

Congenital TORCH Infections in Pediatric Patients and their Proximity to Anterior Circulation Territories of Brain: An Observational Study with Case Illustrations

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Abstract

Background: Congenital TORCH infection is not uncommon in neonates. They constitute approximately ten percent of pregnancies, which transmit infection to fetus since gestation to birth. Their neurological sequelae are leading diversified anatomical complications of brain, focusing over anterior circulation territory of brain.

Materials and Methods: Infants admitted were investigated and diagnosed as congenital TORCH infection. We studied CT brain and MRI of brain of infants. Total 15 cases of symptomatic congenital TORCH infection were studied and analyzed. Ten of them were having CMV infection and two of them were infected *T. gondii*. three of them were rubella and HSV1. We studied the patients from July 2012 to June 2017.

Results: All patients with CMV infections had hydrocephalus, four patients had microcephaly inspite of hydrocephalus. Patterns of hydrocephalus were significantly atypical and lissencephaly-pachygyria were present. However posterior fossa abnormality seems insignificant with compared to cerebral complications in all patients with CMV infection and *T. gondii* as well.

Conclusion: Clinical symptoms of infants and radiological features of brain were studied in details. most of the infants develop symptoms at age of weeks to months. Most presented at age of two months. This study is aimed to relate the congenital infection with the territories of brain affected but not to predict the outcomes. anterior circulation of brain hampers much than posterior circulation.

Keywords: TORCH Infection; *T. gondii*; Brain; Congenital Cytomegalovirus (CMV)

Introduction

TORCH refers to the most common congenitally acquired infections: toxoplasma, rubella, cytomegalovirus, and herpes simplex virus [1]. More than 15% of pregnancies are complicated by infection at some point during the course of pregnancy or delivery. When these infections are transmitted to the developing fetus or newborn, they are called congenital infections. Congenital infections can occur "at any time from conception through birth" [1,2]. Congenital cytomegalovirus (CMV) infection is the leading cause of congenital viral infection and brain disease in children in developed countries, occurring in approximately 1% of all live births (from about 0.3% to 2.4%). Mother-child transmission is mainly the result of primary maternal CMV infection, which carries a risk of transmission varying from 14.2% to 52.4% (combined prevalence of 32.4%). Ten per cent of congenitally infected newborns are symptomatic at birth, and permanent neurological injury occurs in up to 60% of these infants [3].

Congenital CMV infection results in several pathologic and anatomical changes to the brain, including ventriculomegaly, microcephaly, cortical anomalies, calcification, subependymal cysts, and cerebellar hypoplasia. These MRI findings are not pathognomonic of congenital CMV infection and there are several diseases that should be considered as differential diagnosis of congenital CMV infection such as brain developmental disorder (e.g. lissencephaly, pachygyria), leukoencephalopathy [4-6], cerebral palsy and other congenital central nervous system infection. There have been previous clinical reports on the factors associated with poor outcomes in patients with congenital CMV infections.

T. gondii infections range from 0.8 to 20 per 10,000 live births. Congenital infection is usually a result of primary maternal *T. gondii* infection during or immediately preceding pregnancy [5].

T. gondii is a result of maternal parasitemia leading to infection of the placenta and then the fetus. Congenital toxoplasmosis is sub-clinical in approximately 75% of infected infants and, as noted, is inversely related to the gestational age at which maternal infection is acquired. The most common manifestations of severe congenital infection include developmental delays, intracranial calcifications, seizures, hydrocephalus, chorioretinitis, anemia, and jaundice [6]. Microcephaly is noted in 5 - 15% of severely symptomatic congenitally infected infants, and microphthalmia in 1 - 2%. The unique phenomenon of acute chorioretinitis manifesting in individuals between 15 and 20 years of age with mild or asymptomatic congenital infection, remains not well explained; as does the predilection for the macula, basal ganglia, and periventricular areas of the brain in severe congenital toxoplasmosis [5,6]. Ocular toxoplasmosis is more often bilateral in congenital disease than in acquired disease. In other, often subclinically, congenitally infected individuals who manifest acute chorioretinitis during adolescence [7], it is thought that subtle changes in their cell-mediated immune status may allow an ocular *T. gondii* cyst to reactivate and rupture. Of particular interest is the fact that microcephaly may be unrecognized in congenital toxoplasmosis at birth and be recognized between 12 and 24 months of age. Some of these infants, with delayed recognition of microcephaly, were thought to have a subclinical congenital infection. This suggests that antimicrobial treatment may be important in limiting the ongoing destruction of CNS tissue. The efficacy of treating congenital toxoplasmosis is supported by the excellent results of collaborative studies [5,6,8,9].

Subjects and Methods

Data collection

This study was performed prospectively between July 2012 and June 2017. Samples and data were collected from patients from patients with possible congenital CMV infection and toxoplasmosis who showed neurological symptoms such as intellectual disability, hearing impairment, cerebral palsy, microcephaly, periventricular calcifications and epilepsy.

Age	Sex	Male	Female	CMV	Toxoplasmosis	Combined
Weeks to months	M:F	10	05	10	02	03
(mean 02 months)	2:1					

Clinical presentations	Radiological presentations	Multi-system involvement
Microcephaly	Hydrocephalus	Umbilical hernia
Macrocephaly	Asymmetrical ventriculomegaly	Scrotal hernia
Cerebral palsy	Lissencephaly-pachygyria	Anemia
Epilepsy	Septations and cavitations within ventricular system	
Others congenital anomalies	hydraencephaly	

Study design

This is an observational study carried out in department of neurosurgery, Bangabandhu seikh mujib medical university. Bangladesh, Dhaka.. The patients were from age of few weeks to months, usually presented at age of two months male pre-dominance is seen.

Investigation design

All patient were done CT brain, MRI of brain, screening of TORCH infection of infants and mother was done, urine viral DNA load (polymerase chain reaction, PCR) was done for few patients. All other baseline investigations were also done to rule out multisystem involvement. This study is aimed to conclude the association of brain damage in TORCH infection, most commonly in CMV infection and toxoplasmosis, over anterior circulation territory than posterior circulation territory of brain.

Results and Discussion

In our series we studied clinical presentation, birth history and the CT scan and MRI of brain of TORCH infection positive infants, most of them were CMV positive and two of them were *T. gondii* positive. The anatomy of brain of these infants were studied thoroughly, hydrocephalus, ventriculomegaly, microcephaly, macrocephaly, lissencephaly-pachygyria were common findings. This study is mainly focused on analyzing the distortion of brain anatomy and pattern of hydrocephalus and ventriculomegaly, that is atypically different from other varieties of hydrocephalus and ventriculomegaly. Cortical damage also most prominent in cerebral cortex. In all patients with CMV infection ventriculomegaly was present and all of ventriculomegaly had asymmetry, cystic septations, CSF cavitation and very poorly defined blood vessels. This kind of similar brain damage and ventriculomegaly draw the attention of neurosurgeon for the surgical planning and their outcomes. However the reason behind this kind of presentation on CT and MRI were studied extensively but our study focus on differentiating the anatomic distortion of brain in CMV infection and Toxoplasmosis with differentiating features in between supratentorial and infratentorial compartments of brain. Since their blood circulation system is different phylogenetically. Some studies shows that brain

damage in CMV infection starts in gestation period and are inflammatory in nature, relationship of chorioamnionitis and fetal brain damage has been also described [10]. The pattern of damage has been also studied which follow white matter of cerebrum, germinal layer, microglial cell, ependymal cells of ventricles and blood vessels [3]. Infections are associated with recurrent abortion, intrauterine growth retardation, intrauterine death, preterm labour, early neonatal death and congenital malformations [2]. In our series of observation we found the anatomical distortion of brain most prominent over cerebrum and supratentorial following anterior circulation than posterior fossa and infratentorial of posterior circulation territory.

The below illustrations are studied in details and found the pathologies as described in their respective sections. Our study aims to prove the radiological findings mentioned above and are also illustrated below. The prevalence of supratentorial findings are found relatively common than infratentorial involvement. Thus the obvious reason for this kind of supratentorial involvement were not well known, but most of cases only has very lesser extent of infratentorial involvement.

Case Illustrations

Case 1: CMV infection with macrocephaly

A two months old male baby presented in our emergency department with history of intermittent low grade fever and vomiting. The baby was born by normal vaginal delivery in local hospital. No history of post-partum birth asphyxia. During pregnancy mother has no history of fever and she was having regular checkup and used to take regular iron, folic acid and calcium supplements. Gradually parents noticed the size of the head increasing in size. There is swelling over umbilical region and scrotal region. No history of consanguineous marriage. Normal bowel and bladder functions.

- Anemic look.
- Poor sucking reflex
- Normal cry
- GCS-E4V4M6
- Pupil -normal.
- No focal neurological deficit.
- OFC-40 cm on admission, 42 cm after 4 days of admission.
- Setting sun sign was present
- Anterior and posterior fontenelle were open and tense.
- Umbilical and scrotal hernia.



Figure 1: Showing macrocephaly.



Figure 2: Showing umbilical hernia.



Figure 3: Scrotal swelling.

CT head revealed gross congenital hydrocephalus with hydroencephaly

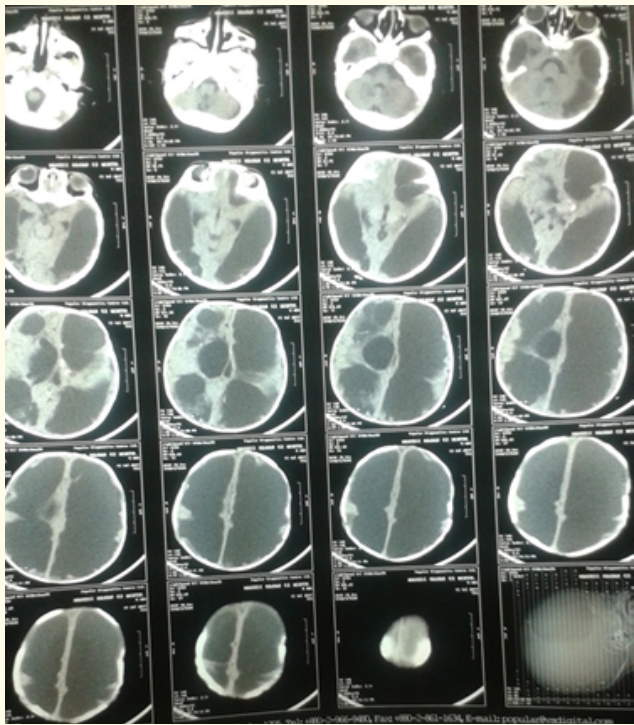


Figure 4

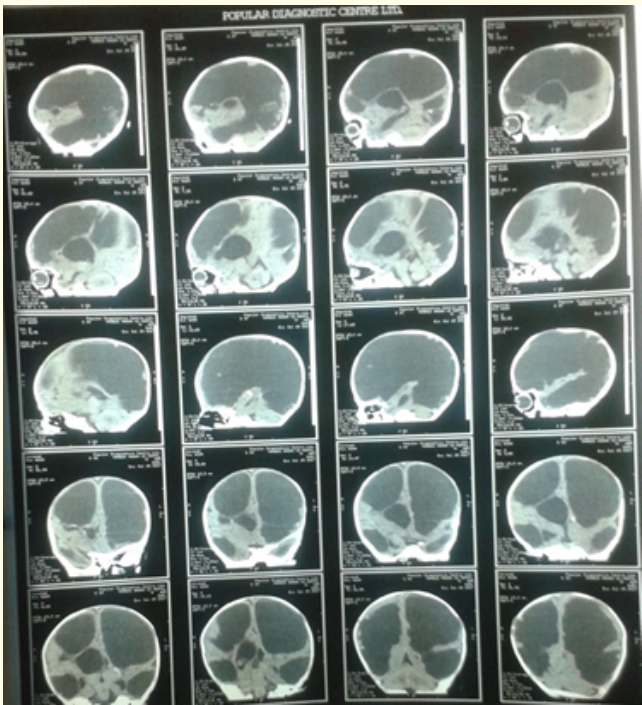


Figure 5

Congenital CMV infection revealed by blood investigation and Mother was also found CMV, rubella and HSV1 positive.

MRI brain was performed to rule out the associated congenital anomaly and anatomic agenesis. MRI brain shows gross ventriculomegaly with septations, cavitations, microgyria, lissencephaly-pachygyria [3,11]. However posterior fossa shows unremarkable findings. Thus congenital CMV infection hampered anterior circulation territories of brain in this patient.

Symptoms seen in this patients are due to supratentorial anatomical distortion of brain due to target viral load that found in urine of patient.

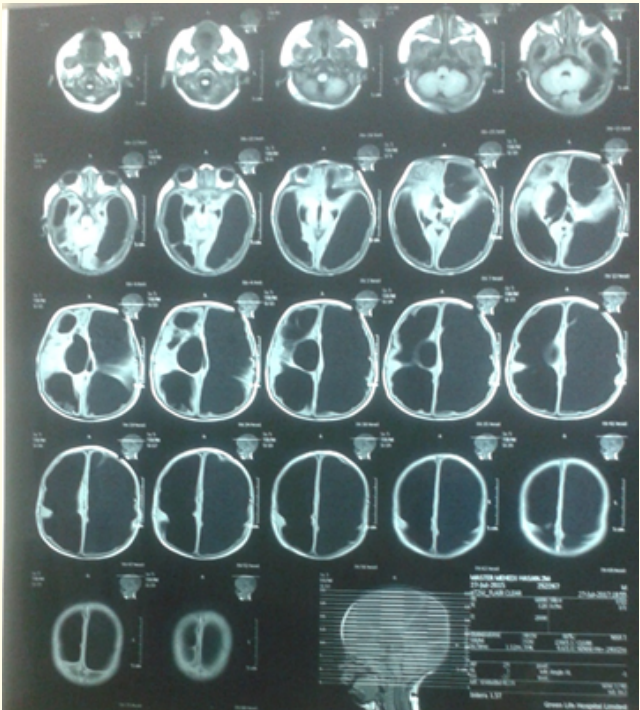


Figure 6

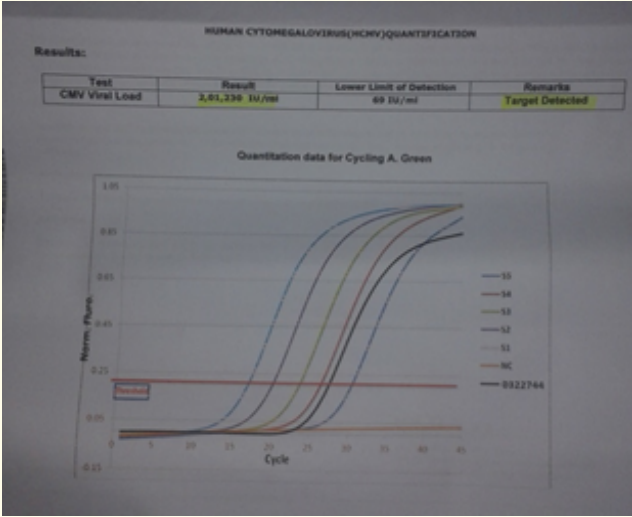


Figure 7: Target viral load.

CMV viral load target detected in this patient through PCR of urine and antiviral therapy was started and patient improved without CSF diversion.

Case 2: A case of congenital toxoplasmosis

A 12 years old male boy presented with history of gradual deterioration of vision and high grade fever, nausea and vomiting. History of five times ventriculo-peritoneal shunt for obstructive hydrocephalus. Post admission suspected for nonfunctioning shunt due to infection. Further work up was done. Ocular examination revealed finding different from hydrocephalus, which leads to investigate further from birth history to present blood sample for TORCH infection.



Figure 8



Figure 9

Right ocular toxoplasmosis leads to right eye blindness [9].

CT head shows multiple calcifications on either side of basal ganglia and in the aqueduct, leads to obstructive hydrocephalus [5,8] eccentric target sign on computed tomography of brain [9]. However posterior fossa shows insignificant changes of toxoplasmosis, indicates anterior circulation territories affected likely than posterior circulation territories of brain.

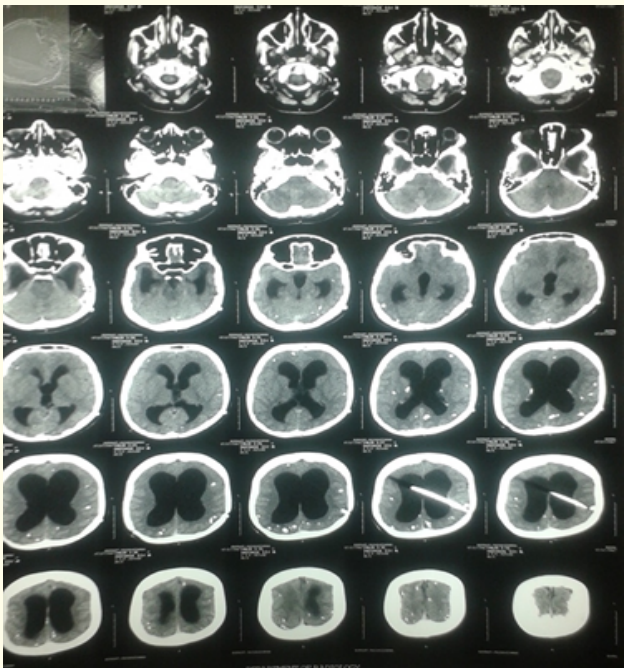


Figure 10

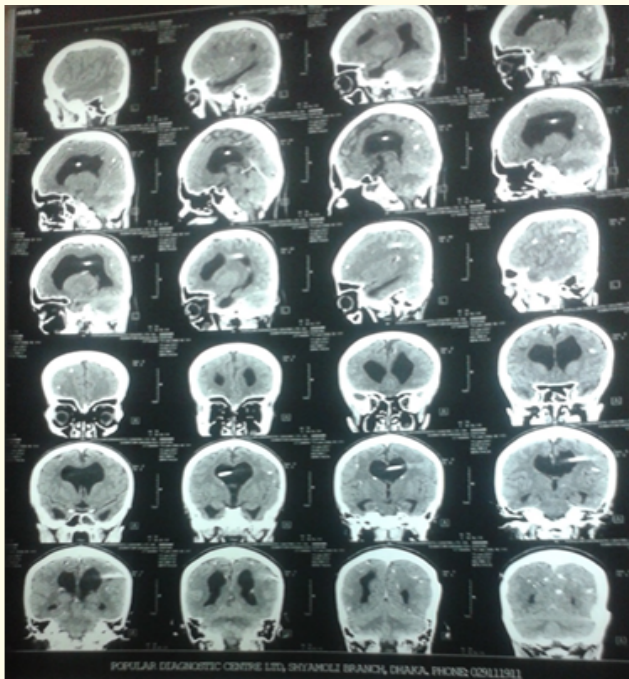


Figure 11

Patient was treated with clindamycin, azithromycin, steroid and antiepileptic for toxoplasmosis after the shunt infection has been resolved after the two weeks therapy of broad spectrum IV antibiotics like meropenem and vancomycin.

The boy was discharged with medications for toxoplasmosis but re-admitted with complaint of two episodes of convulsion and vomiting. CT head was repeated.

Ultimately the patient died of repeated shunt infection and convulsion, leading to cardiorespiratory failure.

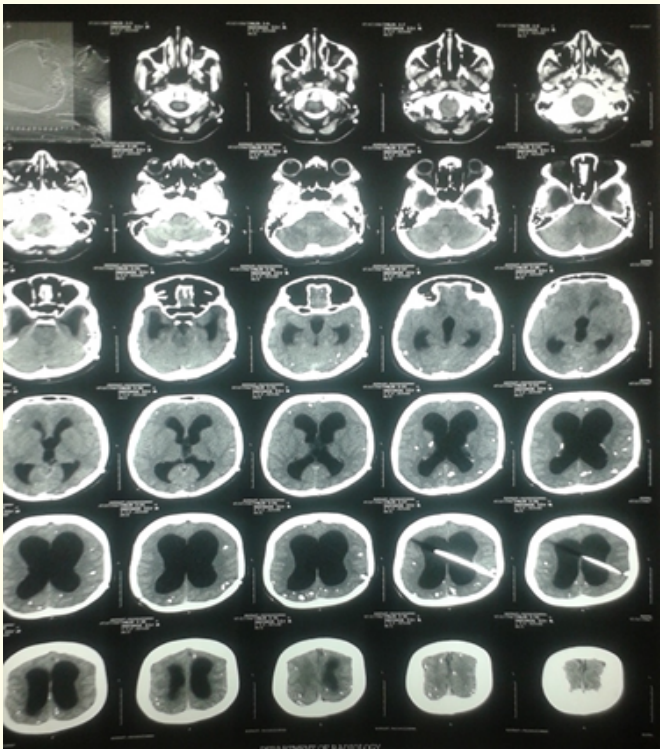


Figure 12

Case 3: A Case of rubella and HSV 1



Figure 13

A one month baby presented with history of macrocephaly following CSF leak from posterior fontenelle, resulting dysfigure of cranium. Setting sun sign present. Baby was investigated and found positive for rubella and HSV1, CT head was done it revealed atypical patterns of hydrocephalus, hydranencephaly

Case 4: A case of CMV infection with CSF diversion failure

A case of congenital CMV infection, a ten months baby presented with macrocephaly, first CT brain shows asymmetrical ventriculomegaly, cavitations and septations of ventricular system, hydranencephaly. Second CT head done after seven months of ventriculoperitoneal shunt which shows not significant changes of brain. However in both CT head done subsequently shows posterior circulation territories affected comparatively less.

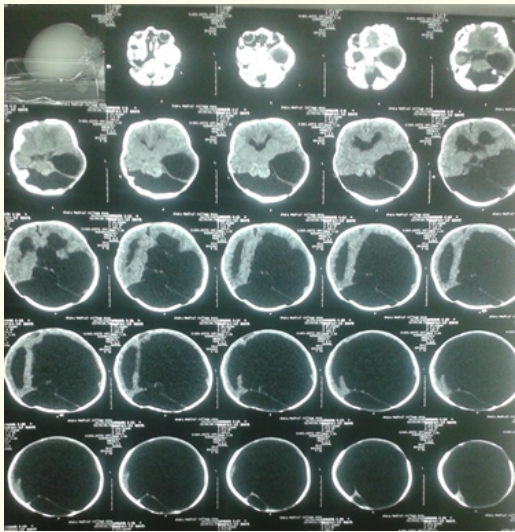


Figure 14



Figure 15

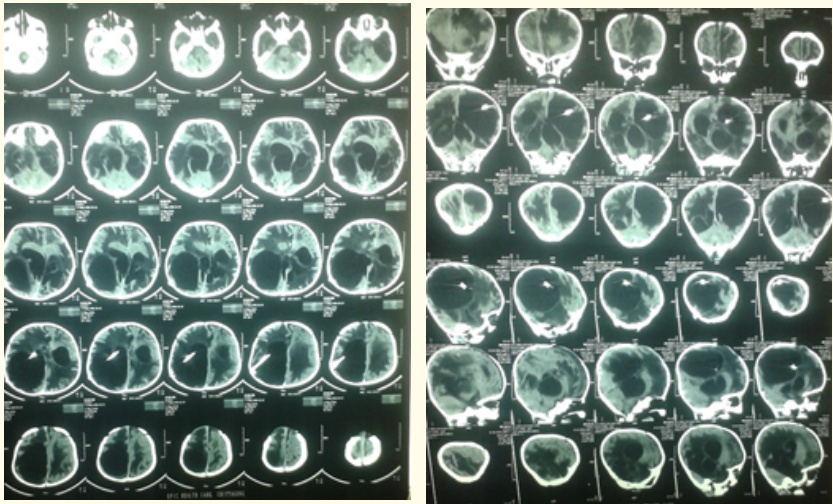


Figure 16

Case 5: A case of congenital CMV infection.

A two months male baby was admitted with history of macrocephaly, investigated and found congenital CMV infection of positive mother.

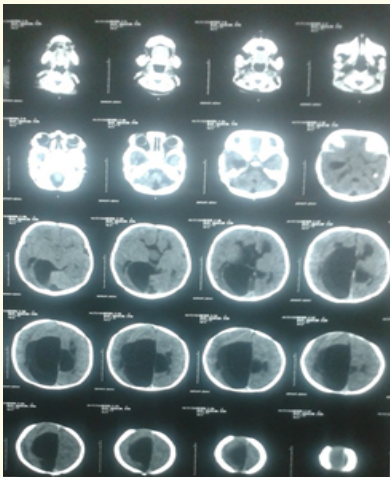


Figure 17

CT head shows asymmetrical ventriculomegaly, however posterior fossa shows unremarkable changes. MRI of brain was also done to study the anatomical distortion in details.

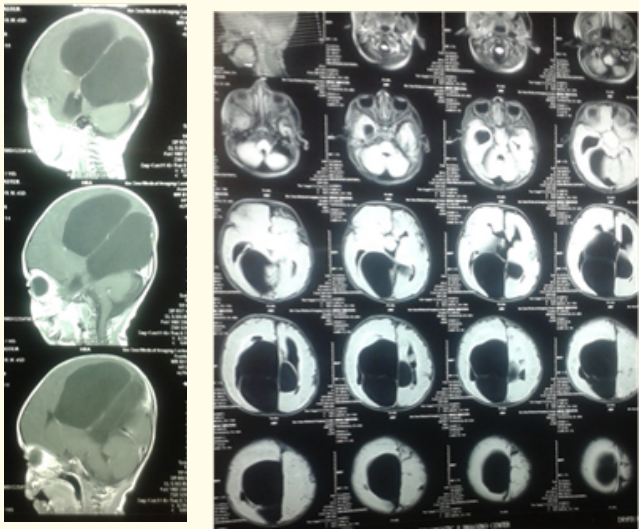
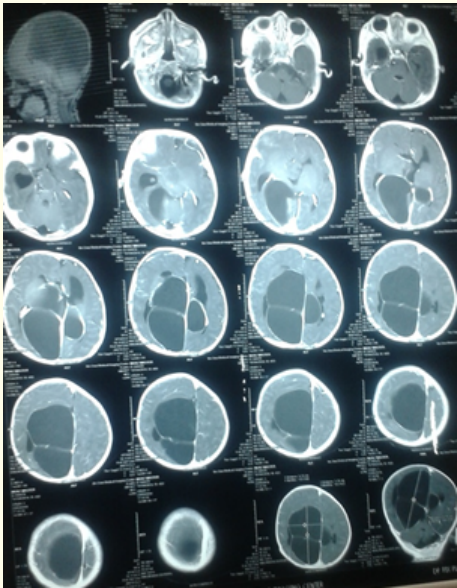


Figure 18

MRI off brain shows features of asymmetrical ventriculomegaly, septations of ventricular systems, hydranencephaly. In this case also we found the posterior fossa affected less and found comparatively less anatomical distortion other than vermian agenesis [12-16].

Conclusion

Congenital TORCH infection usually transmitted during pregnancy to birth to fetus. Among them most common is CMV infection, we studied the anatomical damage of brain in infected patients in details. We found a common atypical pattern of ventriculomegaly and hydranencephaly with others congenital anomalies too. It was found that TORCH infection involve multisystem of patients, however brain damage and its anatomical distortion depends on viral load of infected patients, which has been proved in many other studies. In our observational study we found the pattern of anatomical damage in congenital TORCH infection follows anterior circulation of brain than posterior circulation. However outcome of such patients with or without surgical interventions not varies significantly and role of antiviral therapy might be helpful in some cases. Since this is an observational study, the above shown cases are studied and analyzed in details. Though exact reason for abnormalities of cerebral cortex and ventricular system are not known, we can explain the variations of abnormalities in brain of pediatric patients. The study is based on to evaluation of patients and their management with prognosis. Role of surgery do not change the outcome except in selective cases. The management of these patients are very much critical and may need multidisciplinary approach often. Congenital abnormalities were obvious in these patients, most of mothers were also found positive for TORCH screening, thus modalities of management differs this kinds of patients from rest of the hydrocephalus patients with devastating outcome. This study aims to differ the vision regarding management but not the mechanism of change of architecture of brain in pediatric patients.

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