Long-Term Outcome of Children with Acute Cerebellitis

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Abstract

Background Acute cerebellitis (AC) is characterized by cerebellar symptoms and magnetic resonance imaging (MRI) changes primarily confined to the cerebellum.

Objective To analyze the neurological and cognitive long-term outcome of children with AC.

Methods Children with AC diagnosed by typical clinical features and MRI findings were included in this retrospective study. Medical charts were reviewed and neurological deficits were assessed by neurological examination or by the expanded disability status scale telephone interview. Cognitive outcome was evaluated with a parental questionnaire (Kognitive Probleme bei Kindern und Jugendlichen).

Results A total of 11 children (6 boys, 5 girls; age range: 3 years to 14 years and 10 months) were included. Of them, six children had a severe disease manifestation including mental status changes and neurological symptoms. Of the rest, two children had a moderate and three children had a mild form of AC. MRI of the cerebellum was obtained in the acute phase revealing signal alterations with different patterns. The average follow-up period was 4 years and 4 months. A complete recovery was observed

Keywords
- children
- acute cerebellitis
- long-term outcome
- MRI

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in five children. Neurological sequelae were reported in five children ranging from ataxia to mild tremor. Cognitive deficits were found in six patients. The affected areas of cognition did include spatial visualization ability, language skills, and concentration.
Conclusion Neurological and cognitive sequelae are common in children with AC and underline the role of the cerebellum in cognition.

Introduction

Acute cerebellitis (AC) constitutes one of the important causes of acute cerebellar dysfunction in childhood.[1] It is considered to be an inflammatory syndrome often caused by direct infection or postinfectious autoimmune mechanisms.[2,3] Frequently identified organisms are Varicella-zoster virus (VZV), Epstein-Barr virus (EBV), pertussis, diphtheria, and coxsackie virus.[1]

In the initial phase of AC, often generalized symptoms such as headache, nausea, and altered mental status are present, followed often, but not always, by cerebellar signs, such as ataxia, nystagmus, or dysmetria.[4] The diagnosis of AC requires visible changes in the cerebellum with the modality of choice magnetic resonance imaging (MRI), usually demonstrating altered signal intensity and abnormal diffusion-weighted imaging of the cerebellum and surrounding areas.[5–7] Cerebellar swelling is present in selected cases and can lead to life-threatening complications.[8,9] Symptoms such as mental status changes and MRI abnormalities of the cerebellum sets AC apart from the disease entity termed "acute cerebellar ataxia (ACA)." ACA is also frequently seen in conjunction with a viral infection and, in particular, VZV, but it is not associated in general with mental status changes or signal alterations.[7,10] The diagnosis of ACA is made on clinical grounds and its prognosis is regarded as excellent. In view of the good prognosis, MRI studies are not performed possibly leading to the fact that MRI changes in ACA are underreported. Because of similarities in the clinical presentation and the association with VZV, ACA and AC encompassing mild and severe forms are regarded by some authors as a continuum with similar disease mechanisms.

There is no accepted consensus regarding the treatment of AC ranging from symptomatic medical care in mild cases to surgical intervention with posterior fossa decompression in fulminant cases.[11–13] Often children with moderate and severe AC are treated with immunmodulatory drugs, such as steroids in addition to standard antimicrobial therapies. Surgical intervention with decompression of the posterior fossa is only performed in life-threatening cases and associated with a poor outcome.[2] AC is generally thought to be associated with a complete recovery in most cases,[2,9] although reports are also on record of AC being associated with severe course of the disease including death and neurological handicap.[2]

Here, we describe the neurological and cognitive long-term outcome of 11 children with AC with a special focus on the initial clinical presentation and long-term sequelae.

Patients and Methods

Patients

Eleven children with AC from eight different hospitals in Germany and Austria were included in this retrospective study, all fulfilling the following criteria: acute onset of symptoms such as mental status changes and/or cerebellar symptoms (e.g., ataxia) combined with magnetic resonance signal changes primarily confined to the cerebellum and no previously reported neurological or cognitive impairment. Children with additional minor MRI changes affecting extracerebellar structures that were thought not to be responsible for the main clinical manifestation of the disease were included in the study ($n = 3$).

Methods

Pediatric neurologists from different pediatric hospitals in Germany and Austria were asked if they had treated children with AC in the past, fulfilling the criteria as earlier described. After a 6-month period of recruitment, 14 children were identified. Three patients were subsequently excluded because two had an initially normal scan in the acute phase and one patient had a preexisting mental retardation. Medical records of each child were reviewed systematically including the neuropsychological test results of four children. In each case, the following data were collected: sex, age, symptoms at disease manifestations, length of hospital stay, symptoms at discharge, and information about treatment. Symptoms at disease manifestation were divided into generalized symptoms, such as, fever, emesis, nausea or vertigo, and neurological symptoms, such as, ataxia or dysarthria. All children had serological and immunological (e.g., white blood cells, C-reactive protein [CRP], erythrocyte sedimentation rate, antinuclear antibodies) and cerebrospinal fluid (CSF) (cell count, oligoclonal band testing by isoelectric focusing, lactate, protein, viral studies [e.g., herpes simplex virus: HSV]) work-up at initial manifestation. Most children also had a metabolic screen including creatine kinase, liver/thyroid function tests, serum lactate, amino acids, and urine organic acids.

All initial and follow-up MRI studies were reviewed. The following sequences were available in all MRI studies: T_1-weighted ± contrast-medium, T_2-weighted and fluid-attenuated inversion recovery axial and coronal, diffusion-weighted images, and apparent diffusion coefficient (ADC) maps.

According to their initial symptoms, the severity of AC was divided into three categories. A child with one neurological symptom only (e.g., intention tremor, ataxia) and not more than two generalized symptoms (e.g., fever, nausea) was grouped as mild or category 1. A child with one neurological

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symptom and at least three generalized symptoms or, alternatively, two or more neurological symptoms was classified as moderate or category 2. A child with seizures, need for intubation or mental status changes, such as irritability, apathy, somnolence or mutism in addition to neurological symptoms was described as severe or category 3.

Neurological outcome at follow-up was evaluated with a standardized telephone-based interview assessing the expanded disability status scale (EDSS) score.[14,15]

Cognitive outcome was assessed by a standardized parental questionnaire "Kognitive Probleme bei Kindern und Jugendlichen" (KOPKIJ).[8]

The study was approved by the Ethics Committee of the Medical Faculty of the University of Innsbruck, Austria. Families and adult patients had to give written consent before the telephone interview.

Statistics

The correlation between the age of onset, the severity of AC in the acute phase, days in hospital, MRI findings such as unilateral or bilateral cerebellar involvement, and the neurological and cognitive outcome, respectively, were evaluated by generally accepted statistical methods (Analysis of Variance [ANOVA], the Spearman rank correlation test, Kruskal–Wallis test).

Results

Clinical Data

A total of 11 children (6 boys and 5 girls) were included in the study. At the time of disease onset, patients were aged between 13 months and 14 years and 10 months (median 6.7 years) (►**Table 1**). Eight of 11 patients had a preceeding illness (►**Table 1**).

Symptoms in the acute phase ranged from generalized to characteristic cerebellar symptoms of AC. Meningism with neck stiffness appeared in three patients. Two patients had seizures associated with fever classified as tonic-clonic convulsions. In two children, frontal headaches were the main complaint associated with bilateral papilledema on eye examination.

Six children had changes in mental status including irritability, apathy, somnolence, or mutism (patient 7).

Cerebellar symptoms at the initial presentation were reported in nine children. In eight children truncal and/or gait ataxia were the main presenting symptom. Five children had a bilateral intention tremor. Further cerebellar symptoms were nystagmus ($n = 2$), dysarthria ($n = 3$), or problems with swallowing ($n = 1$).

Main Laboratory Findings in the Acute Phase of Acute Cerebellitis

Four patients had a raised serum CRP level ranging from 2.1 to 27.3 mg/dL (< 1.0 mg/dL). An increased number of leukocytes in the white blood cell count was seen in only one patient. All children had an extensive serological work-up (e.g., VZV, EBV, HSV, enteroviruses, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*). Only in four children, serological studies revealed a recent infection with adenovirus ($n = 1$), VZV ($n = 1$), rotavirus/enterovirus ($n = 1$), and *Borrelia burgdorferi* ($n = 1$) associated with an intrathecal synthesis of IgG antibodies against *B. burgdorferi* in the CSF. Most patients had raised CSF cell count, ranging from 5 to 108 cells/µL. Three patients had an increased amount of protein ranging from 55 to 85 mg/dL and lactate levels were only mildly raised in two CSF samples (2.6 and 2.8 mmol/L). CSF glucose was normal in all patients.

Magnetic Resonance Imaging Findings in the Acute Phase

MRI of the cerebellum was performed in the acute phase revealing signal alterations with different patterns in all children (►**Table 2**). The pattern most often present was bilateral involvement of the cerebellum ($n = 6$). Three children had involvement of cerebellar white matter and cortex ($n = 3$), and the remaining three patients hat lesions confined to the cerebellar cortex ($n = 3$), one of them with additional meningeal involvement. One cerebellar hemisphere was affected in five children. Four of five patients had unilateral involvement of cerebellar white matter and cortex, and in one of five patients, solely the white matter was affected (►**Figs. 1**, **2**, **3**). In one child with signal alterations in a single hemisphere (right), contrast enhancement was found along the cortex of the same hemisphere.

Additional involvement of the brainstem ($n = 2$), left locus caeruleus ($n = 1$), and right superior cerebellar peduncule ($n = 1$) was noted in three patients.

The evidence of cerebellar edema including downward displacement of cerebellar tonsils ($n = 2$; patient 4 and 11), narrowing of the fourth ventricle or disappearance of CSF spaces surrounding the cerebellar cortex was found in nine patients (patients 1, 2, 4, and 6 to 11). In five children, diffusion-weighted imaging and ADC maps revealed a cytotoxic edema. In four children with AC, vasogenic edema in the acute MRI was noted.

Magnetic resonance angiography performed in four patients was without any detectable abnormalities.

In seven children, computed tomography (CT) scan of the brain was performed. In only two children, abnormalities such as cerebellar swelling were observed initially (patients 2 and 6). In the other five (patients 1, 4, 5, 7 and 9) children, the CT was reported as normal despite significant abnormalities in the subsequently performed MRI.

Treatment

Information about treatment was available from 10 of 11 patients. In most cases, a therapy with antibiotics and/or acyclovir was administered. A combination of both medications was given in seven patients (patients 2 to 4 and 6 to 8). Three patients had antibiotic therapy only (patients 1, 5, and 9), and one patient received acyclovir only (patient 11). Worsening of symptoms of AC despite treatment with antibiotics and/or acyclovir was noticed in two patients (patients 5 and 7). Treatment with steroids (dexamethasone [$n = 2$] and prednisolone [$n = 1$]) was applied in three patients (patients 6, 8, and 11) and led to a distinct improvement of the clinical condition in two. Increased intracranial pressure noticed in two children was treated with diamox (patient 5) or mannitol

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Table 1 Clinical and outcome data of the 11 children with acute cerebellitis included in the study

Patient	Age/gender	Preceeding illness	General symptoms in the acute phase	Acute neurological symptoms	Follow-up, y	EDSS score	Neurological sequelae	Cognitive deficits
1	4.5/Male	Angina tonsillaris	Fever, somnolence	Ataxia, intention tremor, dysmetria, tonic clonic convulsions	10	2.0	Intention tremor left hand, ataxia	Attention, language, behavior control
2	3.0/Female	Gastroenteritis	Fever, apathy, hypotonia,	Ataxia, right hemiparesis	1	0.0	No abnormalities detected	No abnormalities detected
3	8.10/Male		Nausea, emesis, headache, vertigo	Horizontal nystagmus	5	0.0	No abnormalities detected	Memory, spatial visual ability, behavior control, school performance
4	3.0/Female	Gastroenteritis	Fever, irritability	Ataxia, dysmetria, intentrion tremor, dysarthria, seizure	10	3.0	Dysarthria, tremor, balance problems	Language, spatial visual ability, behavior control, attention, school performance
5	14.10/Male		Headache, nausea, emesis, fever,		8	0.0	No abnormalities detected	No abnormalities detected
6	5.10/Male	Gastroenteritis	Bifrontal headaches, somnolence, emesis, vertigo	Nystagmus	6 mo	0.0	No abnormalities detected	No abnormalities detected
7	14.3/Female		Fever, cough, nausea, somnolence	Ataxia, intention-tremor, mutism	1.8	3.5	Dysarthria, ataxia, intention tremor	Language, attention
8	4.5/Female	Chickenpox	Fever, respiratory problems with intubation	Ataxia	1	3.5	Intention tremor left hand	Attention
9	7.10/Male	Neuroborreliosis	Frontal headache, emesis		3	0.0	No abnormalities detected	No abnormalities detected
10	4.3/Male	Gastroenteritis	Weakness	Progressive ataxia, dysarthria, dysmetria	5	2.0	Right hand: tremor, problems in fine motor function, change of handedness from right to left	Spatial visual ability
11	8.6/Female		Frontal headaches, emesis, somnolence		5	0.0	No abnormalities detected	No abnormalities detected

Abbreviation: EDSS, Expanded Disability Status Scale.

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Table 2 Neuroimaging findings of the 11 children with acute cerebellitis at the initial manifestation and follow-up

Patient	Age/gender	First cMRI	Interval between first and second cMRI	Second cMRI
1	4.5/Male	Signal changes white matter and cortex of left cerebellar hemisphere, parts of brainstem with edema	8 y	Atrophy left cerebellar hemisphere, hyperintensity left cerebellar hemisphere
2	3.0/Female	Cerebellar swelling, hyperintense signals in white matter and cortex: upper vermis, right pedunculus cerebellaris; left locus caeruleus	1 mo	No significant changes
3	8.10/Male	Hyperintense lesions: white matter and cortex of right cerebellum, lobus centralis (white matter)	4 mo	Improvement
4	3.0/Female	Bilateral signal changes and swelling of cerebellar cortex, downward displaced cerebellar tonsils	14 d	Less swelling and signal alterations
5	14.10/Male	Bilateral cerebellar cortical signal changes; fine nodular leptomeningeal contrast-enhancement		
6	5.10/Male	Bilateral edema of cerebellar white matter, swelling cerebellar cortex, downward displaced cerebellar tonsills	4 mo	Less signal alterations and swelling, slight ascending tonsils, mild cerebellar atrophy
7	14.3/Female	Meningeal contrast-enhancement both cerebellar hemispheres, edema cerebellar cortex	1.6 y	Cerebellar atrophy, 4th ventricle enlarged
8	4.5/Female	Cerebellar and brainstem signal changes in white matter and cortex	8 mo	No signal alterations or swelling noticed
9	7.10/Male	Swollen left cerebellar hemisphere, hyperintense signal alterations in both cerebellar hemispheres confined to white matter	3 mo	Minor signal alterations in cerebellar cortex
10	4.3/Male	Signal alterations white matter and cortex of right cerebellar hemisphere, with contrast enhancement, swelling right cerebellar hemisphere	1 y	Less signal alterations, cerebellar atrophy
11	8.6/Female	Swelling both cerebellar hemispheres, hyperintense signal alterations white matter and cortex, downward displaced cerebellar tonsils		

Abbreviation: cMRI, cerebral magnetic resonance imaging.

(patient 11). Phenobarbital was administered in one patient because of abnormal EEG findings. Melatonin and diazepam were used for sedation and sleeping problems in one patient.

Five patients continued to receive physio-, occupational, or speech therapy after discharge to improve their remaining neurological symptoms (patients 2, 4, 7, 8, and 10).

Neurological and Cognitive Long-Term Outcome

Follow-up interval was between 6 months and 10 years (median: 4.3 years) after the acute phase of AC (►**Table 1**).

Neurological outcome was evaluated with a telephone-based EDSS interview. Six patients had a normal neurological assessment (EDSS score: 0) and five had persisting neurological findings ranging from mild tremor to profound ataxia.

Patient 1 continued to have a tremor of the left hand and mild ataxia 10 years after the illness in addition to attentional difficulties (EDSS score: 2.0). Patient 10 with an EDSS score of 2.0 suffered from clumsiness and a tremor of the right hand. Patient 4 had an EDSS score of 3.0 characterized by abnormalities in speech, concentration, and balance, as well as an intention tremor.

Two patients were evaluated by neurological examination: Patient 7 still suffered from trunk and gait ataxia, dysarthria, and an intention tremor on the left side (EDSS score: 3.5). An intention tremor on the left side was found in patient 8 in addition to problems with concentration (EDSS score: 3.5).

Cognitive outcome was assessed by a parental questionnaire KOPKIJ[8] in 11 children. According to their parents, six patients showed normal results and five patients revealed abnormalities (►**Fig. 4**). One child had detailed neuropsycholical testing at the time of the study, which revealed marked attentional problems (patient 8).

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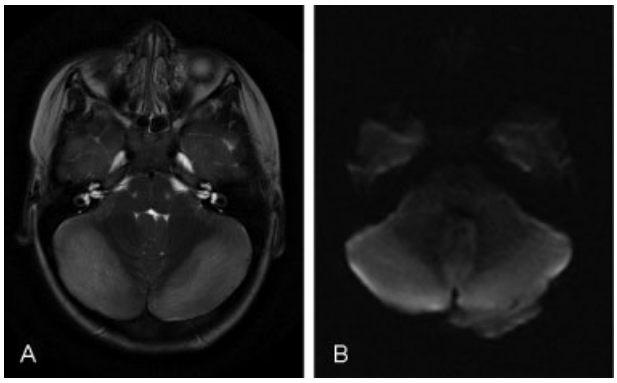

Fig. 1 (A, B) Cerebral magnetic resonance image of a 5-year-and-10-month-old patient (patient 6), who was admitted with signs of meningism, nystagmus, and emesis, showed swelling of both cerebellar hemispheres in axial T_2-weighted images (A). In the corresponding ADC maps, bright signal changes were seen indicative of a vasogenic edema (B). ADC, apparent diffusion coefficient.

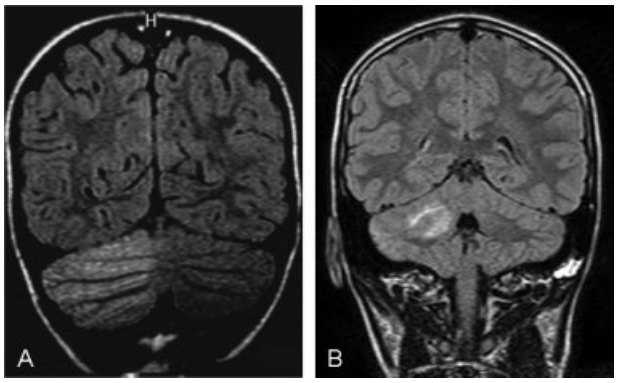

Fig. 3 (A, B) MRI of a 4-year-and-3-month-old boy (patient 10) with distinct cerebellar symptoms showed unilateral signal changes in the right cerebellar hemisphere predominantly affecting the cortical area (coronal FLAIR) (A). Cerebral MRI of an 8-year-and-10-month-old boy (patient 3), who was admitted with nystagmus and generalized symptoms such as nausea and vertigo, showed unilateral hyperintense lesions predominantly affecting the white matter of the right cerebellar hemisphere (coronal FLAIR) (B). FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging.

In the parental questioniare, problems were reported concerning spatial visual abilities (patients 3, 4, and 10), behavior control (patients 1, 3, and 4), and language (patients 1, 4, and 7). The abilities in concentration (patients 4 and 7) and school performance (patients 3 and 4) were impaired in two children. In one child, parents reported problems with memory (patient 3).

Three of five patients (patients 3, 4, and 7) with reported difficulties had been tested with different standardized neuropsychological test batteries (Rey–Osterrieth complex figure test; Wechsler Intelligence Scale for Children–Fourth Edition; Snijders–Oomen Nonverbal Intelligence Test Revised) 12 to 24 months prior to the parental questionnaire. Neuropsychological tests revealed language problems in two patients (patients 4 and 7) in addition to visual-spatial deficits in one (patient 4). Neuropsychological testing in one patient further showed problems with attention (patient 7). In two patients, the neuropsychological results described school problems (patients 3 and 4). Two children (patients 4 and 7) who had neuropsychological testing had a borderline IQ score of 72 and 74, respectively.

Follow-Up Magnetic Resonance Imaging Findings

Follow-up MRIs were performed in 9 of 11 patients. The interval between the onset of AC and the last performed MRI ranged from 14 days to 8 years (►**Table 2**). Complete improvement of the initially described cerebellar signal changes was noted in only two patients (patients 8 and 9). In seven patients, a range of signal abnormalities and/or atrophy of the cerebellum continued to be present in the follow-up study. Improvement of the initial signal changes was noted in two children (patients 3 and 4). Unchanged signal abnormalities with swelling in the upper vermis and pedunculus were still observed in one child (patient 2) 1 month later. Cerebellar atrophy was reported in four children (patients 1, 6, 7 and 10).

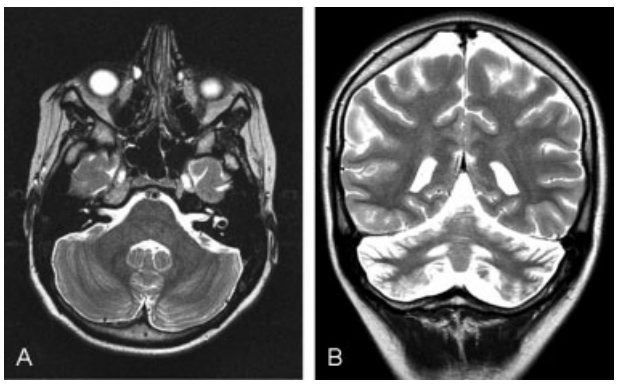

Fig. 2 (A, B) In the magnetic resonance imaging studies of a 14-year-and-3-month-old girl (patient 7) with ataxia, intention tremor, and mental status alterations signal changes in both cerebellar hemispheres were noticed (axial T_2) (A). After 20 months, marked cerebellar atrophy was observed in the same child (coronal T_2) (B).

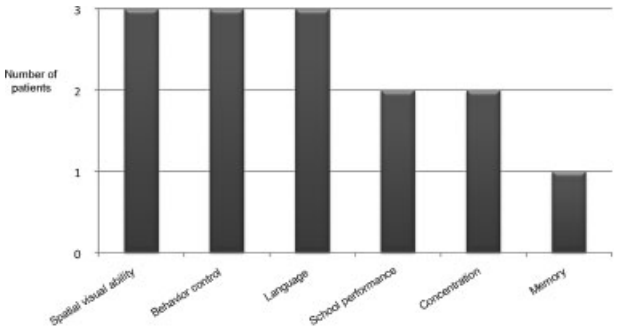

Fig. 4 Five of 11 children had at least one area of cognition affected as detected by the parental questionnaire "KOPKIJ." One child further had marked problems with attention as revealed by neuropsychological testing. KOPKIJ, Kognitive Probleme bei Kindern und Jugendlichen.

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Predictors of Long-Term Outcome

One aim of the study was to assess the neurological and cognitive outcome in children with AC and to detect variables that were associated with a worse outcome (►**Table 3**).

We therefore analyzed if age at initial presentation, severity of the initial phase of AC, and number of days in hospital were associated with a poor neurological or cognitive outcome.

We also analyzed if unilateral versus bilateral cerebellar MRI changes or presence of cerebellar swelling in the initial MRI study had an influence on the subsequent course of the disease.

Age at initial presentation had no influence on the neurological or cognitive outcome ($p = 0.613$ and $p = 0.869$, respectively). Age at initial presentation was also not associated with severity of AC ($p = 0.769$).

The severity of the initial illness showed a linear correlation with the neurological ($r = 0.726$; the Spearman rho) but not with the cognitive outcome ($p = 0.056$; ANOVA).

The number of days in hospital was documented for all patients with AC and was significantly longer in children with neurological problems (median: 22.3 days) than in cases with no neurological sequelae (median: 8.7 days, $p = 0.006$).

MRI changes such as bilateral cerebellar signal changes in the initial phase of the disease were not correlated with a worse outcome.

Discussion

In this retrospective multicenter study, we examined the neurological and cognitive outcome of 11 children with an episode of AC. Our study revealed that more than half of all children had persisting neurological and/or cognitive deficits even years after the initial event. We further showed that the negative predictors for the long-term outcome were the severity at initial presentation and length of hospital admission.

Only few studies so far examined the sequelae of AC mainly addressing neurological problems in the immediate follow-up period.[6,9] Reported neurological symptoms in the early phase include symptoms such as intention tremor, ataxia, or problems in fine motor function.[6,16,17] More detailed information about the long-term outcome is available in children with ACA. Connolly and coworkers in their study found that children with an episode of ACA had overall an excellent neurological outcome.[10] Most of their 66 patients (91%) had complete neurological recovery after four months.[10] It is important to note that Connolly and coworkers predominately included children without mental status changes and normal imaging studies clearly setting this group apart from children with AC.

Although there is most likely a clinical overlap between ACA and AC, it is important to separate both disease entities because of the clinical implications of the latter. Children with AC whose hallmark is the striking radiological appearance of diffuse and focal signal changes in the cerebellum in addition to mental status changes are at risk of serious complications due to posterior fossa swelling.

Cognitive outcome after AC is mentioned only in few case reports describing problems, for example, with expressive language skills.[17] In our cohort, 6 of 11 children showed cognitive deficits in one or more area. The most frequently affected areas of cognition were spatial visualization ability, behavior control, and language. Problems in concentration and school performance were also reported. In three children

Table 3 Correlation between age of patient, severity of illness, days in hospital and long-term outcome

Patient	Age at onset	Severity[a]	Days in hospital	Neurological outcome (EDSS)	Cognitive outcome: 0, *No sequelae*; 1, *sequelae*
1	4 y, 5 mo	3	16	2.0	1
2	3 y	3	14	0.0	0
3	8 y, 10 mo	2	12	0.0	1
4	3 y	3	47	3.0	1
5	14 y, 10 mo	1	19	0.0	0
6	5 y, 10 mo	3	9	0.0	0
7	14 y, 3 mo	3	9	3.5	1
8	4 y, 5 mo	3	17	3.5	0
9	7 y, 10 mo	1	3	0.0	0
10	4 y, 3 mo	2	ni	2.0	1
11	8 y, 6 mo	1	2	0.0	0

[a]1 indicates mild severity of illness: not more than one neurological symptom (e.g., ataxia, dysarthria) and not more than two generalized symptoms (e.g., fever, nausea). 2 indicates moderate severity of illness: one neurological symptom and at least three generalized symptoms or two or more neurological symptoms. 3 indicates severe severity of illness: in addition to neurological symptoms, mental status changes (such as irritability, apathy, somnolence, mutism)/seizures/intubation.

Severity of the initial illness showed a linear correlation with the neurological ($r = 0.726$; the Spearman rho) but not with the cognitive outcome ($p = 0.056$; ANOVA). Days in hospital was significantly longer in children with neurological problems (median: 22.3 days) than in cases with no neurological sequelae (median: 8.7 days, $p = 0.006$).

Abbreviations: ANOVA, analysis of variance; EDDS, Expanded Disability Status Scale; ni, no information.

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with cognitive problems as documented by the parental questionnaire detailed previously obtained neuropsychological testing was available. The overall neuropsychological test results support the findings of the parental questionnaires.

The importance of the cerebellum in motor functions is well known; however, the role of the cerebellum in cognition has not been explored to the same degree, yet.[18] Several studies and reviews recently have shown that different cerebellar disorders can result in impairments in mental flexibility, multitasking, visual-spatial organization, linguistic processing, and mood in adults and children.[19–21]

Recently, functional MRI studies of the cerebellum could show that there is a topographic organization of motor execution and cognitive/emotional domains within the cerebellum of a single individual. This suggests that different neuronal circuits that are localized in separate anatomic areas of the cerebellum are associated with different task domains.[18,22,23,]

Schmahmann and coworkers summarized deficits in higher-order function resulting from damage confined to the cerebellum and from affected cerebrocerebellar circuits as cerebellar cognitive affective syndrome (CCAS).[19] Our parental questionnaire, KOPKIJ, includes questions concerning the following four affected areas of cognition, characterizing the CCAS: disturbance of executive function, impaired spatial cognition, personality change, and linguistic difficulties. Our results indicate that each patient had long-term deficits in at least one area, one patient had deficits in all four areas characterizing CCAS.

Radiological abnormalities in the cerebellum showed a range of patterns in the initial imaging studies. Both cerebellar hemispheres were affected in six and only one hemisphere was affected in five children. Involvement of anatomical structures in addition to the cerebellum was noted in three patients and evidence of cerebellar edema was found in nine patients. The range of anatomical structures affected possibly explains the variability of clinical symptoms and neuropsychological sequelae of children with AC. Interestingly, the difference between unilateral and bilateral cerebellar involvement did not seem to influence the neurological and neurocognitive outcome. Two children with bilateral involvement of the cerebellum had continuing neurological and neurocognitive sequelae, and two children with unilateral involvement of the cerebellum had lasting deficits in both areas, which was however not statistically significant.

Follow-up MRI of the brain was performed in 9 of 11 patients. Complete improvement of cerebellar signal changes was only seen in two children. Eight children continued to have signal abnormalities in the affected cerebellar areas. Cerebellar atrophy ranging from mild to marked was found in 4 of 11 children, of whom, 3 continue to suffer from sequelae including ataxia and cognitive deficits, underscoring the impact of the disease process on the cerebellum.

CSF studies were preformed in nine children. In five children, mental status changes were reported but no signs of papilleoedema or MRI changes suggesting raised intracraniel pressure. It is important to note that children with cerebellitis associated with cerebellar swelling are at great risk of herniation, in particular, in conjungtion with a lumbar puncture. The pros and cons of a lumbar puncture should therefore be discussed in every child with a cerebellitis.

AC associated with swelling of the cerebellum is an emergency sometimes requiring intensive care and neurosurgical intervention. Only three children in our cohort were treated with steroids. High-dose pulses of methylprednisolone as administered in other neuroimmunolgical diseases affecting the cerebellum (e.g., opsoclonus-myoclonus syndrome) are most likely the best medical option to ameliorate swelling and to avoid surgical intervention.[11–13,24]

In the initial work-up, a CT scan of the brain was performed. In most children, revealing abnormalities only in two, despite major findings in subsequently performed MRI. The low detection rate in addition to the higher risk in children from radiation-induced side effects on the developing brain should emphazise the role of MRI as the modality of choice.

The following limitations of our retrospective study need to be addressed. First, our cohort included predominately children who were severely affected and therefore had an MRI scan representing possible selection bias. On the contrary, we did not include children with AC who died in the acute phase due to complication of posterior fossa swelling. Second, the number of children who developed a cerebellar atrophy in our study is most likely too low, due to the short time interval between the initial and follow-up MRI in at least three children. Third, evaluating neuropsychological deficits with questionnaires is a potential problem because the results depend on the realibility of the rater (i.e., parents). Nevertheless, questionnaires provide an opportunity to screen for neuropsychological deficits and are therefore widely used.

Conclusion

Children with AC are at risk of significant neurological and cognitive sequelae. Our results also suggest an association between the duration and severity of AC in the acute phase and long-term outcome. MRI studies are the gold standard in the diagnosis of AC but do not seem to predict the long-term outcome.

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