Original Article

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Congenital Brain Tumors, A Series of Seven Patients

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Abstract

Objective: Congenital brain tumors are very rare. We review these tumors in patients younger than 2 months diagnosed in our Department.

Material & Methods: Seven congenital brain tumors were diagnosed during five years. Clinical and radiological findings and prognosis are analyzed.

Findings: The study included 5 female and two male infants. Two cases were diagnosed antenatally by means of ultrasonography. All patients presented with intracranial hypertension. The tumor was non-homogenous with cystic and solid components in all neuroimaging, except for the case with choroid plexus papilloma. Hydrocephalus was evident in all of them. Most findings were infra-tentorial lesions. There were three teratomas, one primitive neuro-ectodermal tumor, one ependymoblastoma and one choroid plexus papilloma. Six patients were operated on, with one intra-operative death. Two passed away postoperatively with aspiration pneumonia. One patient died due to complications of chemotherapy and another one due to tumor recurrence one year after surgery. Only the patient with choroid plexus papilloma is alive after 2 years.

Conclusion: Today, the availability of noninvasive imaging procedures such as computerized tomography scan and magnetic resonance imaging has improved the diagnosis of congenital brain tumors. Inspite of development in prenatal diagnosis, appropriate pre and post operative management, the mortality associated with these tumors still remains high. The final prognosis in these patients is still discouraging despite early surgery and operative and anesthetic improvements. Choroid plexus papilloma accompanies the best prognosis, whereas teratoma and primitive neuroectodermal tumors have the worst prognosis.

Key Words: Congenital brain tumor, Teratoma, Imaging, Prognosis, Adjuvant therapy

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Introduction

Brain tumors presenting within sixty days after birth are rare and are considered as congenital. They differ from intracranial tumors occurring in older children and adults in their mode of presentation, location, biological behavior, response to therapy and histological types[1]. Whatever the cause and nature, the overall prognosis has been poor, as the outcome is largely related to the size and location of tumor, the general condition of the infant at the time of diagnosis, surgical resectability, and limitations of adjuvant therapy[1,2]. Remarkable advancement in diagnostic techniques for early and on time diagnosis of these special tumors has been made, but still the outcome is generally poor. The younger age of the patients, absence of a well accepted protocol along with the approach of the child's parents make the management more challenging and difficult to deal with. We present a case series, which includes seven infants who were diagnosed of having intracranial neoplasm in the first 60 days of life. We have also tried to highlight the most common signs and symptoms, location, poor outcome along with treatment limitations.

Material & Methods

A retrospective study was conducted in the neurosurgery department of Children's Medical Center in Tehran for cases referred from July 2000 to 2005. During this period, 7 cases of congenital brain tumors were admitted. The patients were included on the basis of the age at which the symptoms developed, rather than the age of referral. Data was collected from hospital records. The results were analyzed for age at the beginning of symptoms and signs, age on the day of admission, sex, location of the lesion (as interpreted by computerized tomography scan [CT] or magnetic resonance imaging [MRI] findings), serum and cerebrospinal fluid (CSF) alpha feto-protein (αFP) levels, histopathology, treatment modality including surgery or chemotherapy and their related complications, the duration of hospital stay, condition of the patient at the time of discharge and the final outcome.

Findings

The study included 7 infants, with female to male ratio of 5:2. The mode of delivery was normal vaginal for 4 cases and cesarean section for 3. The age of the patients at the onset of symptoms varied from 1 day to 1 month (mean 17 days). The age on hospital admission was 10 days to 3 months (mean 45 days). The symptoms had developed 10 days to 2 months (mean 27 days) before admission. All patients presented with intracranial hypertension (Table 1). Apart from hydrocephalus, no other external congenital anomalies were found. The most common presenting signs and symptoms were head enlargement (7 patients), tense and bulging fontanel (6 patients), persistent vomiting (5 patients), poor feeding (5 patients), decreased neonatal reflexes (5 patients), decreased gag reflex (3 patients), sunset eyes (3 patients), seizures (3 patients), respiratory signs and symptoms (2 patients) and fever (2 patients).

Prenatal diagnosis has been done in two cases by ultrasound. The initial diagnosis for all seven cases was made by CT scan. In six of them MRI was further performed to reveal the exact location and the characteristics of the lesion. Hydrocephalus was evident in all imaging (Fig. 1). The tumor was non-homogenous with cystic and solid components consisting of hypo-, iso-, and hyper-dense masses in six CT scans (Fig. 2). Amorphous pointed calcifications were found in 3 cases who were later diagnosed as teratoma (2 cases) and one with ependymoblastoma. Hemorrhage was found in the case with third ventricle teratoma extending to both lateral ventricles (Fig. 3A-C). Only the case with choroid plexus papilloma (CPP) showed a homogenous isodense lesion (Fig. 4). The majority of tumors showed a non-homogenous enhancement after contrast medium injection (Fig. 5).

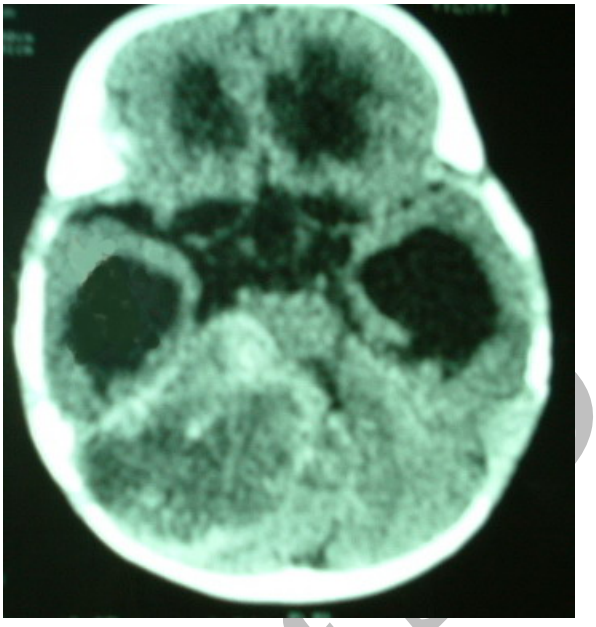

Fig. 1. Ependymoblastoma of CP angle with fourth ventricle involvement. Computed tomography scan shows a large non-homogenous mass with scattered calcifications and severe hydrocephalus.

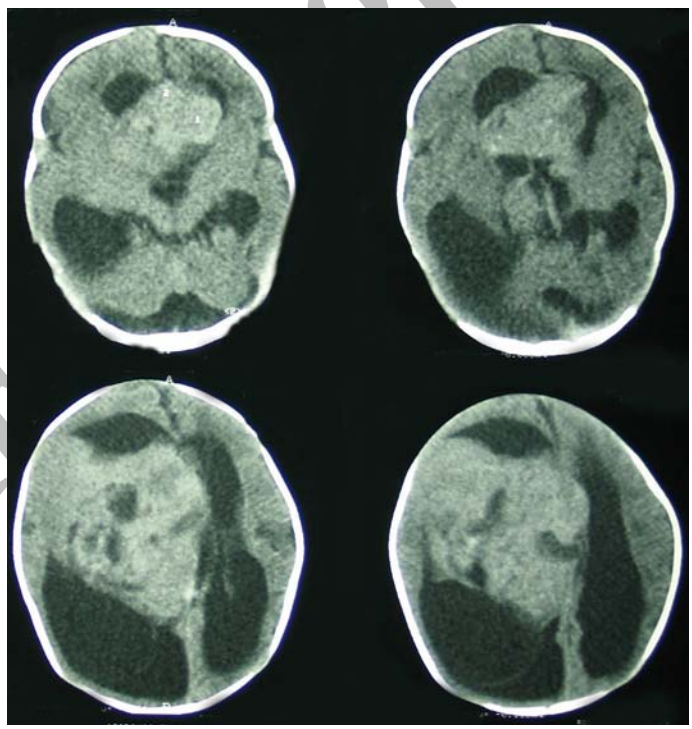

Fig. 2. Cranial CT scan in axial views shows a large non-homogenous right ventricular mass with cystic and solid components which are hypo-, iso-, and hyper-dense along with pointed calcification and severe hydrocephalus

No	Age (day)		Initial symptoms and signs	CT scan findings	MRI findings	Location	Pathology	Treatment	Hospital stay (d)	*Outcome*
	Presentation	Admission								
1	15	30	↑HC, RICP PF, Seizure LCNP	Hydrocephalus, Non-homogenous mass	Hydrocephalus, Non-homogenous mass	IT (Fourth ventricle)	unknown	EVD	6	***Pre-operative death***
2	1	15	↑HC, RICP, PF	Hydrocephalus, Non-homogenous mass, calcification	Hydrocephalus, Non-homogenous mass	ST (Lateral ventricle)	Mature Teratoma	EVD+GTR	4	***Intra-operative death***
3	28	90	↑HC, RICP	Hydrocephalus, Homogenous mass	Hydrocephalus, Isointense-T1, Hyperintense-T2, Homogenous enhancement	ST (third ventricle) Lateral ventricle extension	CPP	EVD+GTR	13	***Alive after 2 years without tumor***
4	30	58	↑HC, RICP, PF	Hydrocephalus, Non-homogenous mass, intratumor hemorrhage	---	ST (third ventricle) Lateral ventricle extension	Atypical Teratoma	EVD+GTR	29	***Chemo-therapeutic complications and death***
5	14	22	↑HC,RICP, Fever, PF, Seizure, LCNP,FNP	Hydrocephalus, Non-homogenous mass, Non-homogenous enhancement	Hydrocephalus, Non-homogenous mass, Non-homogenous enhancement	IT (Fourth ventricle) ST extension	PNET	EVD+STR	27	***Post-operative aspiration pneumonia and death***
6	1	11	↑HC, RICP, PF, LCNP	Hydrocephalus, Non-homogenous mass, Non-homogenous enhancement, calcification	Hydrocephalus, Non-homogenous mass, Non-homogenous enhancement	IT (Fourth ventricle) ST extension	Atypical Teratoma	EVD+STR +VPS	50	***Tumor recurrence after one year and death***
7	30	89	↑HC, RICP, PF, LCNP, FNP	Hydrocephalus, Non-homogenous mass, Non-homogenous enhancement, calcification	Hydrocephalus, Non-homogenous mass, Mixed signal intensity	IT (CP angle) Fourth ventricle extension	Ependymoblastoma	EVD+STR	28	***Post-operative aspiration pneumonia and death***

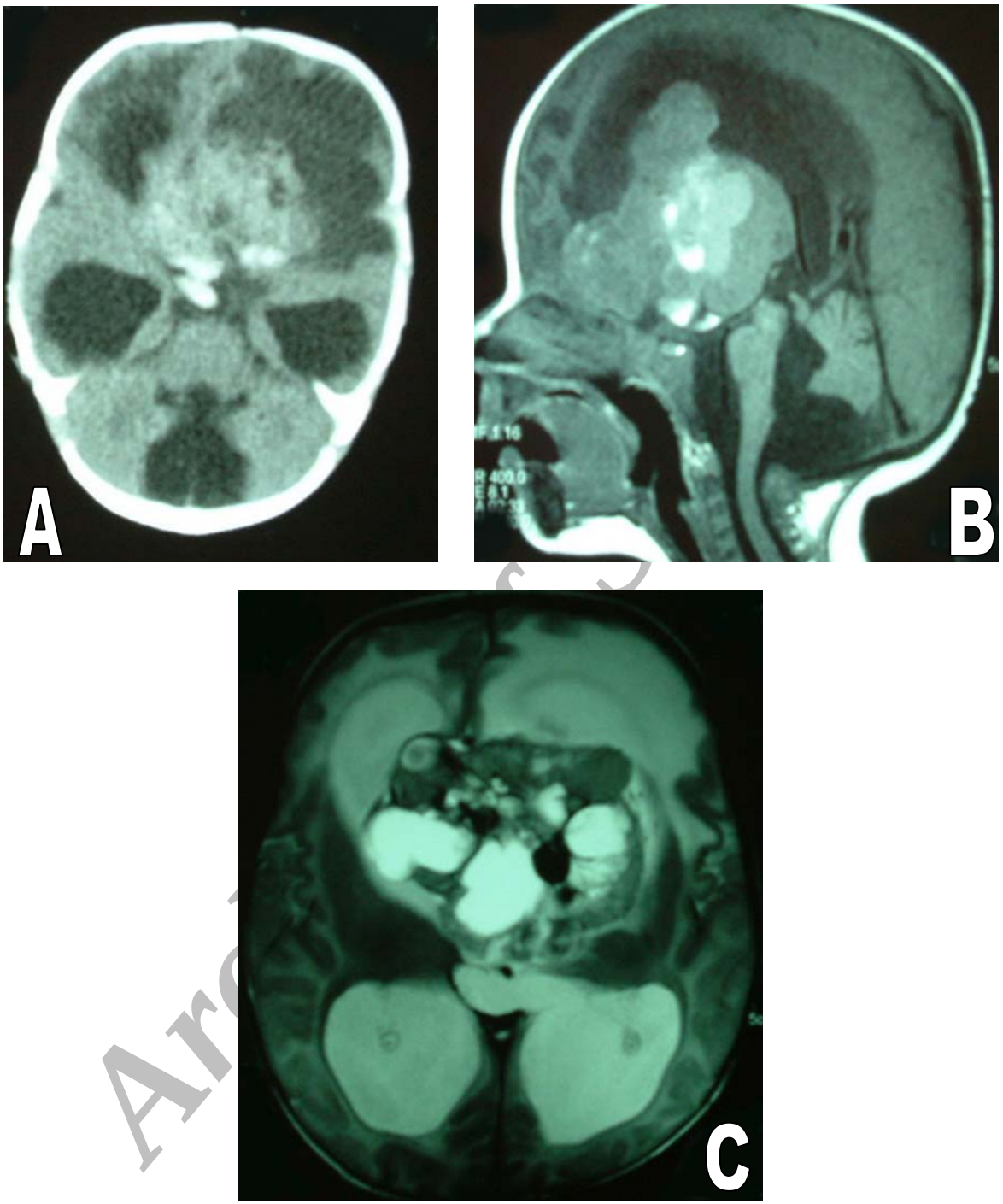

Fig. 3. A. Cranial CT scan in the axial plane reveals a lobulated non-homogenous mass. The hyperdense patches inside the tumor are suggestive of hemorrhage that was confirmed intraoperatively. Histologically, the tumor was an immature teratoma. B. T1-weighted, sagittal view and 3. axial view of this patient's MRI demonstrating different components of the tumor

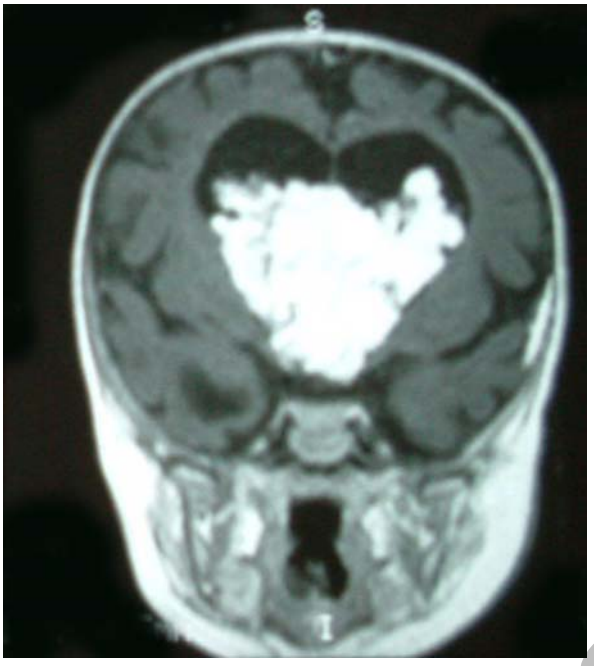

Fig. 4. Congenital choroid plexus papilloma is displayed. T1-weighted magnetic resonance imaging with gadolinium enhancement shows a cauliflower-like mass filling the dilated third ventricle and its extension to both lateral ventricles with homogenous enhancement.

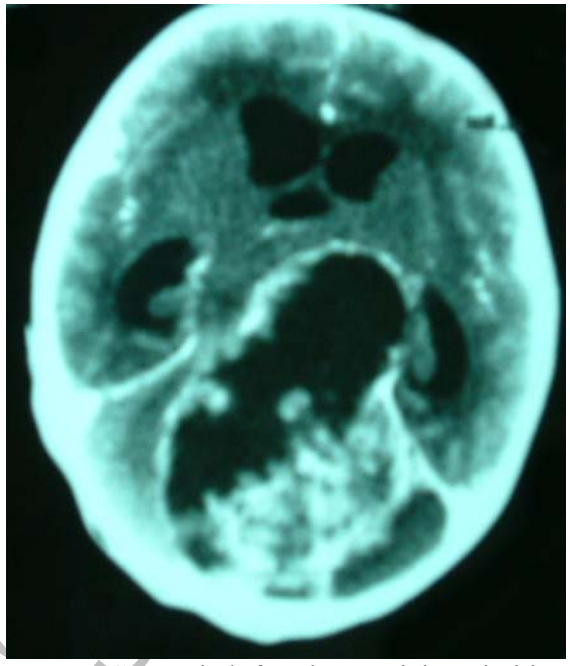

Fig. 5. Congenital fourth ventricle primitive neuroectodermal tumor. CT scan reveals a large non-homogenously enhancing mass, along with a large cyst filling the posterior fossa and extending to supratentorial area accompanied with anterior displacement of the third ventricle and severe hydrocephalus.

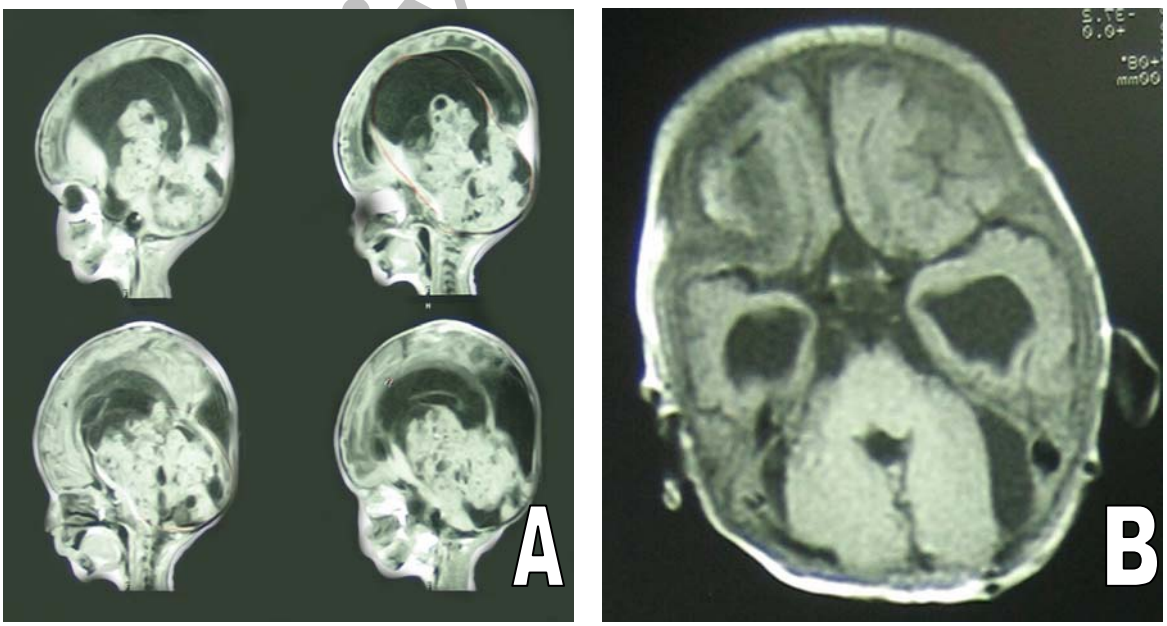

Fig. 6. A. Sagital T1-weighted MR images show a large mass with heterogeneous signal intensity arising from the fourth ventricle filling all infratentorial space with extension to supratentorial area with protrusion into the lateral ventricles, the severe brain stem compression due to the mass is worth noticing, which was well decompressed postoperatively (B).

MRI demonstrated mixed signal intensity (Fig. 6) in 4 of the 6 cases.

As far as the location of the tumor is considered, all were intraventricular. The tumor was purely supratentorial in 3 cases and infratentorial in 4. Two tumors originally infratentorial extended to the supratentorial region.

In 2 patients with teratoma αFP level was high in serum and CSF taken from the lateral ventricle. External ventricular drainage (EVD) was inserted in all cases pre-operatively to decrease the intracranial pressure (ICP) before main surgery. Surgical approach to the tumor was performed in 6 cases, in only 4 of these, a total resection was possible. In the remaining 2, subtotal resection was done due to the attachment of the tumor mass with the fourth ventricular floor. Only one patient required shunting post-operatively. In the rest of them, hydrocephalus was managed temporarily with EVD. The most common pathology was teratoma (Table 1), whereas for one case no specific pathological diagnosis could be made due to severe necrosis of the brain tissue at the time of autopsy done 4 days after being declared as brain dead.

One of the patients expired before operation, subsequent to intractable seizures, inspite of good management of intracranial hypertension. Another passed away in the operation theater after total resection of the mass due to severe blood loss. Two infants expired post-operatively in the pediatric intensive care unit due to aspiration pneumonia caused by lower cranial nerves dysfunction. One passed away due to the refusal of parents for further treatment of a totally resected immature teratoma which recurred one year later. One of the patients died three months after tumor resection due to complications of chemotherapy (anemia and leukopenia). The duration of hospital stay varied from 4 to 50 days (mean 22). Only the case with CPP is alive with good development and without any intracranial problems two years after surgery.

Discussion

Although congenital intracranial tumors are uncommon and rarely reported, the medical, social, and emotional effects caused by them cannot be overlooked. According to the definition proposed by Arnstein et al., tumors that present within 2 months after birth are considered congenital[3]. These have also been sub-classified into three categories; definitely congenital tumors, those presenting or producing symptoms at birth; probably congenital within the first week of life; and possibly congenital within the first months of life[3].

These tumors comprise 18% of brain tumors presenting during the first year of life and only about 0.5-1.5 % of those in childhood[3]. Approximately 10% of all perinatal tumors arise from brain, as compared with tumors in other sites diagnosed in the perinatal period. Overall, central nervous system neoplasms are the cause of 5-20% of deaths in the fetal and neonatal period[1].

As the number of cases referred and diagnosed is trivial, only a few series about them have been published so far. Their mode of presentation, location, histology, behavior, response to therapy and outcome all differ from those of older children and adults. These unique and specific characteristics make them to be classified separately.

Congenital intracranial tumors manifest clinically in several ways. Sometimes they are detected incidentally on routine prenatal ultrasonography. Cases born with these tumors frequently present with a large head, bulging fontanel, vomiting, irritability, seizures, flaccidity, hypotonia, cranial nerve palsy, eye signs (sunset eyes, strabismus), wheezing and regurgitation. Among the patients referred to our center, large head and signs of increased ICP were present in all. These have also been reported as the most common findings in other studies, which are not at all related to histology and location of the tumor [1]. The reason can be the tumor mass itself, which fills intracranial space and distorts normal structures, hydro-cephalus caused by an intraventricular lesion leading to CSF flow disturbance, or due to

associated tumor hemorrhage which is reported to be 14-18%[3,4].

Neonates and infants with rapidly growing neoplasm often exhibit signs of increased ICP with a possible delay, which results from the immaturity of the brain, the ability of the infant's skull to expand and accommodate the rising ICP and the incapability of these patients to complain specific symptoms. These not only delay the diagnosis but also give the tumor ample time to expand and fill most of intracranial space, making surgical resection nearly impossible[5].

Thus, neonates presenting with an abnormal increasing head circumference with or without signs of rising ICP should have an urgent neuro-imaging, at least cranial ultrasound, to rule out intracranial pathology. Among other clinical findings, facial and lower cranial nerve palsies have a specific importance which can help in localization of tumor mass. We only found these deficits in infratentorial lesions.

Fever was observed in 2 cases. As a systemic manifestation of brain tumors it can occur secondary to tumor hemorrhage or necrosis, depositing blood or necrotic debris into CSF.

In most series the location of these tumors has been reported as supratentorial and only a few cases of infratentorial location have been mentioned[1,3,6]. Most of our 7 patients had an infratentorial location. No specific reason for this could be explained as the presentation, tumor behavior and histopathology of our cases were similar to that of other series.

Among the reported congenital tumors in literature, teratoma is the most common, comprising more than one third of all cases [3, 7] and 0.5% of all intracranial neoplasms[8]. The next common reported pathologies are medulloblastoma, then astrocytoma, CPP, and ependymoma or ependymoblastoma[3].

Teratoma also was the most common pathology in this series. It may arise from several locations in the central nervous system and comprises tissues originating from all three germinal layers[7,8]. This entity is suggested when a rapidly growing hydrocephalus with a central calcified and vascularized mass is found in imaging. Regular cerebral structures usually cannot be detected. Early diagnosis in such cases is of immense clinical importance as the prognosis of congenital intracerebral teratoma is generally very poor.

Most cases with antenatally diagnosed intracranial teratoma die shortly before or after birth and have the lowest survival rates of all patients with perinatal brain tumors[1]. In this series for all prenatally diagnosed cases the pathology was teratoma.

The ability to diagnose intracranial tumors antenatally helps the parents as well as the surgeon in the management according to the tumor characteristics in the diagnostic modality. If such a tumor is detected at the time of legal permitted abortion, termination of pregnancy can be considered[9].

The readily available imaging modality is the ultrasonographic study, where antenatal diagnosis of an intracranial mass lesion or hydrocephalus can be made. CT scan can demonstrate the possible location and boundaries along with calcification. MRI is the best diagnostic modality because, through its multiple imaging planes and absence of bony artifact, delineates better the extent of the tumor, especially within the posterior fossa[4]. Disadvantages of MRI in neonates are the longer time needed to complete the process and frequent requirement of general anesthesia. Except for the case with CPP all other lesions in our series demonstrated heterogeneous components and a non-homogenous enhancement after contrast medium injection in CT or MRI. Along with other studies we suggest preoperative prediction of teratoma or malignant tumors such as PNET according to radiological findings of a heterogeneous mass[4].

Tumor markers such as beta human chorionic gonadotropin (β-HCG) and αFP in addition to imaging help us to reach a more certain preoperative diagnosis, especially for mature or immature teratoma. Generally, children with unphysiologically high levels of β-HCG or αFP and proven tumor are considered to suffer from a malignant disease [10]. In 2 of the 3 teratoma cases in our series

αFP level was significantly high.

As most cases present with symptoms of intracranial hypertension, patient management is directed towards relieving hydrocephalus which usually needs urgent CSF drainage because of rapid deterioration. This also reduces brain tension and allows sufficient brain retraction during the operative procedure. Determining the histopathology of the lesion and removing the tumor mass are the other important steps. Inspite of good decompression it may be prudent to leave a ventricular drain in-situ postoperatively for several days to monitor ICP to find whether shunting is required.

It is mostly recommended that these tumors should be removed by complete surgical resection, whenever not feasible, it should be followed by adjuvant therapy. Moreover, recent researches have shown a better prognosis for brain tumors, when other therapeutic modalities are combined with surgery. Irradiation is generally not recommended in children under 36 months of age because of the high risk of cognitive sequelae and endocrine dysfunction. Rapid advances in the field of radiotherapy may provide delicate focal radiation effects without damage to surrounding normal brain tissue in these patients in the near future[5].

Chemotherapy remains a much accepted and well tolerated method of choice in this age group and has been proven beneficial as an adjuvant therapy in many tumors once the mass is resected incompletely[5], or in cases with malignant pathology inspite of complete resection. The possible neurotoxicity of chemotherapy, including mental retardation and leukoencephalopathy, in these neonates concerns the pediatric oncologists[11]. It also allows delayed irradiation and prolongs survival in majority of patients with minimal neurotoxicity[12]. However, a standard, effective and well accepted treatment protocol for optimal management of neonatal brain tumors is yet to be defined.

The survival rate of neonates with brain tumors has been poor overall[1,6]. The best prognosis was evident with choroid plexus papilloma, the worst with PNET.

Most reports have shown a better prognosis for supratentorial location .This may be due to the site, which offers a more accessible surgical approach and the more benign histopathology of supratentorial tumors[5]. It has been shown that the degree of surgical resection is one of the important treatment parameters with complete resection offering the best prognosis. However, surgical resection has been associated with a higher rate of operative mortality ranging from 26-33 %[5]. This poor prognosis is not only related to the surgery but also due to the risk in anesthesia (hypothermia, bleeding), the difficulties in post-operative care (lack of voluntary control of water and electrolytes) along with the pessimistic attitude of the parents in seeking treatment or during follow-up[2].

The best prognosis with long tumor free survival was present only for CPP in our series. We lost the other 6 patients despite adequate facilities present in our setting, with pre-operative problems, intraoperative complications, postoperative aspiration, chemotherapeutic adverse effects and lack of follow-up.

Inspite of improvement in prenatal diagnosis, modern imaging facilities, appropriate pre and post operative management, advancements in therapeutic intervention including surgery and adjuvant therapy, the mortality associated with these tumors still remains high.

Conclusion

Today, the availability of imaging procedures such as CT and MRI has helped in earlier detection of congenital brain tumors. However, the clinical diagnosis is delayed due to skull ability to accommodate the rising ICP, immaturity of the brain and inability of neonates to complain specific symptoms. The overall prognosis depends on the condition of the patient at the time of diagnosis, the size and location of the tumor, surgical resectability, and tumor histology. Despite improvements in prenatal diagnosis, modern imaging facilities, early surgery and operative and anesthetic improvements, outcome is still discouraging. Due to the extreme rarity of congenital brain

tumors and lack of a well accepted protocol, we suggest all centers in the world to submit their findings on the different aspects of these tumors, in order to share their experiences for reaching an agreement for better management of these patients.

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