Brain Tumors with early childhood onset: Three Cases Reports

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Résumé :

Introduction : les tumeurs cérébrales de découverte précoce chez l'enfant sont principalement congénitales (TCC). Elles sont le plus souvent définies comme des tumeurs diagnostiquées dans les premiers 60 jours de vie. Elles sont extrêmement rares et ne représentent que 0,5 à 4% de toutes les tumeurs cérébrales de l'enfant. L'approche diagnostique et thérapeutique n'est pas encore consensuelle malgré plusieurs études. Nous avons rapporté les cas de CBT gérés dans notre unité.

Patients et méthodes : Une étude rétrospective sur quinze ans (2001-2015) concernant les patients avec TCC hospitalisés dans notre unité. Les données cliniques, radiologiques et histopathologiques ont été étudiées.

Résultats : Nous avons recensé trois cas de TCC, deux garçons et une fille. Le diagnostic a été effectué au cours de la période postnatale pour les trois cas. La TCC a été révélée par un état de mal convulsif réfractaire survenu au premier jour de vie pour le premier cas, un retard de la marche pour le deuxième cas (à 18 mois) et un bombement des fontanelles à deux mois de vie pour le troisième cas. Le diagnostic histologique chez le premier patient a révélé un astrocytome pilocytique grade I et l'évolution a abouti à un état végétatif après résection retardée de la tumeur (8 mois). Le deuxième patient avait un épendymome grade II et a subi une résection réussie de la tumeur et est encore vivant avec des troubles de concentration. Dans le troisième cas c'était un astrocytome desmoplastique infantile grade I, la chirurgie a été effectuée avec succès à deux mois et 26 jours de la vie.

Conclusion: Cette étude met le point sur les difficultés diagnostiques anténatales et néonatales et thérapeutiques des TCC, et rappellent les caractéristiques histologiques et évolutives des CBT. D'autres études sont nécessaires pour clarifier ses caractéristiques cliniques et établir des recommandations thérapeutiques pour une prise en charge optimale.

Abstract

Background and aims : Brain Tumors with early childhood onset are mostly congenital (CBTs). They are most often, defined, as tumors presenting within 60 days after birth, are extremely rare. Even after several investigations have been performed, a clear direction for diagnosis and treatment of fetal intracranial tumors is still lacking. We reviewed the cases of CBTs managed in our unit.

Methods : A 15-year retrospective study (2001-2015) of the cases of CBTs hospitalized in our unit was performed. Clinical, radiological with magnetic resonance imaging, histopathological findings and outcome were analyzed.

Results : We identified three cases of CBT diagnosed in two male and one female infant. The diagnosis was performed in postnatal period for the three cases. CBT was revealed by refractory status epilepticus at day one of life for first newborn, delayed walking for the second newborn (at 18 months) and bulging fontanels at two months of life for the third newborn. Clinical outcome in the first case with pilocytic astrocytoma grade I diagnosis resulted in vegetative state after delayed resection of the tumor (8 months). The second patient with ependymoma grade II underwent successful resection of the tumor and is still alive with concentration disorders. In the third case with infantile desmoplastic astrocytoma grade I diagnosis, surgery was successfully performed at two months 26 days of life.

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Conclusion : This study sheds light on the difficulty of prenatal diagnosis, neonatal diagnostic, histological, prognostic, and therapeutic characteristics of CBTs. Further studies are needed to clarify its clinical characteristics and establish recommendations for management.

Mots clés : nouveau-né - néoplasie – tumeurs cérébrales – congénitale -

Key words : brain stem neoplasms – primary – congenital – tumors – intracranial –newborn – infant

BACKGROUND AND AIMS:

Brain Tumors are the most common solid tumors in children. Brain Tumors with early childhood onset are mainly congenital (CBTs). They are most often, defined, as tumors presenting within 60 days after birth, are extremely rare and account for only 0.5 to 4% of all pediatric brain tumors.
The astrocytomas then embryonal tumors and ependymomas are the most frequent histological types. We report three cases of brain tumors with early postnatal revelation.

METHODS:

We performed 15-year retrospective descriptive monocentric study of the cases of CBTs managed in the Neonatal Resuscitation and Intensive Care Unit in coordination with the department of Neurosurgery in Military Hospital of Tunis between 2001 and 2015. We included all patients for whom the histologic diagnosis of CBT was made regardless the age of declaration. We excluded other solid tumors localized elsewhere. Clinical, radiological with magnetic resonance imaging (MRI), intraoperative surgical and histopathological findings and outcome were analyzed.

RESULTS:

We identified three patients with CBT, one female and two male infants. The three patients here described represented 0.16 ‰ of all hospitalization and three of the five cases of congenital solid tumors managed in our unit during the study period.

Case 1 : a male newborn was hospitalized at birth for status epilepticus. The pregnancy was uneventful and birth was at term by programmed caesarean section with 9/10 Apgar score. He was eutrophic with a head circumference of 36 cm. The newborn presented at 15 minutes of life a rebellious status epilepticus of koejewnikoff kind. Brain MRI (day 4 of life) objectified an intra-ventricular expanding process in fourth ventricle extended to the left Lusaka hole measuring 23 by 30 cm (figure 1).

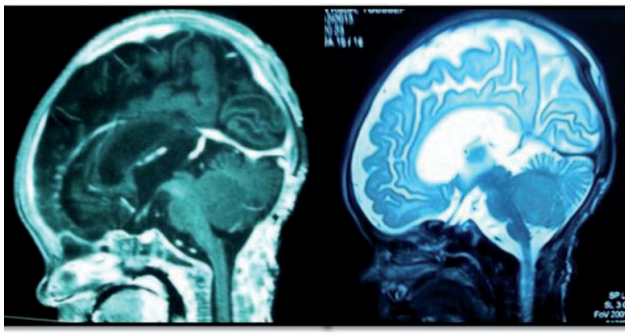

Figure 1: MRI at Day 4: Expanding process of the posterior fossa

Surgical excision tempted at day 35 of life has not been completed because of a severe hemorrhagic that stroke from the incision. The evolution was marked by the occurrence of a refractory fixed convulsive encephalopathy. At seven months, another head MRI was performed and showed a subtentorial process with cortical atrophy (figure 2).

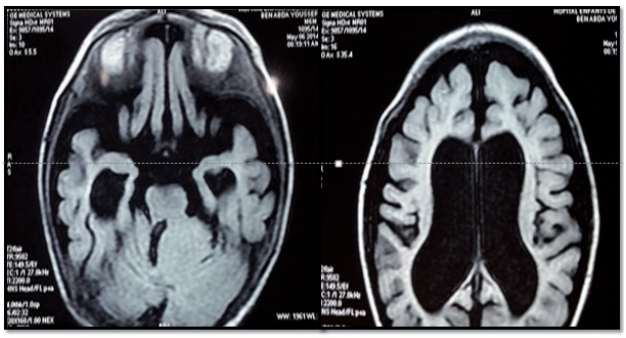

Figure 2: Head MRI (T1) at 7 months:
Infra-tentorial process with dilation of the 4th ventricle and cortical atrophy

Neurosurgery was performed at eight months of life. Pathological examination concluded to a pilocytic astrocytoma grade I (WHO classification). After a two-year evolution, the infant kept a neuro-vegetative state even palsy was relatively stable.

Case 2 : a male newborn was hospitalized at birth for supervising of a diabetic mother newborn. Birth was vaginal and at term with 9-10 Apgar score. Physical examination was normal and weight, height and head circumference (35 cm) were congruent. Monitoring and screening were normal and the infant was released after 24 hours. Subsequent control noted frequent falls and a left foot external rotation while stepping from the age of 11 months without signs of intracranial hypertension. A delayed walking, which was acquired at 18 months was also noted. The growth of head circumference, the rest of psychomotor development and physical examination were normal. A brain MRI performed at the age of 2 years and 3 months objectified a tumor in the posterior fossa associated with ventricular sorting hydrocephalus (figure 3).

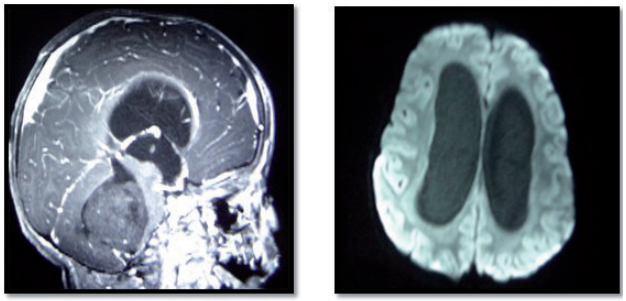

Figure 3: Head and medullar MRI: (a- Axial section, b- Sagittal section)
Tumor of the posterior fossa and triventricular hydrocephalus

Complete tumor resection was performed at the age of 2 years and 3 months. Pathological examination concluded to an ependymoma grade II (WHO classification). The postoperative course was uneventful with rapid acquisition of a more stable walking. After four years, the child kept only minor learning and concentration disabilities.

Case 3 : a female infant was admitted at the age of two months and 25 days of life for a brain-tumor perioperative care. The pregnancy was uneventful. The birth was vaginal, at term and took place without incidents. Head circumference at birth was not mentioned. At the age of two months, her mother noted a 'big cranium'. Physical examination showed intracranial hypertension signs (sunset-looking and bulging fontanel), no eye-pursuit, non-reflective pupils and abnormal upper limbs movements. Brain MRI revealed a supra-tentorial tissue process in the right hemisphere with cerebral herniation (mass effect) and active supra-tentorial hydrocephalus (figures 4 and 5).

Tumor complete resection was carried out at the age of 2 months and 26 days.

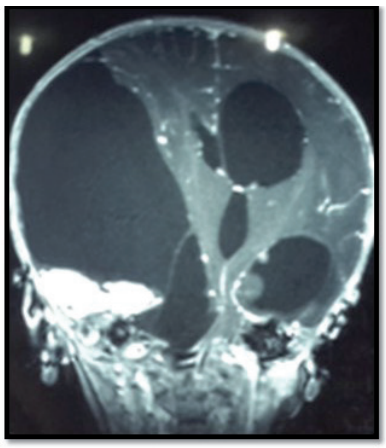

Figure 4: Head MRI at 2 months and 25 days: (Diffusion axial section)
Supratentorial right tumoral process with mass effect

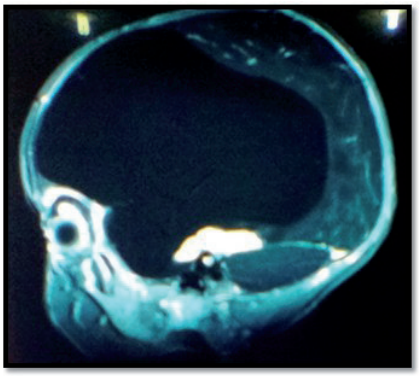

Figure 5: Head MRI at 2 months and 25 days: (sagittal T1 section)
Supratentorial right tumoral process with mass effect

Histological study concluded to a desmoplastic infantile astrocytoma grade I (WHO classification). After two years, the infant has a sequelar motor retardation with an adequate psychic development (good connection) and no seizures occurred under anticonvulsive therapy (Valproic acid).

COMMENTS:

Classification

The first cases of brain tumors ever reported in newborns were in 1951 (1). They were identified as expanding processes that break-out within two months of life and they were defined as congenital (2, 3). Numerous classifications were held so CBTs were distributed into three groups. The first: definitely congenital, tumors diagnosed immediately after birth (case 1 in our sample); the second: probably congenital, those who became symptomatic within seven days of life; the third: possibly congenital, those discovered after few months (2) (case 3 in our sample). Other authors suggested later to include infants older than 12 months whose initial signs began within the first year (case 2 in our sample for whom histological findings confirmed the congenital nature). Although such classifications were unfounded, there was no doubt that tumors presenting at birth are congenital. Thereafter, their congenital origin correlation weakens with increasing delay between birth and onset (2).

Epidemiology:

The CBT are known to be extremely rare (2,4). In fact, only three cases were noted through the last fifteen years with a very low prevalence of 0.16 ‰ of all hospitalization. In literature, total neonatal rates from malignancies are extremely rare according to multiple studies. They were estimated to 1 per 6.24 million live births (2). CBTs represented 7.2% to 10.9% of all perinatal tumors and 0.4 to 1.5 % of all pediatric tumors (2,3,5,6).
Some authors reported that maternal smoking, diet and infections may increase risk of developing neonatal brain tumors (3). Thus, this causal link statement needs further researches. However, genetic predispositions as part of neurofibromatosis,

Li-Fraumeni, von Hippel-Lindau, Tuberous sclerosis are surely involved (2). In our study, the pregnancies were uneventful suggesting the lack of any acquired predisposing factors. Furthermore, there was no statistically significant sex predilection according to larger surveys (2,4).

Clinical features:

The antenatal diagnosis was negative for the three patients here described. Although, simple antenatal ultrasound scan could be sufficient to show intracranial mass, abnormal echogenicity in the head, macrocephaly and/or hydrocephalus (1,6). These abnormalities would be confirmed by performing fetal MRI. Clinical symptoms were nonspecific and began in perinatal and neonatal periods and the first recognizable sign is often macrocephaly defined as increasing head circumference. It may be the result of hydrocephalus or the size of the tumor mass or both (2,5,7). Only one of patients described presented increased intracranial pressure signs (bulging fontanel, sunset look, vomiting, papilledema). Authors noted that these signs are infrequent because in neonates as freely expanding calvaria can accommodate a volume excess (7). Some other series reported frequent increased intracranial pressure at onset (2,6,8). Atypically, in one case we found a unilateral stepping abnormality. In this sense, focal neurologic changes were absent in most cases of neonatal brain tumor despite the large head size and hydrocephalus (2,7).

Imaging features:

All the three patient were diagnosed with MRI, and no-one had CT although tumor calcifications could be spotted easier on CT. MRI have all proved useful for displaying these lesions suitably for surgery through its multiple imaging planes and absence of bone artifact, better delineated the extent of the tumor, especially within the posterior fossa (5).
The majority of our cases (two out of three) were supratentorial which was in accordance with other surveys findings (60 %) (3).

Histopathological findings:

For brain tumors, gliomas are the most frequent (56.9%) especially astrocytomas (cases 1 and 3 in our sample) and other neuroepithelial tumors (37%) such as ependymomas (case 2 in our sample), choroid plexus papillomas, medulloblastoma, and pineoblastoma (1).Tumors originating from meninges, peripheral nerves, and craniopharyngiomas were rare, accounting for only 4% (1).
All three cases were defined as grade I and II of the WHO classification (9) and consequently considered as benign unlike grade III and IV that had been considered as aggressive/malignant and they subsequently had worse outcomes.

Management:

The mainstay of the treatment in CBT is surgery (7,10). It is based on the widest possible surgical excision; it affects the prognosis, even more than histologic grade. When functionally possible, complete resection should be the aim. Surgery can be technically challenging, if possible at all, and the sensitivity of the developing nervous system to the side-effects of radio- and chemotherapy has limited their utility as adjunctive treatments (7). The risk/benefit equation in the planning of treatment of neonatal tumors using these modalities is further complicated by the fact that these tumors are often histologically benign, of large dimensions, but are often situated in locations that lead to a fatal outcome (1).
In one of these cases reports, surgery was delayed because of a massive hemorrhage, which agreed with authors who noted that the prevalence of spontaneous bleeding into the tumor mass was high (18 %) (5).

Prognosis:

The prognosis is guarded in all neonates with brain tumors (3), despite modern imaging methods and surgery, probably because of the large size. Thus, the entire cranial cavity may be filled with the tumoral mass.
The most common outcome of a CBT in neonatal patients is death within five years of diagnosis. The overall survival rate was 14 to 28% (2,6,7). However, the survivors are likely to suffer long-term morbidity (Cerebral palsy, seizures and learning/concentration troubles) (1,10). Astrocytomas had a favourable prognosis (4). In our survey both patients with astrocytomas survived the first year but had sequelar neurological disorders.

CONCLUSION

We reviewed the epidemiological facts, diagnosis, treatment and outcomes of intracranial tumors in neonates. The apparent prevalence and age distribution of CBT are changing with an earlier referral and diagnosis made possible with the advance of neuro-imaging. Pediatrician-neonatologist and pediatric neurosurgeons are major co-executives in the management of these tumors that should be held in experimented multidisciplinary centers.

Antenatal diagnosis could offer more therapeutic options and better outcomes, but and it is unfortunately still lacking. The true incidence, the influence of genetic and environmental factors as well as histological and biological properties should been clarified by further multicentric studies.

Conflicts of interest:

The authors declared no potential conflicts of interest with respect to the authorship and/or publication of this article.

Abréviations :

Congenital Brain Tumors: CBT, Magnetic resonance imaging: MRI
World Health Organization: WHO

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