Pediatric Central Nervous System Tumors in Nepal: Retrospective Analysis and Literature Review of Low- and Middle-Income Countries

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■ BACKGROUND: **Central nervous system (CNS) tumors are the most common cause of cancer-related death in children. Little is known about the demographics and treatment of pediatric brain tumors in low- and middle-income countries (LMICs).**

■ METHODS: **We performed a retrospective chart review of all pediatric patients who presented to the neurosurgical service at Tribhuvan University Teaching Hospital in Kathmandu, Nepal from 2009–2014 and collected information on patients <18 years old who received a diagnosis of a CNS tumor. We analyzed age, gender, clinical presentation, extent of surgical resection, histopathology, and length of hospital stay. We also conducted a literature review using specific terminology to capture studies of pediatric neuro-oncologic epidemiology conducted in LMICs. Study location, length of study, sample size, study type, and occurrence of 4 common pediatric brain tumors were extracted.**

■ RESULTS: **We identified 39 cases of pediatric CNS tumors, with 62.5% observed in male children. We found that male children (median = 13 years) presented later than female children (median = 8 years). The most frequently observed pediatric brain tumor type was ependymoma (17.5%), followed by astrocytoma (15%) and medulloblastoma (15%). Surgical resection was performed for 80% of cases, and gross total resection reported in 62.9% of all surgeries. More than half (54.1%) of patients had symptoms for more than 28 days before seeking treatment. Symptomatic hydrocephalus was noted in 57.1% of children who presented with CNS tumors. The literature review yielded studies from 18 countries. Study length ranged from 2–20 years, and sample sizes varied from 35–1948. Overall, we found more pronounced variation in the relative frequencies of the most common pediatric brain tumors, compared with high-income countries.**

■ CONCLUSIONS: **We present the first operative series of childhood CNS tumors in Nepal. Children often had delayed diagnosis and treatment of a tumor, despite symptoms. More comprehensive data are required to develop improved treatment and management algorithms in the context of a given country's demographics and medical capabilities for childhood CNS tumors.**

INTRODUCTION

In high-income countries (HICs), pediatric cancers are cured at a rate of 80%. This rate does not hold for low- and middle-income countries (LMICs).[1] Given that cancer is the leading cause of disease-related mortality in children residing in HICs,

Key words
- Brain tumor
- Epidemiology
- Global surgery
- Low-income country
- Nepal
- Pediatric

Abbreviations and Acronyms
CNS: Central nervous system
ETV: Endoscopic third ventriculostomy
GTR: Gross total resection
HIC: High-income countries
LMIC: Low- and middle-income countries
NRA: National registry analysis
RCR: Retrospective chart review
STR: Subtotal resection
TUTH: Tribhuvan University Teaching Hospital
VP: Ventriculoperitoneal
WHO: World Health Organization

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the efforts of medical professionals, researchers, governments, and communities to continue raising the 80% cure rate are a distinct need. Specifically, central nervous system (CNS) tumors are the most common cause of cancer-related death in children.[2]

Efforts to provide better care for children with CNS tumors are increasingly needed in LMICs as well.[1,3] Although there have been efforts to better understand and treat cancer in LMICs, childhood CNS tumors have largely been ignored, due to underdiagnosis, poor clinical assessment, and barriers to access of higher levels of care and multidisciplinary treatment facilities.[4]

After completing a comprehensive literature review, we identified no prior studies of pediatric CNS tumors in Nepal. Our endeavor was 2-fold: (1) understand the demographic characteristics, tumor distribution, and clinical presentation of CNS tumors in children at Tribhuvan University Teaching Hospital (TUTH) in Kathmandu, Nepal and (2) compare our findings to reports of pediatric CNS tumors in other LMICs. Diagnosis and management of cancer are complex and multidimensional. Here, we illustrate that pediatric CNS tumor patients must be managed in the context of their own country's experience with the disease and medical resource capabilities. Efforts to understand pediatric CNS tumors in LMICs are under way but need further attention.[4] Further studies are required to first understand and then optimize diagnosis and management of children with brain tumors specific to geographic location and socioeconomic realities.

METHODS

Patient Population

TUTH is a tertiary care center in Nepal. Patients from throughout the country are included in this study.[5]

Study Design and Chart Review

We performed a retrospective chart review of all pediatric patients who presented to the neurosurgical service at TUTH. We analyzed the information of patients <18 years old who received a diagnosis of a CNS tumor. The study period ranged from 2009–2014, a period of 5 years. We analyzed age, gender, clinical presentation, extent of surgery, histopathology, and length of hospital stay.

Literature Review

We conducted a systematic literature search to find studies analyzing pediatric CNS tumors with a focus on low- and middle-income countries. To survey the literature, we searched the NCBI PubMed database and Google Scholar employing the Boolean operators 'AND' and 'OR' with the terms 'pediatric,' 'childhood,' 'brain tumor,' 'neurosurgery', 'neuro-oncology', 'oncology', 'cancer,' 'developing country,' and 'low income country.' We additionally performed the searches above along with the terms 'South America,' 'Central America,' 'North America,' 'Asia,' 'Australia,' 'Europe,' or 'Africa' to identify studies conducted in specific regions worldwide. From the references of these studies, we identified additional studies. Our inclusion criteria included studies published from 1990 to the present that provided epidemiologic data on pediatric CNS tumors in LMIC ($n = 18$). If multiple studies from a country were available, we selected the study with the largest sample size, most reliable data collection method, and relatively recent completion. We excluded studies that did not provide information regarding specific brain tumor types. LMICs were identified following World Bank categorization.[6]

Institutional Review Board Approval

Approval to conduct this study was provided by the Institutional Review Board (IRB) at both TUTH and Stanford University School of Medicine. All patient information and data were collected and managed in compliance with IRB-approved protocol.

Statistical Methods

Data preparation and analysis were performed using R: A Language and Environment for Statistical Computing (version 3.0.2; 2013-09-25).

RESULTS

Patient Demographics and Clinical Presentation

We identified 39 cases of pediatric primary CNS tumors in 248 pediatric neurosurgeries (19.8%) performed by the neurosurgical service at TUTH over the course of 5 years. Male children comprised most these observations (61.5% had tumors). The overall average age of presentation was 10.0 years, with male children presenting later (10.7 years) than female children (8.7 years). The most common presenting symptoms were headache (27%), hemiparesis/plegia (24.3%), and vomiting (21.6%). Symptoms were present for more than 14 days in 78.4% of cases and more than 28 days in 54.1% of cases (Table 1).

Tumor Histopathologic Distribution

Thirty-six tumors were histologically analyzed by the pathology department at TUTH. The most frequently observed tumor type was ependymoma, comprising 19.4% of the tumor burden at TUTH. Other common tumors were pilocytic astrocytoma (16.7%) and medulloblastoma (16.7%) (Table 2). Of 18 tumors for which a World Health Organization grade was determined, 8 were identified as WHO grade IV. Within 3 predetermined age groups, the number of tumors did not vary greatly. However, the most common tumor in each group varied. In the youngest age group, medulloblastoma was most common. The middle age group most frequently experienced pilocytic astrocytoma, while the oldest group was most likely to experience ependymoma.

Operative Characteristics and Length of Stay

Surgical microscope was available for all operations, and surgical resection was performed for 80% of cases. Neuronavigation was not available at TUTH. Gross total resection (GTR) was reported by the surgeon in 62.9% surgeries and subtotal resection (STR) in 17.1%. Biopsy alone accounted for 5.7%, and tumor surgery was not performed in 14.3% of cases (Table 3). Postoperative imaging was not routinely performed to verify GTR versus STR. More than half (52.5%) required additional surgeries in the form of cerebrospinal fluid diversion procedures. Ventriculoperitoneal (VP) shunt was inserted in 17 cases compared with endoscopic third ventriculostomy (ETV) in 4 cases. Average length of stay was 22.9 days with a range of 6–85 days with no meaningful difference between males (22.6) and females (23.3).