Medication Used in Neurologic Disorders Associated and/or Concomitant with Cerebral Arachnoid Cysts in Children

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Arachnoid cerebral cysts can create great anxiety to families of the affected child. In children prospective studies of arachnoid cerebral cyst series are focused on the surgical treatment and no medication associated tot this pathology was analysed until yet. We want to show how medication for neurological disorders found in children which have had also arachnoid cysts was used, and that not only surgery is the first line treatment in all types of arachnoid cysts.There are not extensive studies yet for the different contexts which are involving arachnoid cerebral cystsin children. This study was made for the first time in the cabinet of neurology from the Children Clinic Emergency Hospital Sfantul Ioan Galati in a 111 case series under clinic-imagistic surveillance and EEG between 2014-2017. A male predominance is seen as also a prevalence at the ages of 6-10 years of age and 2-5 years of age. Treatment were of different types due to the neurologic disorder which the children have had (antiepileptic, neurotrophic, antiiinflammatory, nonsteroid and steroid and migraine treatment) after the international guidelines in use.The formulation of a diagnosis of epilepsy must be done with great responsibility because of many parioxistic nonepileptic events, where can exist associated arachnoid cysts, but we can have particulary family structures , because of the parents working places , so the waiting of the next paroxistic events and observing of the child is a wise attitude.But arachnoid cerebral cysts can be considered cerebral structural marker in some of the analysed cases.

Key words: Epilepsy, arachnoid cerebral cysts, cerebral structural marker, children, medication

Disability is a notion which includes concepts about conditions, limitations and restrictions , referring to the negative aspects of the interactions between the person (with a health condition) and the contextual factors of the person (environmental or personal) [1]. Epilepsy after ILAE has the following operational definition: epilepsy is a disease of the brain which is defined with each of the following conditions: 1.Minim 2 unprovoked seizures (or reflex) which appear at a difference of over 24 h.2.One un provoked seizure (or reflex) and a probability of new seizures similar to the general risk of recurrence (minim 60%) after two un provoked seizures, and which appear in the following next 10 years after the first seizure. 3.Diagnosis of an epileptic syndrome [2]. Neurologic disorders are progressive or nonprogressive. The concept of cerebral palsy was introduced in 1953 and belong to the non-progressive disorders. Cerebral palsy is defined as a group of permanent disorders of the development of movement and posture, and determine the limitation of the activity, which are due to nonprogressive disorders which appeared in the fetal or child's brain.The majority of patients with cerebral palsy have imaging changes in 77% at tomography and 89% at MRI [3]. Language disorders often bring the child to child neurologist and they are associated to the neurologic and/or psychiatric disorders of the children. Language disorders in childhood are the most common disabilities from childhood affecting 1/12 children or 5-8% of the preschool children.They include the articulation of sounds, verbal fluency and voice disturbances as also language disorders which affects the utilization of the oral system (or written) covering grammar and phonology, semantic and the function of the language (the pragmatism of the language)[4]. Figure 1 shows the algorithm of evaluation fo the child with languagei disorders.

Intracerebral arachnoid cysts represent 1-2% from all intracerebral lesions in pediatric patients, most of them

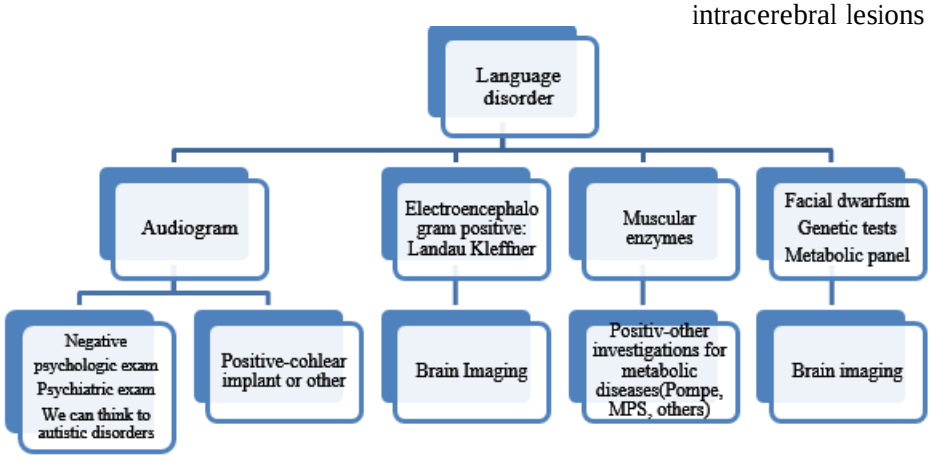

Fig. 1 Diagnosis of language disorders in children

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are congenital but they can appear also de novo. [5]In the general population the prevalence is 0,5% [6]In the fetal period the cerebral cysts can pe diagnosed at 28 weeks (some of them even at 19 weeks) [7]. Suprasellar arachnoid cysts represent 9-21% of cerebral arachnoid cyst in children. [8]Congential arachnoid cysts have epilepsy associated in 18% of the cases [9]. The medium age at which the surgical cases were operated was 8,7 years in a study [10]. The incidence of cerebral palsy in children is 2-3/1000 births in Europe in 2000 [11]. On electron microscope there are cysts with normal arachnoid membrane, but others have a dense fibrous tissue covered with a simple epithelial layer while others are aberrant arachnoid cysts have a luminal non-arachnoid epithelium with abundant microvilli and/or cilia as also nervous tissue in the wall of the cyst [12]. SPECT images has shown a hypoperfusion in the left temporal lobe. Dysfunction of the left temporal lobe determine langauage delay and learning difficulties [13]. Language disorders in children with arachnoid cysts are sometimes generated by left temporal lobe anomalies [14]. The term apoptosis was replaced by the term active cell death while the term necrosis was replaced by the term of passive cell death. Recently researchers formulated the concept of neurovascular unit formed by endothelial cells, pericyte, neurons, glial cells and proteins of the cell matrix which are working all together through biochemical signaling. Excitotoxicity, apoptosis are the core mechanism in neurologic diseases and their modulation is efficient in the neuroprotection in different diseases [15]. Neuromodulation is given by genetic variations and anomalies in function of some genes, which are responsible for the activities, the protection and the homeostasis of the neurovascular unit of the central nervous system [16]. Arachnoid cysts are more frequent in patients with focal epilepsy than in general population but many authors cannot specify if there is a association of epilepsy and arachnoid cysts or it exists a condition that include both [17]. With caution we can keep arachnoid cerebral cysts in mind as an alternative cause of seizures [18]In drug resistant epilepsy and arachnoid cerebral compressive cyst and the epileptic foci is in the cystic region, than microsurgical treatment of the cyst can stop definitive the seizures [19]. Three stigmata (unique palmar fold, epicanthic fold, wiped philtrum, ear defects, ogivala vault etc) can lead to a genetic exam. Thus if we have two stigmata we can the arachnoid cyst as the third, taking it as a stigmata.The COL4A1 was discovered in a mother with arachnoid cyst which have children with genetic porencephaly associated with renal atrophy, hemiparesis and epilepsy in two brothers [20].When cerebral arachnoid cysts are found in twins and are symmetric they need genetic testing [21.]We can have association between Joubert syndrome and cerebral arachnoid cyst [22].There was found an association between Klippel Feil and arachnoid cyst and a single case described in the literature in an adult [23]. In Proteus syndrome can exist syringomyelia and arachnoid cyst an unique association. [24]6-th nerve palsy can be due to an arachnoid cyst [25]. In one child abducens neuropathy was rep[orted to an arachnoid intracerebral cyst [26].Over 30% of the adolescents and adult patients continue to have epileptic seizures despite of the antiepileptic treatment as one drug or in combination [27]. In many types of epilepsies are implicated the inflammatory mechanisms and recent researches try to identify the best treatments which can treat chronic seizures and interfere with the epileptogenic mechanisms[28]. In neurologic pathologies associated to arachnoid cyst are physical therapies and other like logopedia, ludotherapy, group therapy, ABA therapy, therapy with music and all therapies which bring the child to it's higher functioning after diagnosis.Bobath and Vojta therapies can be used in the same patient [29]. Arachnoid cyst diagnosis pannnics often the family of the child. Prognosis depends after the localization and dimensions of the arachnoid cyst, if there exist neurologic pathology or not, if the cyst is paucisymptomatic or not at the moment of diagnosis, if there are genetic syndromes associated and not at least if the family respects the investigation and monitoring plan.In order to grow compliance the work-time of the parents will be respected and there is a flexibility of the consultations adapted to the learning program of the child. If the child makes sport and has arachnoid cyst, it is not contraindicated to continue sport but after a very careful individual evaluation of the case [30].

Experimental part

Material and methods

Because of imaging techniques and the basic life support get each day higher and higher in quality the target of the child neurologist is to get for his patients the highest functioning level possible for each patients given condition, to preserve the functions of the child in the pathologies which the patient must confront with and on the morphologic cerebral restant basis after the injury to develop the most highest possible competences for the patients and its limitations as also for the anticipated complications of the diseases. On the other hand the children must encompass stigma and for this they need social skills which they gain apart from medical treatments through ludo, kineto and psychotherapy. There are not extensive studies yet for the different contexts which are involving arachnoid cysts, and we want to show how arachnoid cyst can be managed in the complex clinical appearance of a child =, where no surgery is needed but a multidisciplinary approach can help the child and family encompass all the difficutlies given by the condition.

This study was made for the first time in the cabinet of neurology from the Children Clinic Emergency Hospital Sfantul Ioan Galati in a 11 case series under clinic-imagistic surveillance and EEG between 2014-2017 .Inclusion criteria in the clinic prsopectiv study were the positive imagistic criteria for arachnoid cysts despite of their localization, form, or the age of diagnosis. The dimesnions of the cyst were measured and when the cyst were greater than 10 mm or the cyst was noted even when the dimesnions were lower than 10 mm in all diameters. Exclusion criteria were other cystic images (for examples hypohysis cystic lesions or other cystic lesions) that were not arachnoid cysts. We analysed the given medication despite it was antiepileptic, antiinflammatory, or for migraine or neurotrophic or for neuroprotection or other pathologies.

Results and discussions

In the study were included 11 children. A male predominance is seen. Figure 2 schows gender repartition in our case series.

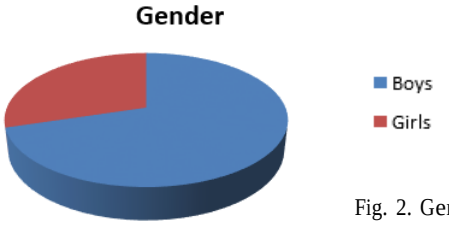

Fig. 2. Gender repartition

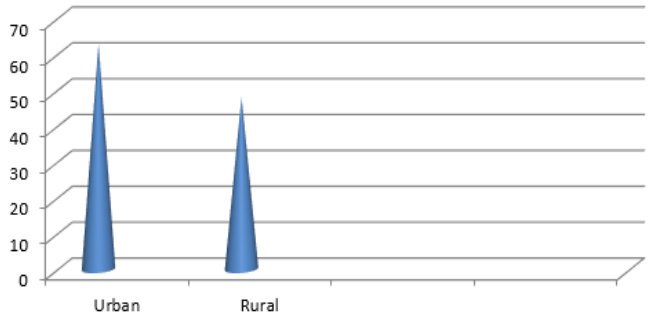

Fig. 3 Medium of provenience

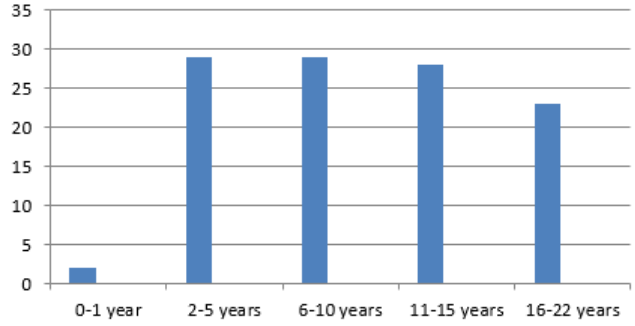

Fig. 4 The age grouping of the children and adolescents having arachnoid cysts in 2014-2017

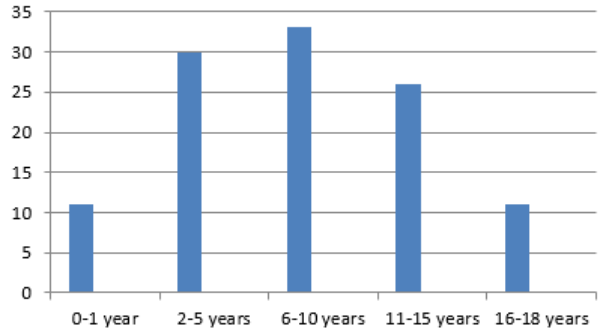

Fig. 5 Age groups of children at the diagnostic moment of the cystic lesions

Medium of provenience:Urban=63 Rural=48 figure 3 shows medium of provenience.

After age groups nowadays with arachnoid cysts the predominance is at the age 6-10 years (29 children) and 2-5 years (29 children) but there are also cases >11-15 year age group(28 children) and respectively 16-22 years (23 children) the lowest frequency is at 0-1 age group(2 children) table 1 shows the age groups of children and adolescents in surveillance with arachnoid cysts in the period 2014-2017 and figure 4 shows the diagram of the age groups of children and adoelscents in surveillance with arachnoid cysts in the period 2014-2017.

Age of the diagnosis is a little different on age groups:6-10 years (33 children) and 2-5 years (30 children) but a great incidence is found also at 11-15 years (26 children) also many are discovered at 16-18 years (11) as also in the little child 0-1 year (11)So table 2 shows ages at diagnosis and figure 5 the chart of ages at diagnostic which differs a little from that of the ages of children in surveillance.

The dimesnions of the cyst We measured in cubic millimeter and had 8 groups: the most often found cysts were the little ones and are retrocerebelous cysts: 1-5.000 mm3 =58 children, 5-10.000 mm 3 =21 children,10-20.000 mm3 =22 children, 20-30.000 mm3 =2 children, 40-40.000 mm3 =2 children, 40-50.000 mm3 =4 children 50-60.000 mm3 =1 child and iar >60.000 is one child with 359.000856 mm3 We take in count the hole cystic mass because there were children with 1,2 or 3 arachnoid cysts. They can exist as combinations between temporal with temporal cysts or temporal with retrocerebellous cyst or bitemporal with retrocerebellous cyst. The great arachnoid cysts we found in the temporal fossa so like they are described in the literature. Figure 6 shows the cystic volumetry distributions.

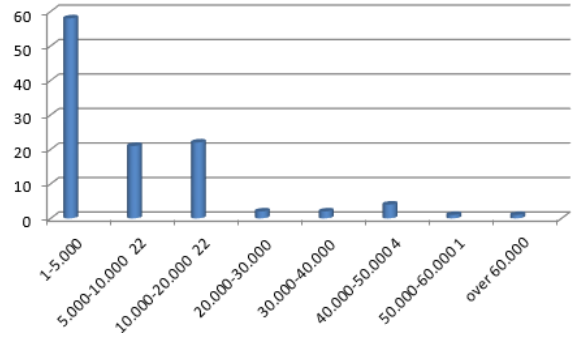

Fig. 6 Cystic volumetry

98 children have had 1 arachnoid cerebral cyst, 8 have had 2 cerebral arachnoid cysts, 5 have had 3 cerebral arachnoid cyst. Localisations were interemisferic, left frontop[arietal, right anterior temporal, temporal suprasellar, retrocereballar, of posterior fossa, pontcerebellar angle, occipital, temporopolar bilateral, frontobasal rightThe mean values of the cyst and the standard deviation of each cyst size are shown in the tables and histograms. Figure 7 is the hystogram of the hole cystic group of 111 subjects.

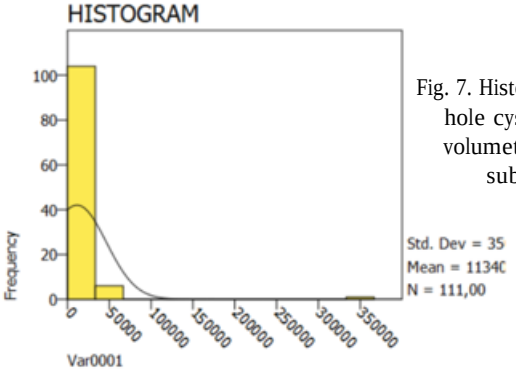

Fig. 7. Histogram of the hole cystic group volumetry of 111 subjects

The second hystogram (fig. 8) shows the distribution between the cyst in the group of cysts with 5.000-10.000 mm^3 and figure 9 that of the cysts between 10.000-20.000 mm^3 .

AGE GROUPS	0-1 year	2-5 year	6-10 year	11-15 year	16-22 year
CHILDREN	2	29	29	28	23

Table 1
AGE GROUPS OF CHILDREN IN SURVEILLANCE WITH ARACHNOID CYSTS IN THE PERIOD 2014-2017

AGE AT DIAGNOSTIC	0-1 year	2-5 years	6-10 years	11-15 years	16-18 years
Children	11	30	33	26	11

Table 2
AGE AT THE DIAGNOSTIC IN CHILDREN AND ADOLESCENTS IN SUSRVEILLANCE BETWEEN 2014-2017

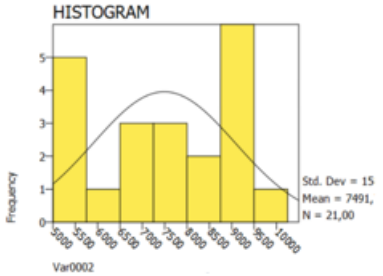

Fig. 8 Distribution between the cysts in the 5.000-10.000 mm^3 cystic group

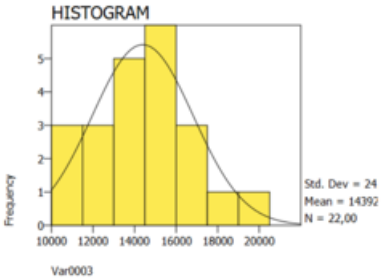

Fig 9 Distribution between the cysts in the 10.000-20.000 mm^3 cystic group

The figure 10 and figure 11 shows the distribution between 20.000-30.000 mm ^{3} cystic group and 30.000-40.000 cystic group and figure 12 between 40.000-50.000 mm^3

Predominant symptoms were headache, but migrains, hemiparesis , triparesis or tetraplegia , voiting and language disturbances and paroxistic phenomena were described but we met also head trauma and endocrinologic disturbances. None of our cases had status epilepticus or coma at presentation.. None of our cases developed psychosis, and none had severe psychiatric symptoms for to need to be in charge in a psychiatric service. Mental retardation was concomitant to (probably) preexisting cerebral palsy, due to perinatal hypoxic ischemic encephalopathy .

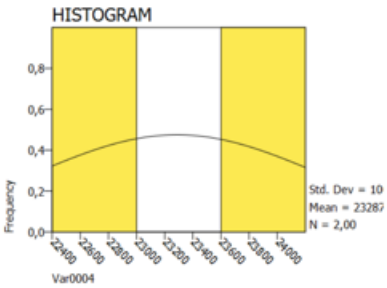

Fig. 10 Distribution between cysts in the 20.000-30.000 mm^3 cystic group

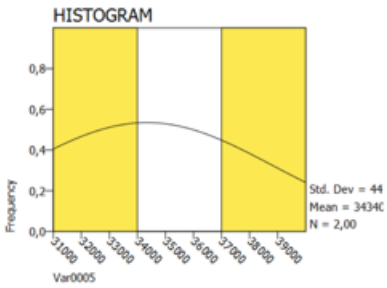

Fig. 11 Distribution between cysts in the 30.000-40.000 mm^3 cystic group

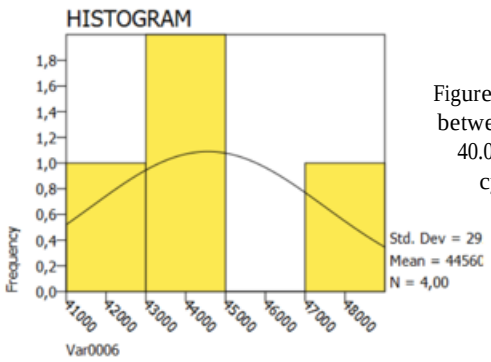

Figure 12 Distribution between cysts in the 40.00-50.000 mm^3 cystic group

Treatament was: antiepileptic drugs after the international guidelines in paractic use for the different types of seizures. Recurrent febrile seizures were treated with valproic acid which is required for 2 years, polimi=orfe tics were treated with Haloperidolum and in migrains anticonvulsivant drugs were associated in little doses, so topiramatum was preferred for migrains in children because of its neuroprotector effect which is associated. 8 children received antiepileptic treatment. First line treatment was valproic acid and Carbamazepine in one case. In two cases biotherapy was needed. EEG and clinical status iprooved at all the 8 children and none of them have seizures any more, but there were patients which have mental retardation associated, learning difficulties, inatention, irritability, which influenced their quality of life. In 4 children with one convulsive episode we maintained indication for diazepam when the child has febrile seizure (intermittent just in the seizure!!!) Antiiinflammatory nonsteroidian treatment was given intermittent in 33 cases for headache or in association for migraine. The treatment is given just in the headache episodes of a intensity that is evaluated bu child and parents and the child is educated to avoid headache and trigger factors like coffe, black tea or sleep deprivation. Antiinflammatory steroid treatment was needed in 4 children with Prednisone and 1 with hemisuccinate thus having all Bells paralysis, one of them the second episode of Bells facial paralysis. All this children became steroid treatment for the Bells paralysis together with vitamins and facial massage, and undergone MRI imaging and arachnoid cyst were found incidentally. Haloperidol received a child with motor tics together with valrpic acid for the modulation of mood and vitamins and psychotherapy and after 4 months the tics ceased without treatment. Benzodiazepins like clonazepam was used for the spasms of crying child and for a child with nocturnl paroxistic events (nonorganic sleep disorders so we denominated them) After 3 montths treatment in minimal doses together with vitamins and family support this symptoms ceased .In one child with migrains we used Topiramatum and in another child with migrains received just antiiinflammatory nonsteroid treatment and was educated to avoid the episodes. Oxybutinine became a child nocturnal enuresis with an incidental diagnosed arachnoid cyst. Acetazolamine was given to a child with recurrent pehomena of intracranial hypertension considered by os not related to the cyst. After two such treated episodes in 6 months he didn't develop any more such episodes and we put the diagnostis benign intracranial hypertension. We gave also different extracts of plants if the anxiety levels didn't need psychiatric treatment and the disturbances needed just psuchological conseilling, changing life style and vitamins. In 13 cases child was just put under surveillance, the presenting symptoms being transitory , not perisisting and family was educated how to observe and educate the child and to come back when new symptoms appear and to come to periodic controls even if there not exist symptoms. Neurotrophic agents were used in combination with physical tehrapies and logopedia in 28 of children under our surveillance. B bomplex vitamin helps the neuronal metabolism,then Guarana Rhodiola was also given, gingko biloba in little and intermittent doses. Aminoacids were given with caution for the kidney function of the little children not to be affected .Extract of calf brain has superoxiddysmutase and helps the metabolic cycle of

glucose and has also pediatric use. The oral posology is an advantage and so we avoid the trauma of injection in children. Piracetam is good for memory and the Gabaergic functions , and products that higher the metabolism of the phosphatidilcholine are also of good effect. Neurotrophic treatment as used secventially not to get a too high excitability of the cortex or not to lower the effect one to each of the substances used. A special attention is given to Calcium and magnesium supply. Lipotimia is very spectacular in children and the worries of a family whiuch think to a neurologic or cardiac cause of the lipotimia to a child are very great and the real diagnosis is hard to put and need great attention from the patient itself , the family and the doctor. Chwostek sign is in many cases positive even if lab blood values of the main iones of the child are normally, but at the interstitial level this elements can be disturbed, so a rational suplly in this elements is of real benefit for the child.

Conclusions

The formulation of a diagnosis of epilepsy must be done with great responsibility because of many parioxistic events where can exist associated arachnoid cysts, but we can have associate particularly family structures , because of the parents working places, so the waiting of the next paroxistic events and observing of the child is a wise attitude. Periodic controls bring their anatomoclinic utility so we see the cyst size and seriated EEG but we can catch ear nose problems otherwise underdiagnosed (sphenoidal sinusitis ethmoiditis) Because of the work on this paper children diagnosed in other places came to us to ask for an advice for the future care of their child. Parents forums must be encouraged even with the risk not always to beapparently favourable for the relation patient-doctor, but so we can grow the networking between sopecialists and parents ahd have better groups of support which can help famliies to accept and manage the status of their children despite of the degree of their disturbances. The smile of a child is always the same with or without ar

The widening of the pericerebral spaces can mean a more subtle pathology associated to arachnoid cerebral cysts in children and in future the association with facieal dwarfism must me held unter surveillance. The cysts greater than 40 mm oligosymptomatic are under neurosurgical surveillance but we can send to the neurosurgeon all the cysts greater than 35 mm in one of the axes, but over 40 mm they can become surgical cysts. In the case when the parents are opposing to the operation we must say them the risk of non-operating, we have had one patient in this situation and nothing worsened in his situation, also his results in school was of high performance. In our case no treatment was needed in the situation of the child just the cyst was under surveillance and we told the parents not to give excitants like chocolate, to avoid sport and head-trauma. In cerebral palsy the arachnid cyst can be incidental , because cerebral palsy is due to prematurity, disturbances of intrauterine growth, intrauterine strokes. When the parents detect the existence of the arachnoid cysts we must reduce their panic. It can happen because nowadays premature babies benefit from maternity of seriated transfontanelar echography, and the spontaneous appearance of a arachnoid cyst is of low probability but cannot be excluded. Children which made sports and have had different pathologies (faintness, unique convulsion) has interrupted sports 1-2 months and afterthat they were allowed to continue moderate exercises but there were excluded sport of contact but in particular situations some children went further to performance sport.

Because of the observed changes like the modifications of the vascularization found in children we can make angio-MRI studies on selected cases. All children which associate facial dwarfism, malformations of the intern organs or dwarfism with familial arachnoid cerebral cysts and/or epilepsy must be investigated by the geneticist and have a separate evidence for the prognosis per se of the child but also for the other family members, if the parents are quite young and want another child and will be advised to test themselves and in some cases the testing is beneficial for the parents for to see the prognosis of the pathology they can have (for example operated spina bifida associated to arachnoid cyst in one of the parents).In the associated neuronal migration disorderlike hemihipertrophy a examination in 3 Tesla MRI is needed to seek also other malformations, they can go to the genetician for genetic advice given to the parents but also to the family. In metabolic disorders form the basic panel the measurement of ammoniemiawhen the child has convulsions, and in the modern therapy the child is evaluated for his hyper amoniemia when we want to introduce valproic acid. If we have ahyperammoniemia de novo we can explore the child for an aminoacidopathy, the following lab tests are urinary aminoacids, electrophoresis of proteins and homocysteine, methylmalonic aciduria. Bilateral arachnoid cysts can be markers for a chronic hyperammoniemia. In twins we can study the presence of arachnoid cysts in the other twin. In the pregnant there wasn't researche with arachnoid cysts and if the pregnancy is influenced by the existence of a cerebral arachnoid cyst, and if the pregnant women knows of the existence of a arachnoid cerebral cyst, it is carefully to consult a geneticist and to have a planed pregnancy. This must be explained to the adolescent girls because pregnancy in teenagers is a public health problem.

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