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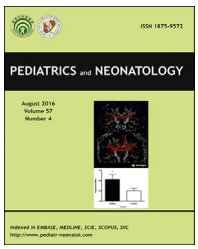

ORIGINAL ARTICLE

Solid Cancers in the Premature and the Newborn: Report of Three National Referral Centers

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neonate;
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Background: Advances in multidisciplinary care for pediatric cancer have resulted in significant improvement in cure rates over the last decades; however, these advances have not been uniform across all age groups. Cancer is an important cause of perinatal mortality, yet the full spectrum of malignant neoplasms in newborns is not well defined.
Methods: The authors have reviewed the clinical features and outcomes of 37 newborns with congenital malignant tumors treated at three referral centers in North, Central, and South Poland between 1980 and 2014. Event-free survival (EFS) and overall survival (OS) rates were estimated by Kaplan—Meier methods and compared using long-rank test and Cox models.
Results: Twenty-two patients were diagnosed prenatally. The most common diagnoses were neuroblastoma (48.7%), followed by malignant germ-cell tumor (16.2%), and Wilms' tumor (8.1%). Neuroblastoma was the most common malignancy among full-term infants, and malignant sacrococcygeal teratoma was the most common malignancy in premature infants. Thirty

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patients (81%) are alive with a median follow-up of 4.8 years from diagnosis. Patients with Wilms' tumor and malignant germ-cell tumors had the best outcomes (5-year OS 100% for both), whereas the worst prognosis was observed for sarcoma patients (5-year OS 72.92%). Premature infants had better outcome than full-term infants (5-year OS 92.8% vs. 72.58%, respectively).

Conclusion: Although rare, neonatal cancers can present with an aggressive clinical behavior, but they have a generally good outcome. Early diagnosis and management by expert multidisciplinary teams that integrate perinatal medicine experts with pediatric and surgical oncologists are critical. Centralized care with clear referral pathways that facilitate early initiation of specialized treatment should be prioritized.

1. Introduction

Cancer in newborns is rare, with an estimated incidence of 3.65/100,000 live births. Although most neonatal neoplasms are considered to have a benign behavior, malignant tumors represent a significant cause of perinatal mortality,[1–3] which may be related to obstetric or postnatal surgical complications, or disease progression.[4] With advances in obstetrical and perinatal care, including fetal imaging, an increasing proportion of these tumors can be identified prenatally, thus allowing for proper planning for delivery and postnatal care.[5] The prognosis is related to the tumor behavior, which may differ significantly between the perinatal period and later ages, suggesting a role for developmental biology factors.[1,6]

The care of newborns with malignant neoplasms requires a state-of-the-art multidisciplinary team that integrates the specialists involved in the care of high-risk pregnancies and newborns with pediatric oncology experts.[5] Herein, we report the experience of three centers providing multidisciplinary care for congenital malignant tumors in premature and neonatal patients in Poland.

2. Materials and methods

2.1. Patients and treatment

This retrospective study included 38 patients with perinatal malignant neoplasms (excluding mature teratomas) treated at three Pediatric Oncology Centers in Poland during the period 1980—2014 (Mother and Child Institute in Warsaw, Central Poland; Wrocław Medical University in Wrocław, South Poland; and Collegium Medicum, Nicolaus Copernicus University, in Bydgoszcz, North Poland). Treatment was conducted according to the existing disease-specific protocols and treatment guidelines, and it included a "watch-and-wait" approach, or different combinations of surgery, chemotherapy, and radiation therapy. All patients had standard imaging and histological procedures for diagnosis, staging, and follow-up. In the case of a prenatal diagnosis, fetal ultrasound (US) and magnetic resonance imaging (MRI) were performed as clinically indicated. "Total resection" was defined as a complete resection of the tumor without macroscopic or microscopic residue, "gross resection" was defined as resulting in microscopic residue, and "subtotal resection" was defined as resulting in macroscopic residual disease. Approval for this retrospective study was obtained from all the relevant institutions in compliance with international regulations for protection of human research subjects.

2.2. Statistical methods

Overall survival (OS) was defined as the time interval from the date of diagnosis to the date of death or last follow-up. Event-free survival (EFS) was defined as the time interval from the date of diagnosis to the date of disease progression, recurrence, second malignancy, death, or date of last follow-up for patients without events. Results distributions were estimated using the Kaplan—Meier method. Factors were examined as predictors of OS using log-rang test. Values of $p \leq 0.05$ were considered significant. Statistical analysis was performed using STATISTICA 10.0 for Windows (StatSoft Inc., Tulsa, OK, USA).

3. Results

3.1. Patient characteristics and treatment

Between 1980 and 2014, 37 patients with congenital malignant neoplasms (mature and immature teratomas were excluded) were referred for treatment to the three oncology centers. The clinical and treatment characteristics are shown in Tables 1 and 2. The median gestational age at the time of delivery was 38 weeks (range 30—41 weeks); 14 patients (37.8%) were born preterm (<38 weeks). Four children were very low birth weight, born at 30—34 weeks of gestational age; three were low birth weight, born at 34—35 weeks of gestational age, one baby was hypertrophic, born at 35 weeks of gestational age, and the others were eutrophic newborns. All 21 cases diagnosed prenatally through standard screening US imaging were monitored weekly by US or MRI as clinically indicated, and an elective cesarean section was performed in 20 women due to rapid tumor growth (11 of them were premature births). Ten cases (out of 14) of preterm labor