Case Report

A Survival Case of Premature Infant with Hepatoblastoma (Fetal Pattern) along with Other Serious Comorbidities and Surgical Interventions

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Abstract

An estimated ratio (i.e., 1 in 10) babies are born too early every year. Roughly 1 million children die each year due to impediments raised pertaining to preterm birth. One such extreme preterm male baby was presented in the neonatal care unit with respiratory distress and grunting. Baby was confirmed to have ventricular septal defect along with patent ductus arteriosus and craniosynostosis which was treated with medications and surgical managements. He was also engaged with various prophylactic and empirical antibiotic therapies to cover the microbial growth. The most disturbing stage here was the appearance of liver mass sizing 5.8 cm × 1.3 cm accompanied with area of necrosis, diagnosed with hepatoblastoma which was evident with the aid of ultrasound. Hence, chemotherapy was commenced which was in accordance with Societe Internationale d Oncologie Pediatrique Epithelial Liver Tumor Study Group-3. Although the existing comorbidities haunted the baby for a long time, he finally made it successfully to get into track by fighting all the hurdles bravely, which was a sheer miracle. Along with the clinicians/surgeons, we Clinical Pharmacists worked hand in hand to ensure the baby to be receiving optimized drug regimen keeping in mind the risk-benefit ratio.

Keywords: Chemotherapy, craniocynostosis, hepatoblastoma, patent ductus arteriosus, preterm, ventricular septal defect

Introduction

Hepatoblastoma is one of the common malignancy in early childhood stage, almost accounting for the 2/3rd of primary malignant liver tumors, especially seen under 4 years of age and more frequently in premature babies with very low birth weights. Alpha-fetoprotein (AFP) level in the blood is the important clinical biomarker for hepatoblastoma. Other diagnostic approaches include computed tomography (CT) scan, magnetic resonance imaging, biopsy, and series of blood tests.

Craniosynostosis, a birth defect where the bones in a baby's skull fuse together in an early stage before the brain is fully developed, this can however limit the growth of the brain if not repaired at an initial stage. In India, the incidence report of its occurrence is estimated to be 1 in 2500 live births. Treatment usually involves a surgical procedure-craniosynostosis correction, where excision of fused sagittal suture takes place.

The high prevalence of ventricular septal defect (VSD) in preterm neonates has been recorded widely in studies done across worldwide. VSD is a defect, which involves a defect in the wall between the heart's lowers chambers. Treatment depends upon the severity of the case. Surgical procedure is accompanied to close the defect. Drugs such as diuretics, antihypertensive medications, and inotropes are required to treat the postsurgical symptoms.

This case report discusses a complex case wherein a preterm baby along with recurrent lung consolidation and VSD was diagnosed with hepatoblastoma. Baby was also confirmed to have asymmetrical craniosynostosis. The stepwise approach

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by the entire neonatal unit team to treat the baby keeping in consideration all the pitfalls was highly appreciable.

Case Report

A moderate preterm baby of 32 weeks' gestation was received in the neonatal intensive care unit after emergency lower segment cesarean section due to the indicated concern of pregnancy-induced hypertension with hypertensive dilative cardiomyopathy. The birth weight was recorded to be 1 kg. Baby was intubated in view of respiratory distress and grunting. Baby was extubated to oxygen through high flow nasal cannula (HFNC) within 24 h of birth, despite this baby continued to have respiratory distress with retractions. Hence, serious chest X-rays were taken at various intervals which showed migrating consolidation in both the lungs. Nebulization with N-Acetylcysteine was given along with a short course of Inj. Furosemide to relieve the distress. Baby responded well to treatment but however required HFNC support till day 103 of life. On clinical examination of the cardiovascular system, baby was having a systolic murmur. ECHO confirmed VSD (sized as 5 mm) and patent ductus arteriosus (PDA). Since, PDA was persistent in subsequent ECHO's; a 5 day course of IV Acetaminophen was ordered. ECHO on the 2nd month of baby's life displayed VSD as 4.3 mm size along with increased pulmonary vascular resistance. Baby underwent VSD closure + PDA ligation successfully, postsurgery he required inotropes for the initial period of 48 h which was slowly tapered before stopping entirely, and he also required inodilators cycling (milrinone + levosimendan) for 10 days.

The blood samples for sepsis screening were sent on day 1 itself, initial white blood cells and platelet counts were low with negative C-reactive protein (CRP), subsequent CRP result showed higher numbers; hence, 7 days of piperacillin + tazobactum course were started. Another blood screen on the 3rd week of life showed highly positive CRP and procalcitonin levels with methicillin-sensitive *Staphylococcus aureus* septicaemia, followed by which he was started with IV antibiotics cefazolin and meropenem; since then CRP showed decreasing trend and the repeat blood culture was sterile. Post VSD surgery, bronchial wash specimen showed growth of extended-spectrum beta-lactamases (ESBL), *Escherichia coli,* and *Ralstonia picketti* for which further antibiotics were given. Ambiguous genitalia were noted at birth, for which karyotyping and Fluorescence *in situ* hybridization [as shown in Figure 1] performed depicted normal karyotyping-46 XY. On follow-up, both the testes were descended in the 7th month of his life. Hypospadias surgery was advised to be done after 1 year of age.

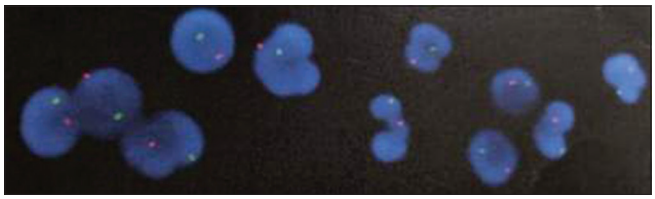

Figure 1: Fluorescence *in situ* hybridization– Report. This test was performed to analyze sex chromosomal anomalies

On the 3rd week of life, the liver was palpable during the clinical examination which was initially attributed to the abscess. Ultrasound abdomen showed a liver mass measuring 5.8 cm × 1.3 cm with the areas of necrosis; CT abdomen was suggestive to hepatic neoplasm. Alpha-fetoprotein was markedly elevated (136,402 ng/ml). Finally, ultrasound-guided liver biopsy done was consistent with hepatoblastoma (fetal pattern). Hence, baby was commenced on chemotherapy which was in accordance with Societe Internationale d Oncologie Pediatrique-Epithelial Liver Tumor Study Group (SIOPEL 3) Protocol, he underwent two cycles of two drug therapy (Carboplatin/Doxorubicin). Baby received one dose of granulocyte-stimulating factor after each cycle in view of significant neutropenia. Alpha-fetoprotein count after therapy was (1350 ng/ml), marking a good response. Right hepatectomy was performed on the 5th month of his life [Figures 2 and 3]. Serum AFP was monitored frequently, and the value showed a decreasing trend. He was given phosphate and albumin correction following Hepatectomy. Posthepatectomy his blood cultures grew ESBL, *Klebsiella pneumonia*; Endotracheal secretions grew *Acinetobacter* and *Klebsiella pneumoniae* and abdominal drain fluid grew *Pseudomonas aeruginosa* for which he received broad spectrum antibiotic for duration of 14 days further. ECHO at this time done showed normal cardiac function. Calcium correction was given intravenously. Renal function tests and electrolytes done periodically were within the normal limits.

Meanwhile, amidst the treatment phase, baby's head continued to grow in an abnormal shape and sagittal suture appeared to be partially fused on the clinical examination. A CT brain was done which confirmed the presence of asymmetrical craniosynostosis. Finally, craniosynostosis correction and excision of fused sagittal suture were done before the 3rd

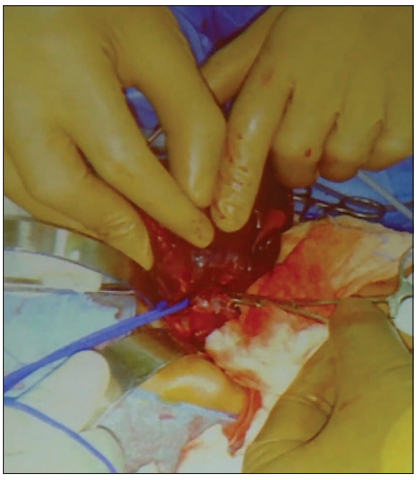

Figure 2: Image showing the abnormal mass which is situated very adherent to the liver. This image was taken during the hepatectomy procedure

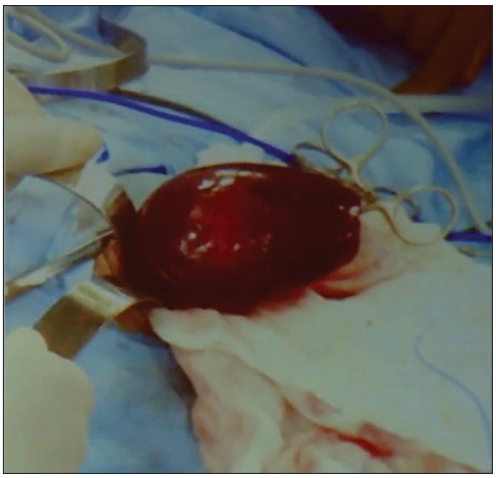

Figure 3: Image showing dissected tumor. The abnormal mass (tumor) has been removed by performing hepatectomy and the image here displays the dissected portion

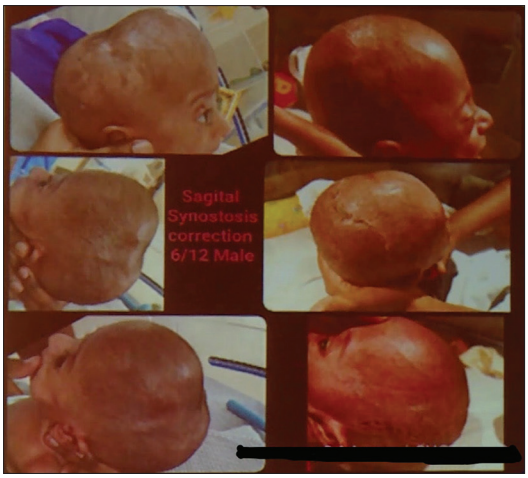

Figure 4: Sagittal synostosis correction before and after images. The figure here shows the before (in the left) and after craniosynostosis correction (in the right) images

and 4th cycle of chemotherapy [as shown in Figure 4]. He was started on prophylactic anti-epileptic (levetiracetam) postsurgery which was advised to be continued for 3 months. Three weeks postcraniosynostosis, he had been given with two more remaining cycles of chemotherapy which according to the guideline was single drug therapy (cisplatin). Final AFP done after the completion of chemotherapy showed value of 38 ng/ml. Baby did responded well to the treatment, he was stable and ultimately got discharged after serving 8 months of his life in hospital.

Discussion

The clinical course of this patient was way too complicated; it indicated us three main clinical manifestations in the treatment approach pertaining to the diagnosis. First of all, treating physicians/neonatologists must be cautious of hepatoblastoma occurrence, especially in neonates with extremely low-birth weight (ELBW). The incidence of hepatoblastoma in ELBW neonates is on a surge according to reports; it might be the reason for an increase in the count of more immature infants with a more sensitive liver.[1] AFP has been shown to correlate with tumor size and volume at the time of diagnosis.[2] Since the AFP levels may be seen at a higher numbers in preterm infants, serial measurements in the transition of AFP levels and its continuous monitoring are meant to be indispensable.[3] Studies show that the incidence of hepatoblastoma is infrequent in the black population when compared to white.[4] In this case, as discussed, connecting the dots in view of infection, baby was believed to be having liver abscess, since the baby was septic from day 1 of life. It was only after performing the essential diagnosing tests; baby was confirmed to have hepatoblastoma.

SIOPEL protocol was followed for the treatment of hepatoblastoma. SIOPEL is a result of an international collaborative effort of a multidisciplinary team originally found in Jerusalem to study these sorts of diseases internationally.[5] In this case, two cycles of two drugs chemotherapy (Carboplatin/Doxorubicin) were ordered before resective surgery and postsurgery 2 more cycles of single drug chemotherapy (Cisplatin) was introduced, this chemotherapeutic approach was in accordance with SIOPEL 3 protocol. For infants <5 kg, Carboplatin and doxorubicin dosage is 11.5 mg/kg and 1.34 mg/kg accordingly. The latter must be given in 48 h continuous infusion. The dose of cisplatin is 80 mg/m^2 continuous infusion for 24 h which is to be run concurrently with 120 ml/m^2/h/day of solution containing glucose/sodium chloride + mannitol, potassium chloride, magnesium sulphate, and calcium gluconate. Since infants are at a higher risk of cisplatin-induced electrolyte imbalance than older children, the need for regular electrolyte monitoring is particularly important. Prior to individual chemotherapy, premedications such as antihistamines and anti-emetics must be given to cope up with untoward symptoms.

Second of all, treating physicians/neonatologists should be well aware of various neurological ill-effects that craniosynostosis holds along with skull deformity. It is often evident that proper neurosurgical management at appropriate time would ensure excellent outcomes for craniosynostosis patients.[6] The aim of surgery is to warrant normal growth of the brain, to prevent increase in intracranial tension and to improve facial and skull appearance without compromising visual and auditory function. The incidence of seizures in patients treated with levetiracetam is relatively less after neurosurgeries.[7] In this case, post craniosynostosis; levetiracetam was ordered for 2 months as a prophylaxis measure to avoid the risk of developing seizure later on. It was advised to taper slowly after 2 months before stopping completely.

Third of all, is to consider cardiovascular examination in preterm neonates predominantly. VSD along with PDA is not something uncommon and accounts for higher percentages in neonates.[8] Repeat ECHO must be done postsurgery to ensure no traces of residual VSD. The septicemia condition, even after 3 major surgeries (Right hepatectomy, craniosynostosis

correction, and VSD closure + PDA ligation) was well treated with definitive antibiotic therapy approach. The baby mentioned herein, fought all the odds well, survived tedious treatments and it's nothing short of miracle. He was finally discharged with regular follow-up strategic plan.

Declaration of patient consent

The authors certify that they had obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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