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Abstract

Whether or not cranial ultrasound (crUS) and cerebral magnetic resonance imaging (MRI) have both a place in the assessment of children with congenital cytomegalovirus infection (cCMV), remains a topic of discussion between research groups. Literature suggests that MRI is indicated only in children with abnormal crUS.

In Flanders, Belgium, combined crUS and MRI was performed in 639 children with cCMV, referred for diagnostic assessment. Cranial US was classified as abnormal in the presence of striatal vasculopathy, calcifications, cysts, cystic germinolysis and/or ventriculomegaly. MRI findings were classified as abnormal in the presence of gyration disorders, cerebellar abnormalities, ventriculomegaly, cysts or pathologic white matter lesions.

One in five children (93/480) with normal crUS showed abnormal findings on MRI. Of them, 85 (91,4%) were classified as symptomatic. In 37 of those 93 children (39,8%) classification as severely symptomatic was made based on MRI lesions alone. One in five children (93/480) with normal crUS showed abnormal findings on MRI. Of them, 85 (91,4%) were classified as symptomatic. In 37 of those 93 children (39,8%) classification as severely symptomatic was made based on MRI lesions alone. MRI and crUS proved to be complementary in the assessment of CNS involvement in children with cCMV. Long-term studies are needed to evaluate the importance of this finding with respect to outcome and benefit of therapy in this particular subgroup of patients with cCMV infection.

Conclusion

Our findings support an enhanced role of MRI in the diagnosis of CNS involvement in children with cCMV infection. The ideal assessment should include both imaging techniques, as the strengths of each test compensate for the other's weaknesses.

Keywords

Congenital cytomegalovirus infection, imaging techniques, central nervous system involvement, management

Introduction

Congenital cytomegalovirus (cCMV) infection is the most common congenital infection worldwide and occurs in 0,3 % to 2,4% of all live births. Congenital CMV has a significant long-term impact on affected children, being the major cause of non-hereditary sensorineural hearing loss and the major infectious cause of neurodevelopmental abnormalities in infants born in developed countries. These infections frequently involve the central nervous system with direct injury to and possible disruption of brain development. [1] This can lead to a wide spectrum of brain abnormalities, including microcephaly, calcifications, ventriculomegaly, intraventricular adhesions, periventricular pseudocysts, gyration disorders, cerebellar abnormalities and white matter injury. This wide spectrum of brain lesions can give cause to a wide variety of clinical manifestations, making counselling very challenging. [1]

All newborns with confirmed diagnosis of cCMV need neuroimaging examination to assess central nervous system involvement. This information will contribute to optimal treatment and follow-up and is helpful in addressing prognosis and counselling of parents. [2,3]

Cranial ultrasound (crUS) and cerebral magnetic resonance imaging (MRI) are both valuable neuroimaging techniques for assessment of children with cCMV infection. [4] Whether or not MRI provides additional information in newborns with normal crUS remains a topic of discussion between research groups. In the European expert consensus statement by Luck et al in 2017 a full agreement was found on performing crUS in every child with cCMV and the majority agreed that cranial MRI should be performed in any baby with cCMV and evidence of CMV disease. Only a minority advocated to perform cranial MRI in all CMV-infected babies. [1] Since 2018, the Flemish consensus states that every child with cCMV should have a crUS and MRI must be performed in case of clinical signs, hearing loss or abnormal crUS. However, there remain differences in the use of CNS imaging between the different centers, which is a reflection of the discussion in worldwide literature. Few studies have been performed to compare MRI and crUS and often these studies were performed in small groups. [3,5] A study by Smiljkovic et al. found that sequential US and MRI were concordant in the majority of cases in their population and that additional MRI/CT after crUS did not influence clinical management of the children. Capretti et al. described that MRI did find additional pathological findings in their children with cCMV. As is suggested, studies with larger groups are needed to clarify whether or not MRI is necessary to obtain a more complete assessment of central nervous system involvement which might influence neonatal management and treatment.

The Flemish CMV registry collects data on prenatal, neonatal management and long-term follow-up in children with cCMV. Between January 2007 and December 2020, 1059 children were included. We compared the results of crUS and MRI of 639 registered children in which both investigations were performed. With this study we aim to assess the diagnostic value of both MRI and crUS compared to crUS alone to detect CNS lesions and to identify those children eligible for therapy.

Patients and methods

Study population

In 2007 the systematic registration of children with cCMV started in 6 collaborating hospitals in Flanders. Children were included in the registry after written informed consent of the parent(s)/legal guardians and only after a confirmed diagnosis of cCMV. Diagnosis in the neonatal period was made by viral isolation and/or PCR on urine taken within the first 3 weeks of life. Retrospective diagnosis (after age of 21 days) was made by PCR on dried blood spot (DBS). The registration was approved by the ethics committee og Ghent University Hospital and was enlisted at the privacy commission. All children included in the registry and who had both crUS and MRI after birth, were eligible for this study.

Methods

Central nervous system imaging was performed by cranial ultrasound (crUS), magnetic resonance imaging (MRI) or a combination of both. Ultrasound was performed in the local center by the attending neonatologist/radiologist with expertise in cranial ultrasound in newborns. CrUS was classified as abnormal in the presence of striatal vasculopathy, calcifications, cysts, cystic germinolysis and ventriculomegaly.
Brain MRI was also performed in the local collaborating center and images were reported by the (pediatric) radiologists with expertise in the field of neonatal brain imaging. Magnetic resonance imaging findings were categorized and scored normal/abnormal according to the presence or absence of cortical malformations, cerebellar anomalies, cerebral calcifications, ventricular dilatation, ventricular adhesions, subependymal cysts and white matter abnormalities. General anesthesia was used in only one center. In other centers, a combination of a very mild sedative and feeding prior to MRI were used to perform MRI.
Based on additional investigations (peripheral blood count, hearing and vision evaluation, CNS imaging) and according to the Flemish consensus, children were categorized as asymptomatic, mildly, moderately or severely symptomatic. All severely symptomatic children were eligible for therapy but ultimately parents decided after

counselling whether or not treatment with (val)ganciclovir was started. Initially, treatment consisted of intravenous ganciclovir during 6 weeks at a regimen of 6 mg/kg, twice daily. Since 2012, oral treatment with valganciclovir for 6 weeks, 16 mg/kg twice daily, has been introduced. Since end of 2017, valganciclovir therapy duration has been prolonged to 6 months.

In moderately symptomatic children therapy could be offered if deemed necessary by the attending physician and after expert opinion.

Results

Between January 2007 and December 2020, 1059 children were included in the registry. Of these 1059 children, 639 underwent both cranial MRI and crUS and were eligible for this study. In 332 only one of the examinations was performed. Eighty-eight children in this population didn't have any form of cerebral imaging. Of 639 children who underwent crUS and MRI, 480 (75,1%) had a normal US. Of those, 93 children (19,4%) had an MRI classified as pathologic. Overall, in 93/639 (14,6%) children with both investigations performed, MRI was abnormal with normal crUS findings. In 56 children lesions on crUS were found which were not detected on MRI. (table 1) The baseline characteristics of all 1059 children in the registry, categorised in 4 groups (no imaging, only crUS, only MRI and both MRI and crUS performed). are listed in table 2. Analysis of these data is restricted to the children with known data on the different topics. No significant differences on these characteristics are found between the different groups. (table 2)

Table 3 shows which lesions were seen on the MRI in those children with normal crUS. The majority of them (79/93, 85%) have white matter hyperintensity and in 1 child cortical anomaly was detected.

The sensitivity of crUS to assess complete CNS involvement is 52,5%, with a specificity of 75, 4%. The positive predictive value (PPV) of crUS is 64,8% and the negative predictive value (NPV) is 80,5%. Table 4 shows the sensitivity, specificity, PPV and NPV of crUS per trimester of seroconversion.

In the group of children with normal crUS and abnormal MRI, 85 (91,4%) children were classified as symptomatic. Forty-seven of them (50,5%) were diagnosed as severely symptomatic.

Of the eight children with MRI lesions who were classified as asymptomatic, one had lesions unrelated to cCMV and 2 were diagnosed at later age (> 28 days). The remaining 5 had very mild white matter hyperintensity on T2 weighted sequence and the attending neonatologist decided to classify those children as asymptomatic.

The majority of the symptomatic children (72/85; 84,7%) in this subgroup is classified as mildly (23,6%), moderately (25%) or severely symptomatic (51,4%) based on abnormal MRI findings alone. Thirteen of them

showed additional abnormal findings (hearing loss and/or clinical signs) that contributed to the diagnosis of symptomatic cCMV infection. (fig. 1) In the group symptomatic children based on MRI findings alone, 37 (51,4%) were diagnosed as severely symptomatic. MRI findings in this group consisted of extensive white matter lesions/leuko-encephalitis and ventriculomegaly. In the mild group, MRI lesions consisted mostly of subependymal cysts or mild white matter abnormalities, referred to as 'suggestive of central involvement of CMV'. The moderate symptomatic group showed moderate white matter lesions with/without cysts. In the subgroup of 93 children with normal US and abnormal MRI, 58 children (62,4%) started therapy. Eleven of 58 (18,9%) had hearing problems or clinical signs beside the abnormal MRI, contributing to the indication for therapy. So, in 81% of the treated children in our subgroup (47/58) MRI abnormalities were the sole reason for starting treatment. (fig 1) Table 5 shows the different described lesions in our study population and this in relation to the imaging modality in which they were detected. In our population, striatal vasculopathy is only detected by crUS. On the other hand, MRI is the only technique to detect gyration disorders, polymicrogyria, cortical atrophy and white matter hyperintensity.

Overall, in our study population of 639 children, 245 (38,5%) were classified as symptomatic of which 72 (29,4%) based on MRI abnormalities alone. Therapy was given in 179/639 (28%) and in 47 of them (26,2%), MRI lesions were the only indication for treatment.

We see a significant higher percentage of abnormal MRI's at first trimester seroconversion (37,3%) compared to third trimester infection (18,3%, p = 0,002). This difference is not significant when comparing second and third trimester seroconversions nor when comparing first and second trimester infections. At third trimester infection, the number of abnormal brain MRI's combined with normal crUS is significantly lower (18,3%) than after infection earlier in pregnancy (33,3%, p = 0.004).

Discussion

Whether or not both cranial US and MRI have a place in the assessment of children with congenital CMV remains a topic of discussion. In the European Expert Consensus Statement of 2017, only a minority agreed that cranial MRI should be performed in all CMV-infected babies. There was a major agreement that MRI should be performed in children with any sign of CMV-disease and a full agreement on performing cranial US in every child with cCMV. [1] In Flanders, we adapted our consensus on diagnosis and indications for treatment according to this European consensus statement in 2018.

crUS is a reliable technique to detect a wide range of cerebral abnormalities suggestive of cCMV, e.g. striatal vasculopathy, periventricular pseudocysts, ventriculomegaly, possible white matter hyperintensity and calcifications. Performing crUS has many advantages: it comes with a relatively low cost, it can be done bedside even in the most critically ill children and it is the safest neuro-imaging technique available. [3,6,7,8] However, crUS also has its limitations. First, there is a poor visualisation of the posterior fossa, cerebellum and sub-tentorial spaces. Moreover, crUS is less performant in detecting cortical or gyral abnormalities, delayed myelinisation and white matter injury. [3,6,7] Secondly, whether cerebral lesions or abnormalities are picked up by crUS, is dependent on the expertise and experience of the investigator. [3,9] This is also reflected in our population where we see that in some children crUS was described as normal in cases where MRI revealed mild ventriculomegaly or cysts.

As for magnetic resonance imaging, it is widely known that it offers greater sensitivity and specificity and enhanced lesion characterization, without the use of ionised radiation (in contrast to CT). [9] MRI is superior to crUS in revealing cortical abnormalities, gyral disorders, cerebellar hypoplasia and white matter injury. [3,6,10,11] Again, this technique also comes with some disadvantages. First, the child has to be transported to the radiology department, which can be challenging in case of a critically ill child. Secondly, the examinations by MRI take a long time and it is important that the child remains still for optimal imaging. In some cases, some form of sedation of the child is necessary. [8] In our population, only in one center general anestaesia was used Last, MRI may detect brain abnormalities with no well-known clinical and prognostic significance which may have implications on counselling. [6]

Studies have revealed that MRI and crUS are complementary investigations to assess the central nervous system in children with congenital CMV infection. [2,4] Oosterom et al. found that migrational disorders may be present in infants with mild crUS findings and concluded that MRI can offer additional information, which can help in more accurate prediction of outcome. [12]

Despite this apparent complementarity between crUS and MRI, still no consensus is found. The debate on whether or not both should be performed in every child with cCMV is still going on, the main question being if, by not performing MRI in every child with cCMV, we fail to detect abnormal MRI findings which could lead to a change in classification in asymptomatic/symptomatic and hence, in counselling of parents, initiation of therapy or not and the follow-up of those children.

In this study, we focused on the group of children in which investigations have been performed. As table 2 shows, there are no significant differences in baseline characteristics between this group of 639 children and the

total population. Hence, we cannot detect any characteristics, specific for our study population, which might have influenced the decision to perform bot MRI and crUS.

Special attention is given to the subgroup of 93 children with normal crUS in which lesions on MRI are found. In 72 children, MRI findings were the only reason to classify those children as symptomatic. Hence, 1 in 3 symptomatic children (29,4%) in our study population would have been classified as asymptomatic and thus not being offered therapy, if MRI wasn't performed. Results show that MRI anomalies are more frequently found after first and second trimester infections compared to third trimester. This is in accordance with the findings of Oosterum et al. [12] In centers where general anesthesia is applied for MRI or where there is no full agreement on performing both investigations in every child with congenital CMV, restricting MRI to first and second trimester infections may be an option. However, our results show that even in third trimester infections, abnormal MRI can be found in children with normal crUS. In these children, only white matter lesions were found. These results suggest that performing both investigations in all children with cCMV could be recommended, regardless of time of seroconversion, to have a complete evaluation of the central nervous system involvement in children with cCMV.

This complete and thorough evaluation of cerebral involvement in children with cCMV is of utmost importance to identify all symptomatic children since this has important implications.

First, being classified as moderately or severely symptomatic makes a neonate eligible for therapy. In Flanders, therapy regimens have changed over the years from 6 weeks of intravenous ganciclovir therapy to 6 weeks of oral valganciclovir treatment to 6 months of oral valganciclovir therapy since 2017. [1,13,14] A review by Goderis et al. showed a delayed onset hearing loss of approximately 18% in symptomatic children, compared to 9% in the asymptomatic group. [15] Moreover, studies have shown that children with CNS involvement have a higher risk for developing hearing loss at later age. [16,17] Literature has shown that early treatment with (val)ganciclovir can prevent hearing deterioration and improve neurodevelopmental outcomes. [1,13,14] These findings suggest that it might be beneficial to identify all children with CNS involvement, as they might benefit from antiviral therapy. In our study population, 18.6% (40) of all treated children would not have been offered therapy if MRI had not been performed.

Second, the recommended follow-up in our Flemish consensus is different for symptomatic and asymptomatic patients. Symptomatic children are seen more regularly on audiological and neurodevelopmental follow-up. Main reason is the higher risk of developing hearing loss [14] or some degree of neurodevelopmental delay. If

diagnosed timely, patients may benefit from early therapy if necessary (e.g., speech/physical therapy, hearing aid).

Third, the immediate involvement and cooperation of parents is crucial for successful follow-up of the child, underscoring the need of accurate counselling. Counselling parents is often challenging. The mother might be fraught with feelings of guilt, so parents need to be informed as soon as possible. Counselling on outcome starts from the moment the seroconversion is diagnosed, which was the case in the majority of our patients. The investigations offered during pregnancy (e.g., fetal US, amniocentesis, fetal MRI) have their limitations when it comes to detect which children are infected and to what extent. [18,19] In the majority of cases, we are unable to predict neonatal and/or long-term outcome in a precise manner when CMV infection is diagnosed during pregnancy. [19] The anxiety this induces in parents is well-known. So, counselling after birth with knowledge of results of all investigations performed in the newborn is merely a next step in an already ongoing path of prediction of outcome with all its uncertainties. Parents expect to receive more accurate answers to their questions after the baby is born. In our experience, one of the parents' first questions to be answered is what neurodevelopmental outcome to expect in their child. If the diagnosis of cCMV is confirmed and the additional investigations are performed, a more precise prediction of outcome can be offered. In case of symptomatic disease, parents are counselled about the risk of 18-20% for late-onset hearing loss and, depending on what anomalies were detected on CNS imaging, neurodevelopmental outcome can be discussed in more detail. This is however not always 'clear cut' and in case of 'minor' lesions on MRI, it remains difficult to predict outcome in a complete manner. On the other hand, a normal MRI result will reassure parents on the neurodevelopmental outcome and will reduce their anxiety. Fortunately, this is the case in the majority of the children, allowing us to reassure the parents of an expected normal neurological development. The findings in our study illustrate the value of MRI in evaluation and management of children with cCMV.

However, some considerations must be made. The MRI lesions described in the group of 93 children with normal crUS were subependymal cysts (1), mild ventriculomegaly (1) but mostly leuko-encephalitis and other white matter abnormalities. Only one child with cortical defects was found in this subgroup. Where cortical defects and gyration disorders are known to be associated with poor neurodevelopmental outcome, this is not so clear for white matter lesions. [20] Abnormal white matter intensity on MRI is frequently found in children with cCMV and is often made more impeded by partial myelination. [21] It is known that in infants, it may be difficult to differentiate abnormally increased signal intensity of white matter from normal. [8] Moreover, the prognostic role of white matter lesions is still unclear. A review by Buca et al. showed that hyperintensity in the

temporal lobe is more likely to be associated with an adverse neurological outcome than hyperintensity in the frontal and parieto-occipital lobes. [22] Capretti et al found that white matter lesions may be the only signs of cCMV and that these might be related to impaired psychomotor outcome. [3] Kwak et al. described a possible relation between white matter lesions and epilepsy. [10] However, other studies have demonstrated the opposite and state that white matter changes do not correlate with neurological outcome. [6,19] This unknown long-term outcome of white matter lesions might explain the discordance between the finding in our population where MRI lesions are seen even after third trimester infections and what Leruez-Ville et al. described regarding trimester of infection and outcome. [23] They stated that long-term sequelae are only severe in case of first trimester infections and that cerebral lesions are mostly correlated with first trimester infections. As described above, in our population, after third trimester infections only white matter lesions were seen. Our data only describe the presence of white matter lesions on MRI after birth but to evaluate their significance,and possible impact on neurological outcome, long-term follow-up data need to be studied in these children.

Not only the impact of white matter lesions on neurodevelopmental outcome is debated; their impact on hearing outcome is questioned as well. A study by Lanzieri et al. showed that white matter lucency was significantly associated with SNHL at 5 years. [24] Others found that abnormal imaging is not predictive for developing delayed onset hearing loss. [7,25] This controversy demonstrates the need for further studies on the prognostic role of white matter lesions in cCMV.

Routine MRI imaging in newborns with cCMV infection may increase the finding of lesions with unclear impact on outcome. This might induce anxiety in parents. Parents have come a long way when being confronted with cCMV infection and hope to receive clear answers after birth. [26] If MRI reveals anomalies with uncertain prognostic role, counselling remains challenging and uncertain. On the other hand, normal MRI results may reassure parents on the neurodevelopmental outcome of their children. Craeghs et al. showed a negative predictive value of normal crUS and MRI of respectively 91% and 92% on developing delayed onset hearing loss. [25] Although we might induce anxiety in some parents in case of MRI findings with unclear prognostic significance, we will be able to reassure a large part of our parents since MRI is normal in the majority of our population.

A last consideration to be made, is whether it is mandatory to perform an MRI if crUS shows obvious lesions. Obviously, a child will be classified as having symptomatic cCMV and might be offered therapy in cases where crUS is clearly abnormal. However, additional MRI might detect lesions which have an important impact on neurodevelopmental outcome and hence, might influence counselling. As table 5 depicts, serious anomalies such

as gyration disorders, polymicrogyria, cerebellar hypoplasia and cortical atrophy are only detected by MRI and these lesions will influence the neurodevelopmental outcome substantially. Hence, we believe that even in cases of abnormal crUS, it is beneficial to perform an MRI.

This retrospective study has some limitations. The group with normal crUS and abnormal MRI is relatively small. In addition, our population is not the result of universal screening but of referrals to the collaborating hospitals, so our population does not represent the spectrum of the disease in the general population.

We described how results of MRI influenced classification, management and counselling in children with cCMV at birth. However, little is known on the clinical outcome of children with normal crUS and abnormal MRI, so many questions on management and counselling are still unanswered.

Conclusion

Whether or not both MRI and crUS are mandatory in all children with cCMV remains a topic of discussion between various research groups. So far, no studies have proven nor disproven the need of performing both. Our findings support an enhanced role of MRI in the diagnosis of CNS involvement in children with cCMV infection. The ideal assessment should include both imaging techniques, as the strengths of each test compensate for the other's weaknesses. However, a better understanding of the prognostic role of some 'minor' MRI lesions is essential. For this, further studies with long-term observation of a large number of children with cCMV are warranted.

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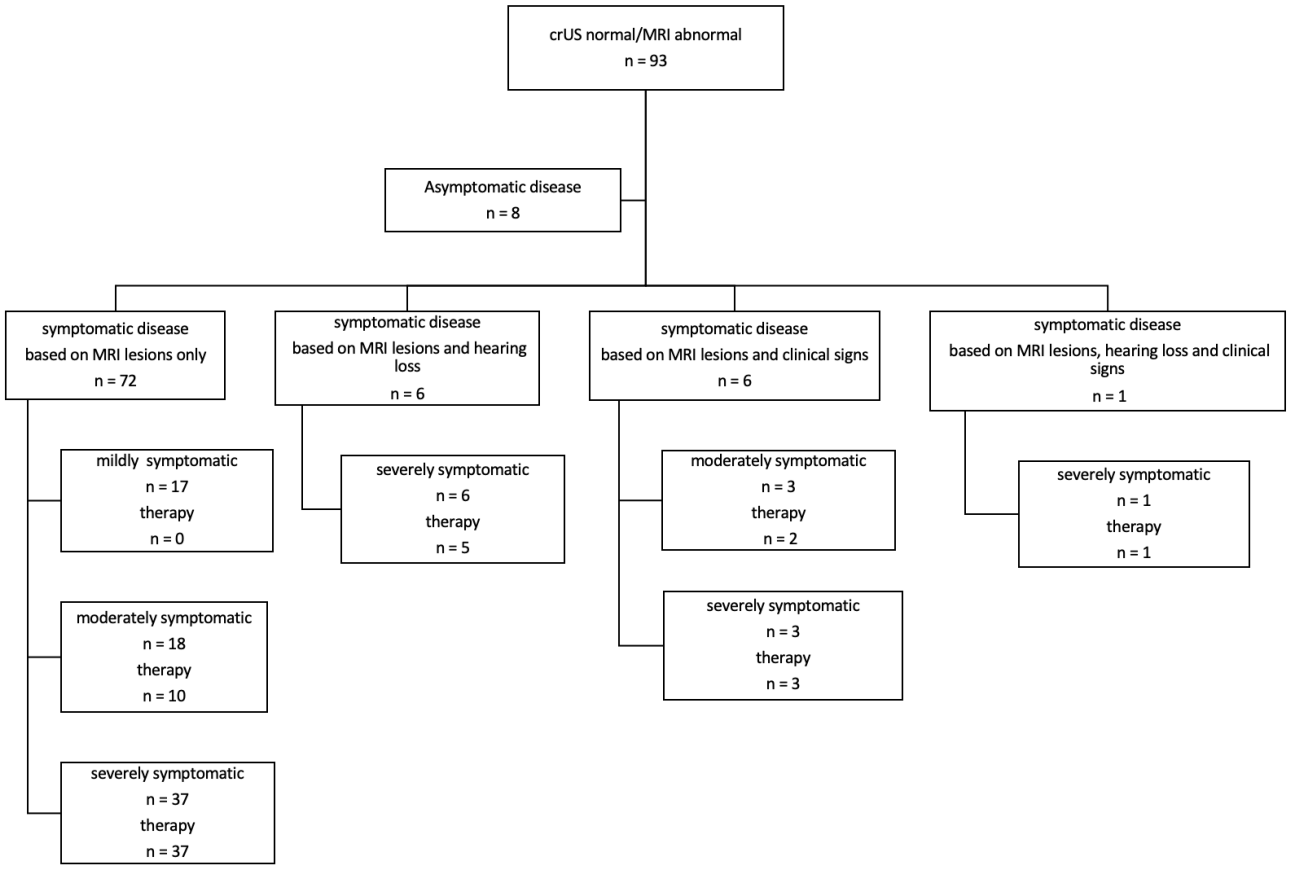

Figure 1. Distribution of asymptomatic/symptomatic disease and therapy in the group of children with normal crUS and abnormal MRI

	normal MRI	abnormal MRI	
normal crUS	387 (60,5%)	93 (14,6%)	480
abnormal crUS	56 (8,8%)	103 (16,1%)	159

table 1. Results of crUS and MRI in 639 children in which both MRI and crUS are performed.

	No imaging n = 88	only crUS n = 273	only MRI n = 59	both MRI and crUS n = 639
GA				
known	32	175	54	633
< 37 weeks	4/32 (12,5%)	30/175 (17,1%)	5/54 (9,3%%)	111 (17,5%)
> 37 weeks	28/32 (87,5%)	145/175 (82,9%)	45/54(90,7%)	522 (82,5%)
unknown	56	98	9	6
Tsero				
known	22	138	26	462
0-13 weeks	8/22 (36,4%)	62/138 (44,9%)	14/26 (53,8%)	206/462 (44,6%)
14-27 weeks	7/22 (31,8%)	47/138 (34,1%)	9/26(34,6%)	169/462 (36,5%)
> 27 weeks	7/22 (31,8%)	29/138 (21%)	3/26 (11,6%)	87/462 (18,9%)
unknown	66	135	33	177
Age at diagnosis				
known	75	186	57	636
<21 days	53/75 (70,6%)	171/186 (91,9%)	34/57 (59,6%)	621/636 (97,6%)
22 days-3 months	15/75 (20%)	11/186 (5,9%)	14/57 (24,6%)	12/636 (1,9%)
> 3 months	7/75 (9,4%)	4/186 (2,2%)	9/57 (15,7%)	3 (0,5%)
unknown	13	87	2	3
Birthweight				
known	28	173	46	626
dysmaturity	4/28 (14,3%)	9/173 (5,2%)	1/46 (2,1%)	29/626 (4,6%)
normal for GA	24/28 (85,7%)	164/175 (94,8%)	45/46 (97,9%)	597 (95,4%)
unknown	60	100	13	13
CMV PCR serum				
known	5	37	12	260
positive	5	33/37 (89,2%)	9/12 (75%)	186/260 (71,5%)
negative	0	4/37 (10,8%)	3/12 (25%)	74/260 (18,5%)
unknown	83	236	47	379
clinical signs				
known	181	273	59	639
present	7/181 (3,8%)	27 (9,9%)	5 (8,5%)	56 (8,7%)
absent	74/81 (96,2%)	246 (90,1%)	44 (74,5%)	583 (91,3%)
unknown	7	0	0	0

Table 2: Baseline characteristics of the 1059 children in the registry.
(GA : gestationa+Q3:U44l age, Tsero : time of seroconversion)

MRI lesions in children with normal crUS	**n = 93**
cortical anomaly	1
periventricular cysts	1
ventriculomegaly	1
Cystic PVL	3
hyperintensity white matter	79
not specified in database	8

table 3. Described lesions on MRI in children with normal crUS

Trimester of seroconversion	sensitivity	specificity	PPV	NPV
< 13 weeks (n=136)	67,1%	85,4%	72,8%	82,0%
14-27 weeks (n=133)	40,8%	86,7%	55,6%	78,2%
> 28 weeks (n=82)	18,7%	97,2%	60,0%	84,1%

table 4. sensitivity, specificity, PPV and NPV of crUS per trimester of seroconversion

type of lesion	only on crUS n	only on MRI n	both MRI and crUS n
periventricular cysts	35	10	15
intraventricular adhesions	2	13	2
striatal vasculopathy	70	0	0
calcifications	12	6	6
hyperechogenic caudal pit	13	0	0
ventriculomegaly	11	15	21
cystic germinolysis	11	0	0
subependymal cysts	5	1	3
cystic PVL	5	9	5
cortical atrophy	0	7	0
gyration disorders	0	16	0
polymicrogyria	0	6	0
vermis hypoplasia	0	5	0
cerebellar hypoplasia	0	2	0
hyperintensity white matter	0	145	5

table 5. Described lesions in the group of 639 children
in relation to the imaging modality in which they were found.