warburg syndrome patients, which might be explained by the high frequency of hydrocephalus, with or without encephalocele [42, 43], as present in one of our patients as an occipital encephalocele. An additional CMD patient with macrocephaly in our series was diagnosed with muscle–eye–brain disease, which is consistent with a previous report [10].

MLSC and CMD generally exhibit distinguishable MR features. However, the observation of a dysmorphic cerebellar cortex, usually polymicrogyric, with small cyst-like structures and a particular pattern of brainstem morphological abnormality, was useful to confirm the CMD diagnosis in our series of patients with dystroglycanopathies and define the discriminating MR features when macrocephaly is associated with ATL cysts. Peripheral cerebellar abnormalities have been associated with dystroglycanopathies [44], whereas brainstem deformities are characterised by a constellation of variable findings, such as the flattening of the ventral portion of the pons, pontine midline cleft, enlargement of the midbrain tectum fusion of the colliculus, mid-pons kink and vermian hypoplasia [43, 45]. Our approach argues that different combinations of these infratentorial features define the specific diagnosis (dystroglycanopathies) among patients with ATL cysts.

Cortical abnormalities were observed in all patients with CMD dystroglycanopathies (05/05=100.0 %) and additionally in three of seven patients with congenital CMV disease (03/07=42.8 %). Congenital CMV disease exhibits abnormalities in the superficial grey matter characterised by the appearance of agyria/polymicrogyria [8, 46]. Cortical abnormalities in CMD patients result from lissencephaly type II (cobblestone complex), ranging from a complete lissencephaly to a more focal pachygyria or polymicrogyria and usually with frontal predominance [39]. The conditions usually exhibit some particularities despite the possible overlap in both entities due to their large spectrum of cortical appearances. In our series, these two entities could be distinguished by head size, the presence of calcifications or the abovementioned typical brainstem and cerebellar abnormalities.

Olivier et al. [15] described NMLSC as a new leukoencephalopathy with bilateral ATL cysts associated with a small or normal head circumference and usually associated with a normal or severe non-progressive delay in motor and speech development. As demonstrated in our series of patients, NMLSC exhibits no systemic involvement, and the head circumference is characteristically normal, although the circumference might decrease as the patient ages [21, 47, 48]. Recently, a deficiency in the gene product of RNASET-2 on chromosome 6 (6q26-q27) was reported in some NMLSC patients. This gene is also implicated in the pathogenesis of congenital CMV disease, which justifies the overlap among the constellation of neuroimaging abnormalities observed in both diseases [49]. Brain WM in NMLSC is predominantly affected around the ATL cystic formations and the parietal lobes, sparing the subcortical and periventricular WM, similar to congenital CMV disease. Differentiating NMLSC and CMV patients can be difficult [49], particularly in normocephalic deaf subjects. Although the presence of periventricular calcifications should a raise suspicion of a viral congenital infection, our approach suggested gyral abnormalities as the most important discriminating feature for congenital CMV disease diagnosis. Furthermore, this laboured differentiation should also consider postnatal negative serological tests and the potential family history of consanguinity, which would favour the diagnosis of an autosomal recessive pattern of inheritance of the NMLSC [9, 49].

The differential diagnoses of brain disorders with ATL cysts might be even larger in the setting of a child with a

neurological impairment than discussed here. We could not find any reports of these rare diseases associating leukoencephalopathy with ATL cysts, but rare pseudo-TORCH syndromes, such as congenital lymphocytic choriomeningitis virus syndrome and Baraister–Reardon syndrome, are reported as almost indistinguishable from CMV [50, 51]. Although head size is a simple distinguishing clinical feature, it might represent a potential limiting factor in the differential diagnosis if considered alone, particularly when advanced brain diseases, older subjects or hydrocephaly are evaluated. The proposed flow chart discriminated all of the individuals in this series of patients from a single institution, but the authors encourage further studies with larger samples of these rare diseases to validate the current approach.

Conclusion

ATL cysts are an uncommon brain MR finding in children that are not essential for diagnosis but represent an additional special feature that might help to distinguish a short list of disorders. Discriminating features for these disorders that are useful for specific diagnosis include head size, brain calcifications, cerebellar cysts, brainstem morphological abnormalities, WM signal intensity and superficial grey matter involvement on MR. The authors encourage the combined interpretation of these imaging features in the approach proposed herein, which confidently determined the final diagnosis in this particular group of disorders associated with ATL cysts.

Ethical standards and patient consent We declare that all human and animal studies have been approved by the Santa Casa de Sao Paulo Medical Ethical Committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. We declare that all patients gave informed consent prior to inclusion in this study.

Conflict of interest We declare that we have no conflict of interest.

References

1. Osborn AG, Preece MT (2006) Intracranial cysts: radiologic-pathologic correlation and imaging approach. Radiology 239(3): 650–664
2. Labrune P, Lacroix C, Goutieres F, de Laveaucoupet J, Chevalier P, Zerah M, Husson B, Landrieu P (1996) Extensive brain calcifications, leukodystrophy, and formation of parenchymal cysts: a new progressive disorder due to diffuse cerebral microangiopathy. Neurology 46(5):1297–1301
3. Naidu S, Bibat G, Lin D, Burger P, Barker P, Rosemberg S, Braverman N, Arroyo H, Dowling M, Hamosh A, Kimonis V, Blank C, Fiumara A, Facchini S, Singhal B, Moser H, Kelley R, DiMauro S (2005) Progressive cavitating leukoencephalopathy: a novel childhood disease. Annals Neurol 58(6):929–938. doi:10.1002/ana.20671
4. Biancheri R, Rossi D, Cassandrini D, Rossi A, Bruno C, Santorelli FM (2010) Cavitating leukoencephalopathy in a child carrying the mitochondrial A8344G mutation. AJNR Am J Neuroradiol 31(9): E78–E79. doi:10.3174/ajnr.A2182
5. Sureka J, Jakkani R (2012) Clinico-radiological spectrum of bilateral temporal lobe hyperintensity: a retrospective review. British J Radiol 85(1017):e782–e792. doi:10.1259/bjr/30039090
6. Rawal S, Croul SE, Willinsky RA, Tymianski M, Krings T (2013) Subcortical cystic lesions within the anterior superior temporal gyrus: a newly recognized characteristic location for dilated perivascular spaces. AJNR Am J Neuroradiol. doi:10.3174/ajnr.A3669
7. Schiffmann R, van der Knaap MS (2009) Invited article: an MRI-based approach to the diagnosis of white matter disorders. Neurology 72(8):750–759. doi:10.1212/01.wnl.0000343049.00540.c8
8. Fink KR, Thapa MM, Ishak GE, Pruthi S (2010) Neuroimaging of pediatric central nervous system cytomegalovirus infection. Radiographics Rev Publ Radiol Soc North Am Inc 30(7):1779–1796. doi:10.1148/rg.307105043
9. van der Knaap MS, Vermeulen G, Barkhof F, Hart AA, Loeber JG, Weel JF (2004) Pattern of white matter abnormalities at MR imaging: use of polymerase chain reaction testing of Guthrie cards to link pattern with congenital cytomegalovirus infection. Radiology 230(2):529–536
10. van der Knaap MS, Valk J, Barkhof F (2005) Magnetic resonance of myelination and myelin disorders, 3rd edn. Springer, Berlin ; New York
11. Raybaud C, Barkovich AJ et al (2011) Pediatric neuroimaging. Wolters Kluwer Health/Lippincott Williams & Wilkins, Philadelphia
12. Tortori-Donati P, Rossi A, Biancheri R (2005) Pediatric neuroradiology. Springer, Berlin ; New York
13. Roche AF, Mukherjee D, Guo SM, Moore WM (1987) Head circumference reference data: birth to 18 years. Pediatrics 79(5):706–712
14. van der Knaap MS, Barth PG, Stroink H, van Nieuwenhuizen O, Arts WF, Hoogenraad F, Valk J (1995) Leukoencephalopathy with swelling and a discrepantly mild clinical course in eight children. Annals Neurol 37(3):324–334. doi:10.1002/ana.410370308
15. Olivier M, Lenard HG, Aksu F, Gartner J (1998) A new leukoencephalopathy with bilateral anterior temporal lobe cysts. Neuropediatrics 29(5):225–228. doi:10.1055/s-2007-973566
16. Biancheri R, Pisaturo C, Perrone MV, Pessagno A, Rossi A, Veneselli E (2000) Presence of delayed myelination and macrocephaly in the sister of a patient with vacuolating leukoencephalopathy with subcortical cysts. Neuropediatrics 31(6):321–324. doi:10.1055/s-2000-12949
17. Gomes AL, Vieira JP, Saldanha J (2001) Non-progressive leukoencephalopathy with bilateral temporal cysts. Eur J Paediatr Neurol 5(3):121–125
18. Battini R, Bianchi MC, Tosetti M, Guzzetta A, Cioni G (2002) Leukoencephalopathy with bilateral anterior temporal lobe cysts: a further case of this new entity. J Child Neurol 17(10):773–776
19. Yalcinkaya C, Yuksel A, Comu S, Kilic G, Cokar O, Dervent A (2003) Epilepsy in vacuolating megalencephalic leukoencephalopathy with subcortical cysts. Seizure 12(6):388–396
20. Anlar B, Yalaz K, Saatci I (2003) Bilateral temporal cysts in a case of subacute sclerosing panencephalitis. Eur J Paediatr Neurol 7(2):81–84
21. Henneke M, Preuss N, Engelbrecht V, Aksu F, Bertini E, Bibat G, Brockmann K, Hubner C, Mayer M, Mejaski-Bosnjak V, Naidu S, Neumaier-Probst E, Rodriguez D, Weisz W, Kohlschutter A, Gartner J (2005) Cystic leukoencephalopathy without megalencephaly: a distinct disease entity in 15 children. Neurology 64(8):1411–1416
22. Grosso S, Cerase A, De Stefano N, Marco LD, Galluzzi P, Galimberti D, Morgese G, Balestri P (2005) Non-progressive

leukoencephalopathy with bilateral anterior temporal cysts: a case report and review of the literature. Brain Dev 27(1):73–77
23. Bodensteiner JB, Kerrigan JF, Johnsen SD (2006) Leukoencephalopathy with bilateral anterior temporal lobe cysts. J Child Neurol 21(5):419–422
24. O'Rourke D, Bradley L, King MD, Ryan S (2010) Leukoencephalopathy with anterior temporal cysts due to congenital CMV infection diagnosed retrospectively. J Neuroimaging 20(3): 292–293
25. Hoffmann C, Grossman R, Bokov I, Lipitz S, Biegon A (2010) Effect of cytomegalovirus infection on temporal lobe development in utero: quantitative MRI studies. Eur Neuropsychopharmacol 20(12):848–854
26. Manara R, Balao L, Baracchini C, Drigo P, D'Elia R, Ruga EM (2011) Brain magnetic resonance findings in symptomatic congenital cytomegalovirus infection. Pediatr Radiol 41(8):962–970. doi:10.1007/s00247-011-2120-5
27. Kamate M, Bhandankar M, Dhaded SM, Hattiholi V (2011) MRI abnormalities of the anterior temporal lobe: a new indicator of congenital cytomegalovirus infection. Indian Pediatr 48(4):325–328
28. Xie H, Wang J, Dhaunchak AS, Shang J, Kou L, Guo M, Wu Y, Gu Q, Colman D, Wu X, Jiang Y (2012) Functional studies of MLC1 mutations in Chinese patients with megalencephalic leukoencephalopathy with subcortical cysts. PLoS One 7((3): e33087. doi:10.1371/journal.pone.0033087
29. Sureka J, Jakkani RK (2012) Clinico-radiological spectrum of bilateral temporal lobe hyperintensity: a retrospective review. Br J Radiol 85(1017):e782–e792
30. Renaud DL (2012) Leukoencephalopathies associated with macrocephaly. Semin Neurol 32(1):34–41. doi:10.1055/s-0032-1306384
31. Koyama S, Kawanami T, Arawaka S, Wada M, Kato T (2012) A Japanese adult case of megalencephalic leukoencephalopathy with subcortical cysts with a good long-term prognosis. Intern Med 51(5): 503–506
32. Uggetti C, La Piana R, Orcesi S, Egitto MG, Crow YJ, Fazzi E (2009) Aicardi–Goutieres syndrome: neuroradiologic findings and follow-up. AJNR Am J Neuroradiol 30(10):1971–1976
33. Barkovich A (2005) Infection of the nervous system. In: AJ B (ed) Pediatric neuroimaging. Lippincott Williams & Wilkins, Philadelphia, pp 801–868
34. Aicardi J, Goutieres F (1984) A progressive familial encephalopathy in infancy with calcifications of the basal ganglia and chronic cerebrospinal fluid lymphocytosis. Ann Neurol 15(1):49–54. doi:10.1002/ana.410150109
35. Aicardi J (2002) Aicardi–Goutieres syndrome: special type early-onset encephalopathy. Eur J Paediatr Neurol 6(Suppl A):A1–A7, discussion A23-25, A77-86
36. Lanzi G, Fazzi E, D'Arrigo S (2002) Aicardi–Goutieres syndrome: a description of 21 new cases and a comparison with the literature. Eur J Paediatr Neurol 6(Suppl A):A9–A22
37. Lopez-Hernandez T, Sirisi S, Capdevila-Nortes X, Montolio M, Fernandez-Duenas V, Scheper GC, van der Knaap MS, Casquero P, Ciruela F, Ferrer I, Nunes V, Estevez R (2011) Molecular mechanisms of MLC1 and GLIALCAM mutations in megalencephalic leukoencephalopathy with subcortical cysts. Hum Mol Genet 20(16):3266–3277
38. Batla A, Pandey S, Nehru R (2011) Megalencephalic leukoencephalopathy with subcortical cysts: a report of four cases. J Pediatr Neurosci 6(1):74–77
39. Bertini EE, D'Amico AA, Gualandi FF, Petrini SS (2011) Congenital muscular dystrophies: a brief review. Semin Pediatr Neurol 18(4):12–12. doi:10.1016/j.spen.2011.10.010
40. van Engelen BG, Leyten QH, Bernsen PL, Gabreels FJ, Barkhof F, Joosten EM, Hamel BC, ter Laak HJ, Ruijs MB, Cruysberg JR et al (1992) Familial adult-onset muscular dystrophy with leukoencephalopathy. Ann Neurol 32(4):577–580. doi:10.1002/ana.410320415
41. Leite CC, Lucato LT, Martin MG, Ferreira LG, Resende MB, Carvalho MS, Marie SK, Jinkins JR, Reed UC (2005) Merosin-deficient congenital muscular dystrophy (CMD): a study of 25 Brazilian patients using MRI. Pediatr Radiol 35(6):572–579. doi:10.1007/s00247-004-1398-y
42. Barkovich AJ (1998) Neuroimaging manifestations and classification of congenital muscular dystrophies. AJNR Am J Neuroradiol 19(8): 1389–1396
43. van der Knaap MS, Smit L, Barth PG, Catsman-Berrevoets CE, Brouwer OF, Begeer JH, De Coo I, Valk J (1997) Magnetic resonance imaging in classification of congenital muscular dystrophies with brain abnormalities. Annals of neurology 42(1):50–59
44. Barkovich AJ (2012) Developmental disorders of the midbrain and hindbrain. Front Neuroanat 6:7. doi:10.3389/fnana.2012.00007
45. Aida N, Tamagawa K, Takada K, Yagishita A, Kobayashi N, Chikumaru K, Iwamoto H (1996) Brain MR in Fukuyama congenital muscular dystrophy. AJNR Am J Neuroradiol 17(4):605–613
46. Lo CP, Chen CY (2008) Neuroimaging of viral infections in infants and young children. Neuroimaging Clin N Am 18(1):119–132
47. Faria EC, Arita JH, Peruchi MM, Lin J, Masruha MR, Vilanova LC (2008) Cystic leukoencephalopathy without megalencephaly. Arq Neuropsiquiatr 66(2A):261–263
48. Henneke M, Preuss N, Engelbrecht V, Aksu F, Bertini E, Bibat G, Brockmann K, Hübner C, Mayer M, Mejaski-Bosnjak V (2005) Cystic leukoencephalopathy without megalencephaly: a distinct disease entity in 15 children. Am Acad Neurol 64(8):1411–1416
49. Henneke M, Diekmann S, Ohlenbusch A, Kaiser J, Engelbrecht V, Kohlschütter A, Krätzner R, Madruga-Garrido M, Mayer M, Opitz L, Rodriguez D, Rüschendorf F, Schumacher J, Thiele H, Thoms S, Steinfeld R, Nürnberg P, Gärtner J (2009) RNASET2-deficient cystic leukoencephalopathy resembles congenital cytomegalovirus brain infection. Nat Genet 41(7):773–775. doi:10.1038/ng.398
50. Wright R, Johnson D, Neumann M, Ksiazek TG, Rollin P, Keech RV, Bonthius DJ, Hitchon P, Grose CF, Bell WE, Bale JF Jr (1997) Congenital lymphocytic choriomeningitis virus syndrome: a disease that mimics congenital toxoplasmosis or cytomegalovirus infection. Pediatrics 100(1):E9
51. Vivarelli R, Grosso S, Cioni M, Galluzzi P, Monti L, Morgese G, Balestri P (2001) Pseudo-TORCH syndrome or Baraitser–Reardon syndrome: diagnostic criteria. Brain Dev 23(1):18–23