Case Report

Neonatal neuroblastoma presenting as recurrent chylothorax in a hydropic baby: A case report

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Abstract

We report here a rare case of neuroblastoma in a neonate who presented as a hydropic baby with respiratory distress due to recurrent chylothorax. The neuroblastoma regressed after six cycles of chemotherapy and the infant was discharged in good condition.

Keywords: Chylothorax, neonatal neuroblastoma, respiratory distress

Introduction

Neuroblastoma is the most frequently encountered malignant cause of mediastinal mass in infancy (under the age of 12 months), and it can arise anywhere along the sympathetic nervous system.[1] It accounts for around 30% of all neonatal tumors, with an incidence of 1 per 10,000 to 1 per 30,000 live-born infants.[2]

Most patients with congenital neuroblastoma are at a favorable stage at diagnosis and have an excellent long-term prognosis. Aggressive high-stage disease tends to be found in patients who are diagnosed after the first year of life.[3-5]

Case Report

A preterm baby boy with a gestational age of 31 weeks + 6 days and a birthweight of 1.835 kg was born via spontaneous vaginal delivery, with APGAR score of 2, 6, and 9 at 1, 5, and 10 minutes, respectively, to a booked 32-year-old primigravida mother who had been diagnosed with gestational diabetes that required only dietary management. Perinatal ultrasound performed at around 20 weeks of gestation showed normal fetal anatomy. A follow-up ultrasound a few days before the onset of labor showed features of hydrops fetalis in the form of polyhydramnios, fetal ascites, and pleural effusion.

After birth, the baby developed respiratory distress, managed with intubation, ventilation, and administration of surfactant in the labor room. Systemic examination revealed generalized body edema and minor dysmorphic features in the form of short fingers of both hands with hypoplastic nails. The baby was transferred to the neonatal intensive care unit, where he was connected to mechanical ventilation. His initial chest X-ray showed bilateral plural effusion [Figure 1]. At Day 2 of life, he developed severe respiratory distress, and his ventilator setting was escalated to high-frequency oscillatory ventilation. Pleural tapping demonstrated the appearance of milky pleural fluid.

The patient was extubated in the third week of life to continuous positive airway pressure, and in the fourth week of life, pleural tapping was again performed due to reaccumulation of pleural effusion. Analysis of the pleural fluid confirmed the diagnosis of chylothorax with the following results: protein level,

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Received: 16-06-2023 **Revised:** 20-08-2023
Accepted: 01-12-2023 **Published:** 28-06-2024

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_992_23

How to cite this article: Alhazmi DS, Bamehrez M. Neonatal neuroblastoma presenting as recurrent chylothorax in a hydropic baby: A case report. J Family Med Prim Care 2024;13:2780-3.

39 g/L; lactate dehydrogenase level, 238 U/L; triglyceride level, 0.25 mmol/L; glucose level, 8.8 mmol/L. Culture results were also negative.

The patient was then started on a protein-based formula with high medium-chain triglyceride (Monogen), and intravenous octreotide at a dose of 1 μg/kg/hour, which was gradually increased to 5 μg/kg/hour according to response. Intravenous octreotide was later switched to subcutaneous route. During the course of treatment, the patient reaccumulated chylothorax for the third time, for which a chest tube was inserted for draining. Following complete resolution of the chylothorax, the chest tube was removed, the patient was gradually weaned off octreotide, and the treatment was discontinued at the end of the ninth week of life.

When the patient was 11 weeks old, he was weaned off the Monogen formula successfully. At the age of 3 months, after serial chest radiographs showed a persistent pulmonary shadow involving the right border of the heart [Figures 2 and 3], a computed tomography (CT) chest scan was performed, which reported a large prevertebral mass in the lower thorax and upper abdomen likely suggestive of neurogenic tumor, especially neuroblastoma [Figure 4]. This was followed by an abdominal magnetic resonance imaging (MRI) scan that showed a "large paravertebral mass in the thorax and upper abdomen with features highly suggestive of neuroblastoma."

At that time, both the pediatric oncology and the pediatric surgery teams were involved in the care of the patient, and the opinion of both was to treat this patient by means of a conservative watch-and-see approach. Although the risks and benefits of surgical intervention were discussed, it was decided that no surgical intervention would be undertaken, as a high percentage of neonatal neuroblastomas have been shown to regress spontaneously and there was a high risk of operative morbidity and mortality due to the size and location of the mass.

Six weeks later, the patient developed respiratory distress, and a CT chest scan was repeated, revealing an increase in tumor size

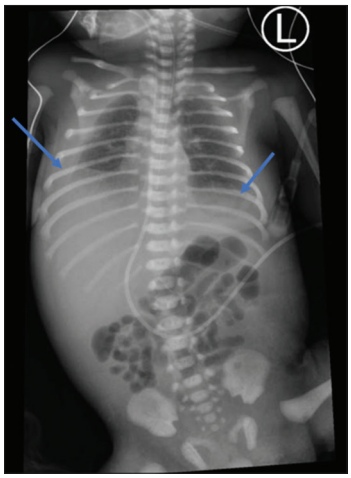

Figure 1: Initial chest X-ray showed bilateral plural effusion

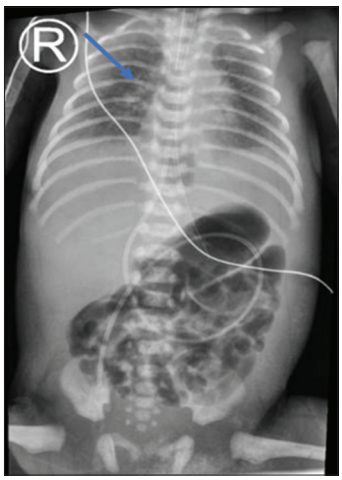

Figure 2: Serial chest radiographs showed a persistent pulmonary shadow involving the right border of the heart

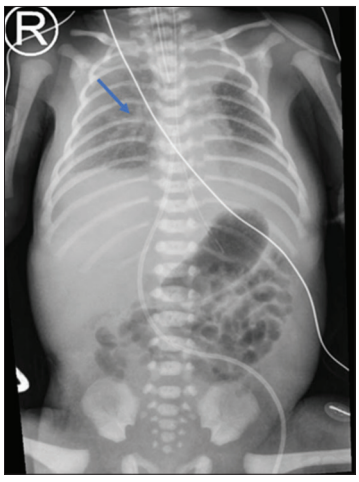

Figure 3: Serial chest radiographs showed a persistent pulmonary shadow involving the right border of the heart

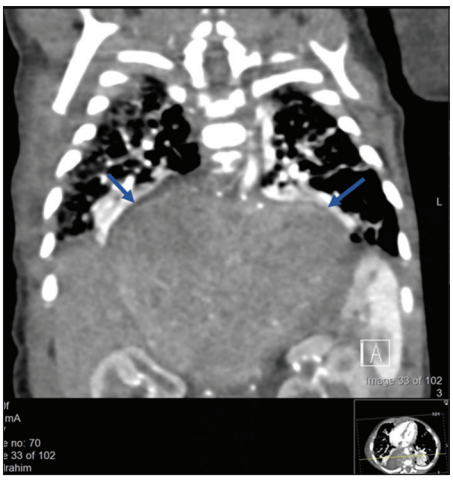

Figure 4: Computed tomography (CT) chest scan showed a large prevertebral mass in the lower thorax and upper abdomen likely suggestive of neurogenic tumor, especially neuroblastoma

by 40%. Given this new finding, a decision was made to start chemotherapy after the results of a CT-guided aspiration biopsy showed a "paravertebral mass with diagnosis of neuroblastoma consistent with undifferentiated type."

Following confirmation of the diagnosis of neuroblastoma, a metastatic workup was done. Metaiodobenzylguanidine (MIBG) scintigraphy showed intense MIBG uptake at the large paravertebral mass in the chest and abdomen in keeping with active neuroblastoma, with no clear evidence of distant abnormal MIBG uptake to suggest distant metastasis. A bone scan reported no clear evidence of skeletal metastasis. Given these findings, the patient was diagnosed with stage III abdominal neuroblastoma of undifferentiated type, and the family was updated.

From the recommendations of the pediatric oncology team, and after family agreement, the patient was initially started on low-dose chemotherapy (stage IVs protocol), including cyclophosphamide 5 mg/kg daily for 5 days × 2 cycles (first cycle starting at the age of 6 months). Following a good response to chemotherapy in the form of a 40% decrease in the size of the tumor and with the protocol being well tolerated by the patient, the decision was made to continue chemotherapy for a total of six cycles. After completion of these cycles, an MRI at 21 days after the last cycle showed: an interval decrease of the previously noted large, solid, midline, paravertebral mass in the lower thorax and upper abdomen, measuring 1.5 cm × 5 cm × 5.5 cm (anterior–posterior [AP] × cranio-caudal [CC] × transverse [TR]), compared with the size reported on the earlier abdominal CT scan of 5.9 cm × 8 cm × 9.5 cm (AP × CC × TR) and no intraspinal extension of the mass or distant metastasis.

Repeat MIBG imaging showed that the tumor had become less active and less avid.

Upon discharge from the hospital, the 10-month-old baby had the following growth parameters: weight 8.240 kg (between the 5th and 10th centile), height 65 cm (below the 5th centile), and head circumference 43 cm (below the 5th centile). The patient was receiving full oral feeding and maintaining saturation on room air. He had motor developmental delay (no head control) with good eye contact and a social smile.

A multidisciplinary team meeting was held prior to the patient's discharge. The team recommended no surgical intervention and no further chemotherapy treatment for the time being. However, close follow-up of the mass via monthly ultrasound was indicated. Parents were involved in the patient management and plan for the follow-up.

Discussion

Neuroblastoma in infants is more likely to be a primary tumor in the thoracic and cervical regions.[1] Clinically, the presenting features of neuroblastoma differ depending on location, size, and extent of tumor spread. Chylothorax is considered a rare presentation of thoracic neuroblastoma,[3] whereas respiratory distress is the most common, as demonstrated in a 2012 case report by Agrawal and Anand, who described a 4-month-old baby boy presenting with a history of cough and shortness of breath for 7 days. A chest X-ray showed plural effusion and a large mass in the right thoracic paravertebral region, and a diagnosis of neuroblastoma was confirmed with CT-guided fine-needle aspiration and the identification of urine metabolites.[3] Prior studies have reported prenatal findings such as the presence of fetal hydrops and polyhydramnios,[5,6] both of which were demonstrated in our case. Antenatal diagnosis by fetal MRI was reported by Blackman SC *et al.* in 2008 in a male neonate born at 36 weeks' gestational age with paraspinal neuroblastoma, which was later confirmed to be poorly differentiated neuroblastoma by an ultrasound-guided needle biopsy of the mass.[7] Other reported presentations include abdominal distension, chyle ascites, and skin rash.[4,8]

Ultrasound can be used as the initial screening for neuroblastoma, but MRI is the preferred imaging modality for abdominal tumors. Markers of tumor bulk that are not specific to neuroblastoma include ferritin, serum lactate dehydrogenase, and neuron-specific enolase levels,[2] whereas urinary catecholamines such as vanillylmandelic acid and homovanillic acid are specific markers.[1]

Neuroblastoma can be classified into three types on the basis of tissue biopsy results: undifferentiated, poorly differentiated, or differentiating.[2] From clinical and genetic information and prognoses, the International Neuroblastoma Risk Group has stratified neuroblastoma into three main risk groups, as follows:

- 30% of all neuroblastomas are low risk with a 95% to 100% 5-year survival rate, and 70% of neonatal neuroblastomas are considered to be in this low-risk category.[1]
- 20% of all neuroblastomas are intermediate risk, with a very good prognosis, as the 5-year survival rate is 85% to 95%.[1]
- 50% of all neuroblastomas are high risk, the best 5-year survival rate being 30% to 40%, but only around 5% of neonatal neuroblastomas fall into this risk category.[1]

The treatment options for neuroblastoma depend on the stage and location of the tumor and may include multi-agent chemotherapy, surgical excision, bone marrow transplantation, and/or no treatment (watch-and-see strategy), as there is a high possibility of spontaneous regression of the tumor.[4] If spinal cord compression is suspected, steroid treatment might be given earlier in the course of the disease.[1]

Neuroblastoma may be lethal in association with prematurity. In 2010, Tesanic D *et al.* reported a case of a premature female baby delivered by cesarean section due to acute polyhydramnios. An ultrasound at 27 weeks of gestation showed a small solid structure in the fetal abdomen. The baby died immediately after birth, and placental histopathological analysis revealed small round blue cells consistent with a diagnosis of neuroblastoma.[2]

Conclusion

We believe that our case of neuroblastoma in a preterm neonate with chylothorax is rare. The tumor was an undifferentiated type stage III abdominal neuroblastoma that was increasing in size. Fortunately, after six cycles of small dose chemotherapy, it decreased significantly and the patient was discharged home at the age of 10 months in good condition.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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