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The clinical management and outcomes of cervical neuroblastic tumors

Jeremy R. Jackson, MD,[a] *Hung C. Tran, MD,*[b] *James E. Stein, MD,*[a] *Hiroyuki Shimada, MD, PhD,*[c] *Ankur M. Patel, DO, MPH,*[d] *Araz Marachelian, MD,*[b] *and Eugene S. Kim, MD*[a,*]

[a] *Division of Pediatric Surgery, Department of Surgery, Children's Hospital Los Angeles, Los Angeles, California*
[b] *Division of Hematology-Oncology, Department of Pediatrics, Children's Hospital Los Angeles, Los Angeles, California*
[c] *Department of Pathology and Laboratory Medicine, Children's Hospital Los Angeles, Los Angeles, California*
[d] *Division of Otolaryngology, Department of Surgery, Children's Hospital Los Angeles, Los Angeles, California*

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ABSTRACT

Background: Although patients with peripheral neuroblastoma (NB; pelvic and thoracic) typically have better outcomes and less aggressive disease compared with patients with abdominal disease, little has been published with regard to the management and outcomes of patients with cervical NB. Herein, we sought to determine the characteristics of cervical neuroblastic tumors and the effect of extent of resection on survival and outcomes.

Methods: We performed a retrospective review of 325 children with neuroblastic tumors at Children's Hospital Los Angeles over a 15-y period (January 1990-February 2015). Data collected from the medical record included location of tumor, age at diagnosis, age at resection, extent of resection, chemotherapy course, International Neuroblastoma Staging System stage, histologic International Neuroblastoma Pathology Classification, and MYCN amplification, a poor prognostic marker. Outcome variables included postoperative complications and overall survival.

Results: Twelve patients (3.6%) were found to have cervical neuroblastic tumors (nine NBs, one ganglioneuroblastoma, and two ganglioneuromas). All had favorable histology, and none (0/12) had MYCN amplification. Of the NB patients, four of nine patients underwent resection, whereas the other five underwent biopsy followed by chemotherapy or observation alone. Of the 12 total patients, six underwent gross total resection, four (67%) of which developed complications. At a median follow-up of 4.4 y, there were no recurrences or deaths.

Conclusions: Cervical neuroblastic tumors represent favorable lesions with good outcomes similar to other peripheral neuroblastic tumors. In our study, survival was excellent regardless of extent of tumor resection. Based on our data, we recommend a minimally aggressive surgical approach in managing children with cervical neuroblastic tumors.

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* *Corresponding author*. Division of Pediatric Surgery, Children's Hospital Los Angeles, 4650 Sunset Blvd, MS #100, Los Angeles, CA 90027. Tel.: +1323 361-8332; fax: +1 323 361-3534.
E-mail address: eugeneskim@chla.usc.edu (E.S. Kim).

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Introduction

Neuroblastic tumors are a heterogeneous group of embryonal tumors derived from neural crest cells. These tumors have been found to develop anywhere along the sympathetic nervous chain and most often arise within the adrenal gland. Neuroblastic tumors are categorized broadly into a spectrum of three histologic categories, ranging from mature to immature: ganglioneuroma (GN), ganglioneuroblastoma (GNB), and neuroblastoma (NB).[1] NB is the third most common pediatric malignancy behind leukemias and central nervous system cancers.[2] Cervical NBs are rare and represent approximately 3%-5% of all NBs.[3,4] Although there have been few published studies on the topic, peripheral NBs, including cervical, thoracic, and pelvic tumors, are generally considered to be more favorable lesions.[3-5] As such, the best management with the least morbidity may differ for cervical neuroblastic tumors than for primary abdominal lesions. Our institutional practice has been to perform gross total resection (GTR) if possible without incurring injury to nearby structures. Given the proximity of cervical tumors to vital structures, such as the vertebral artery, carotid artery, internal jugular vein, trachea, and cranial nerves IX-XII, these tumors can be clinically challenging to resect and may lead to significant postsurgical morbidity.

There is a paucity of literature regarding the clinical and biologic characteristics of cervical neuroblastic tumors given their rarity. Previous studies of cervical NB demonstrate favorable outcomes and support surgical resection as the treatment of choice, but, they do not offer recommendations regarding the extent of surgical resection required in the management of these tumors.[6-8] The purpose of this study was to identify the characteristics of cervical neuroblastic tumors and to determine the effect of extent of resection on the incidence of complications and overall survival in these patients.

Methods

In our study, 325 patients were found to have neuroblastic tumors at Children's Hospital Los Angeles, from January 1990 to February 2015. The medical records (both paper and electronic) were analyzed to ascertain primary tumor sites as determined by contrast-enhanced computed tomography (CT) scan, magnetic resonance imaging, or surgical exploration. Patients with cervical tumors were identified and selected for further analysis, including a review of diagnostic pathologic reports for tumor subtype and mitosis-karyorrhexis index (MKI). Clinical data collected include age at diagnosis, age at resection, extent of resection, chemotherapy course, International Neuroblastoma Pathology Classification, and International Neuroblastoma Staging System (INSS) classification.[9,10] Patient imaging and clinical data were also reviewed to determine International Neuroblastoma Risk Group (INRG) classification.[11,12] In addition, MYCN amplification status, a poor tumor prognostic marker, and metaiodobenzylguanidine (MIBG) avidity were noted. Other serum markers correlating to poor prognosis, ferritin, and lactate dehydrogenase levels were also collected at diagnosis. To determine tumor volume, CT scans at the time of biopsy or resection were reviewed, and the tumor dimensions were recorded. Tumor volume (cm^3) was measured using the following formula: maximal orthogonal tumor length $\times$ width $\times$ height $\times$ 0.52 ($\pi/6$). Medical records were analyzed for overall survival and postoperative complications. Postoperative complications were defined as any surgery-related injuries or adverse events, which manifested within the first 30 d after surgery. Patient records were also analyzed for preoperative tumor-related Horner's syndrome to distinguish from postoperative Horner's syndrome. This study was approved by the Institutional Review Board of Children's Hospital Los Angeles (CHLA-15-00,119).

Results

Of 325 patients diagnosed with neuroblastic tumors, 12 patients (seven females:five males, 3.6%) were identified to have cervical tumors. Specifically, nine patients had a diagnosis of NB (9/12, 75%), one patient with GNB (1/12, 8.3%), and two patients with GN (2/12, 16.6%).

Patients with neuroblastoma

In the NB cohort, at the time of diagnosis, all nine patients were aged under 12 mo, with a median age at diagnosis of 4 (range: 1-7) mo. Among these patients, the median length of follow-up was 3 y (range: 9 mo-15 y). Two patients initially presented with tumor-related Horner's syndrome. All nine patients had favorable histology. None (0/9) of the analyzed NB tumors were found to have MYCN amplification by fluorescent *in situ* hybridization. MIBG avid tumors were seen in 71% (5/7) of studied patients. The median lactate dehydrogenase level was 765 u/L (range: 679-1332; normal 425-975), and the median ferritin level was 43 ng/mL (range: 17-228; normal 10-140). The mean tumor volume was 22.3 cm^3 (range: 2.9-40). All the NBs had a poorly differentiated subtype. Five of nine had a low MKI, three had an intermediate MKI, and one was indeterminate. With regard to INSS staging, five patients were stage II, one was stage III, two were stage IV, and one was stage IV-S. By INRG staging, one patient was stage L1, four were stage L2, two were stage M, and one was stage MS (Table). Of the nine patients with NB, two underwent GTR or a complete excisional biopsy before initiating chemotherapy. One patient (1/2, 50%) in this group developed a postoperative complication after a transoral excisional biopsy of a 35.5-cm^3 tumor, which led to repeated failed extubation attempts, necessitating tracheostomy, and subsequent decannulation after 7 mo. One patient received chemotherapy before GTR of a 10.3-cm^3 tumor, which was complicated by chronic postoperative Horner's syndrome. Four of nine patients with NB underwent a minimal biopsy technique (three incisional, one percutaneous), followed by chemotherapy alone without any further surgical interventions. The average tumor volume of