

Diagnosis and treatment of infantile malignant solid tumors in Beijing, China: A multicenter 10-year retrospective study

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ABSTRACT

Importance: Cancer is the main cause of death by disease in children. Children experience the highest incidence of cancer in the first year of life. However, there is no comprehensive registration system for children with tumors in China.

Objective: To summarize the diagnosis and treatment of infant cancer and analyze the status of standardized diagnosis and management among several treatment centers in Beijing, China, thereby providing evidence to guide further clinical research.

Methods: From January 1, 2010 to December 31, 2019, patients with newly diagnosed infantile malignant solid tumors were admitted to six large tertiary pediatric solid tumor diagnosis and treatment centers in Beijing. The epidemiology, clinical features, and therapeutic effects of tumors in these patients were analyzed retrospectively. All patients were followed up until March 31, 2020.

Results: In total, 938 patients were enrolled in this study. There were 530 boys (56.5%) and 408 girls (43.5%); the median age was 6.0 months (range, 0–12.0 months). The three most common tumors were retinoblastoma in 366 patients (39.0%), neuroblastoma in 266 patients (28.4%), hepatoblastoma in 133 patients (14.2%), and central nervous system tumors in 52 patients (5.5%). The estimated 5-year overall survival rate was 81.3% \pm 1.8%, and the 5-year event-free survival rate was 71.8% \pm 2.9%. The 5-year overall survival rates of non-rhabdomyosarcoma soft tissue sarcoma, neuroblastoma, and retinoblastoma were 100%, 88% \pm 2.2%, and 86.9% \pm 2.1%, respectively. The 5-year event-free survival rates were 81.1% \pm 2.7% for neuroblastoma, 81.6% \pm 9.8% for non-rhabdomyosarcoma soft tissue sarcoma, and 72.7% \pm 14.1% for extracranial malignant germ cell tumors.

Interpretation: The three most common infantile malignant solid tumors were retinoblastoma, neuroblastoma, and hepatoblastoma. Multidisciplinary combined diagnosis and treatment is needed for infantile tumors.

KEYWORDS

Infant, Solid tumor, Malignant, Multicenter, Neuroblastoma, Retinoblastoma

INTRODUCTION

Cancer is the main cause of death by disease in people younger than 20 years of age worldwide.¹ According to the Surveillance, Epidemiology, and End Results (SEER) report, children experience the highest incidence of cancer in the first year of life.² The histological type of two-thirds of infant tumors is embryonic tumors or germ cell tumors. The most frequently diagnosed cancers among infants are neuroblastoma (NB), central nervous system tumors, retinoblastoma (RB), germ cell tumors, nephroblastomas (Wilms tumors), and hepatoblastoma (HB), respectively. Thus far, there has been no comprehensive registration system for children with tumors in China. Attention to cancer in infants is low; most studies focus on single hospitals or single tumors, such that they lack the research impact of multiple centers for treatment of infants with malignant solid tumors. Therefore, we combined data from six large children's tumor diagnosis and treatment centers in Beijing, China. We retrospectively analyzed the clinical data of malignant solid tumors in infants, then summarized their clinical characteristics, diagnosis and treatment status, and existing problems. We also summarized the statuses of standardized diagnosis, treatment, and management to provide evidence to support further clinical studies.

METHODS

Ethical approval

This study was a multi-center retrospective clinical study, which has been registered in the National Medical Research Registration Information System, reviewed and approved by the Ethics Committee of Beijing Children's Hospital, Capital Medical University (Number: 2020-Z-012). Since this was a retrospective study and the data analysis were performed anonymously, the study was exempt from informed consent from patients' guardians.

Study participants

This study included patients with newly diagnosed infantile malignant solid tumors from six large children's diagnosis and treatment centers in Beijing (i.e., Beijing Children's Hospital, Beijing Tongren Hospital, Beijing Tiantan Hospital, Beijing Shijitan Hospital, Peking University First Hospital, and Capital Institute of Pediatrics) between January 1, 2010 and December 31, 2019.

Eligible criteria were as follows: diagnosis of malignant solid tumors and age younger than 12 months. The included diseases were NB, RB, brain tumors (e.g., medulloblastoma, atypical teratoid/rhabdoid tumors,

intracranial primitive neuroectodermal tumor, pinealoblastoma, glioma, choroid plexus papilloma, choroid plexus papillary carcinoma, and intracranial germ cell tumor), HB, renal tumors (e.g., Wilms tumor, rhabdoid renal tumors, and renal clear cell sarcoma), rhabdomyosarcoma, non-rhabdomyosarcoma soft tissue sarcoma, Ewing sarcoma, extracranial germ cell tumors, and other rare solid tumors.

Exclusion criteria were unclear clinical or pathological diagnosis and presence of existing solid tumors.

Treatment and outcome evaluation

All patients were diagnosed based on the primary tumor, tumor markers, and imaging studies. All solid tumors were treated at a single center by means of multidisciplinary combined comprehensive treatment, mainly comprising surgery and chemotherapy. Systemic tumor imaging evaluation was performed to guide selection of surgical resection or direct neoadjuvant chemotherapy, and to identify the tumor invasion site and any distant metastasis. For patients undergoing surgery, pathology and staging analysis were used to determine whether chemotherapy was required. In accordance with their clinical experience, each center adopted different chemotherapy plans for patients with different disease types.³⁻⁶

Follow-up and statistical analysis

All patients who stopped treatment without disease deterioration were withdrawal treatment. Patients who terminated treatment due to disease deterioration were included in the statistical analysis. The most recent follow-up time and disease status were regarded as the end point. The statistical end points were complete remission, progress, recurrence, and death due to disease. All children were followed up to March 31, 2020.

SPSS version 17.0 (SPSS, Inc., Chicago, IL, USA) was used to analyze the data. Overall survival was defined as the time from admission to death or loss to follow-up for any reason. Event-free survival was defined as the time from admission to initial tumor recurrence/metastasis, death, or loss to follow-up for any reason. Data with normal distributions were expressed as mean \pm standard deviation, data with non-normal distributions were expressed as median (range), and survival data were expressed by means of Kaplan–Meier survival analysis. $P < 0.05$ was considered statistically significant.

RESULTS

Characteristics of the patients

Between January 1, 2010 and December 31, 2019, 987 infants with newly diagnosed infant malignant solid tumors were treated in the six participating hospitals. Excluding 11 patients older than 12 months of age, 25

re-enrolled patients (one Wilms tumor, eight RB, and 16 HB, including one patient underwent treatment in three of the six hospitals), and 13 patients admitted to the hospital without treatment, a total of 938 patients were finally included in this study. Among these 938 patients, Beijing Children's Hospital had the largest proportion (501 patients, 53.4%), followed by Beijing Tongren Hospital (367 patients, 39.1%), Peking University First Hospital (31 patients, 3.3%), Capital Institute of Pediatrics (30 patients, 3.2%), Beijing Shijitan Hospital (seven patients, 0.7%), and Beijing Tiantan Hospital (two patients, 0.2%).

Of the 938 patients, 530 (56.5%) were boys and 408 (43.5%) were girls. The median age was 6.0 months (range, 0–12.0 months). The most common tumor was RB in 366 patients (39.0%), followed by NB in 266 (28.4%), HB in 133 (14.2%), soft tissue sarcoma in 59 (6.3%), central nervous system tumors in 52 (5.5%), renal tumors in 44 (4.7%), and extracranial germ cell tumor in 15 (1.6%) (Table 1). Three patients had rare tumors: one each with pleural pulmonary blastoma, poorly differentiated carcinoma of parotid gland, and pancreatoblastoma. Twenty-four patients had a family history of malignant tumor. Thirty-three patients (3.5%) were diagnosed antenatally or immediately after birth.

TABLE 1 Demographic and clinical characteristics of 938 infant patients with solid tumors

Characteristics	Number of patients, <i>n</i> (%)
Sex	
Male	530 (56.5)
Female	408 (43.5)
Diseases	
Retinoblastoma	366 (39.0)
Neuroblastoma	266 (28.4)
Hepatoblastoma	133 (14.2)
Central nervous system tumors	52 (5.5)
Embryonic tumor	13 (1.4)
Medulloblastoma	6 (0.7)
Atypical teratoma/rhabdoid tumor	5 (0.5)
Intracranial primitive neuroectodermal tumor	2 (0.2)
Glioma	10 (1.1)
Others	29 (3.1)
Renal tumors	44 (4.7)
Wilms tumor	30 (3.2)
Clear cell sarcoma of the kidney	5 (0.5)
Rhabdoid renal tumors	9 (1.0)
Soft tissue sarcoma	59 (6.3)
Rhabdomyosarcoma	28 (3.0)
Non-rhabdomyosarcoma soft tissue sarcoma	20 (2.1)
Ewing sarcoma	11 (1.2)
Extracranial germ cell tumor	15 (1.6)
Yolk sac tumor	1 (0.1)
Malignant germ cell tumor	4 (0.4)
Immature teratoma	10 (1.1)
Other rare tumors	3 (0.3)
Family history	24 (2.5)
Other malignant tumors	7 (0.7)
The same tumor	17 (1.8)

The median age of onset was 6.0 months. The numbers of patients with onset age of either 1 month or 11 months after birth were relatively small. Twenty patients were lost to follow-up, with a loss to follow-up rate of 2.1%. The median follow-up duration was 33.0 months (range, 0–124.6 months). The estimated 5-year OS rate was $81.3\% \pm 1.8\%$ for all patients. The estimated 5-year EFS rate was $71.8\% \pm 2.9\%$ of patients with tumors other than RB ($n = 527$) because it is hard to analyze the relapse of the patients with RB.

The sources of patient referrals were widely distributed. In total, 936 patients (99.8%) were from China, whereas two patients were from other nations. The five most common provinces of origin were Shandong (137 patients, 14.6%), Hebei (135 patients, 14.4%), Beijing (102 patients, 10.9%), Henan (82 patients, 8.7%), and Shanxi (46 patients, 4.9%). Diagnosis and treatment of patients were mostly in the northern region of China, centering around Beijing.

Diagnoses, treatment and outcome of specific cancer

Retinoblastoma

In total, 366 patients (198 boys and 168 girls) were diagnosed with RB, which was the most common disease in this study. Two hundred seven patients (56.5%) were diagnosed with bilateral RB and 159 patients (43.4%) were diagnosed with unilateral RB; 360 patients (98.4%) were diagnosed with intraocular RB and six patients were diagnosed with extraocular RB (Figure 1). The median age of onset was 5 months (range, 0–12 months). Fourteen patients (3.8%) had a family history of RB, comprising 58.3% of the 24 patients with a positive family history (Table 2). The average age of diagnosis did not significantly differ between patients with a family history of RB and patients without family history (150.0 ± 102.9 days vs. 194.5 ± 92.3 days, $P = 0.08$).

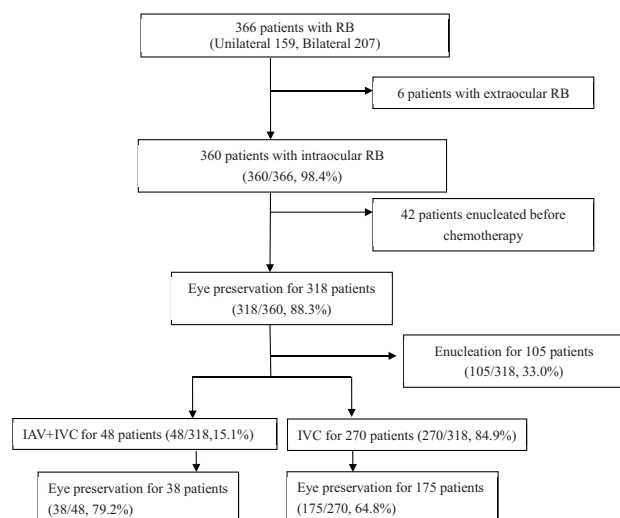


FIGURE 1 Treatment outcomes of 366 patients with retinoblastoma. RB, retinoblastoma; IAC, intra-arterial chemotherapy; IVC, intravenous chemotherapy.

Three hundred eighteen of the 360 patients (88.3%) with intraocular RB underwent eye preservation treatment. In total, 213 (67.0%) eyes underwent successful globe salvage; the median number of chemotherapy treatments was four courses (range, 0–21). One hundred five patients underwent failed eye preservation; the median number of chemotherapy treatments was four courses (range, 0–17). However, there were no significant differences in the number of chemotherapy treatments between patients with successful or failed eye preservation treatment ($P > 0.05$). Forty-eight of the 318 patients (15.1%) underwent systemic chemotherapy combined with intra-arterial chemotherapy (the combined chemotherapy group), the eye-preservation rate was 79.2% (38/48). About 270 of the 318 patients (84.9%) received intravenous chemotherapy with focal treatment; the eye-preservation rate was 64.8% (175/270) (Figure 1). The eye-preservation rate was slightly higher in the combined chemotherapy group, but without statistical significance ($P = 0.51$). The median follow-up duration was 58.4 months (range, 2.0–124.6 months). Thirty-seven patients (10.1%) died, two of which were in the extraocular stage, 21 were in the Intraocular Retinoblastoma Classification (IRC) E stage, and 14 were in the IRC D stage. The number of chemotherapy treatments for death patients was 4.18 ± 3.24 . The estimated 5-year OS rate was $86.9\% \pm 2.1\%$ for patients with RB (Figure 2).

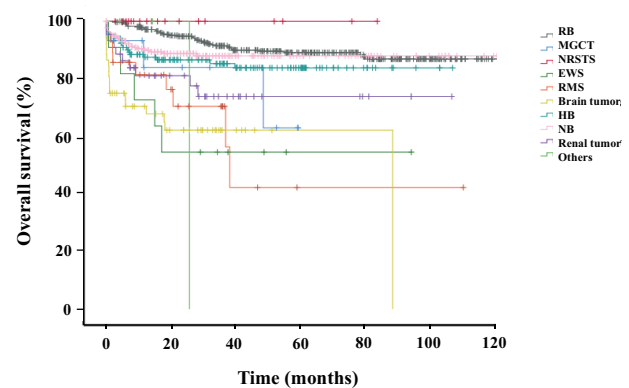


FIGURE 2 Kaplan–Meier overall survival curves by various type of tumor. RB, retinoblastoma; MGCT, malignant germ cell tumor; NRSTS, non-rhabdomyosarcoma soft tissue sarcoma; EWS, Ewing’s sarcoma; RMS, rhabdomyosarcoma; HB, hepatoblastoma; NB, neuroblastoma.

Neuroblastoma

In total, 266 patients (28.4%; 143 boys and 123 girls) were diagnosed with NB (28.4%), which was the second most common disease in this study. The median age of onset was 6.1 months (range, 0–12.0 months). Twenty-three patients (8.6%) were diagnosed immediately after birth, comprising 69.7% of the 33 patients of all the disease diagnosed after birth; none had a family history of malignant tumors (Table 2). The most common primary site was the abdomen in 172 patients (64.7%), thorax in 74

patients (27.8%), cervix in 15 patients (5.6%), and other locations in five patients. There were 91 patients (34.2%) with lymph node metastasis, 61 patients (22.9%) with liver metastasis, 47 patients (17.7%) with bone metastasis, 41 patients (15.4%) with bone marrow metastasis, 25 patients (9.4%) with skin and soft tissue involvement, nine patients (3.4%) with central nervous system involvement, two patients with lung metastasis, and three patients with pancreas involvement. Thirty-nine patients (14.7%) had high-risk status, while 227 patients (85.3%) had intermediate or low-risk status.

Of the 266 patients, 23 (8.6%) did not undergo further chemotherapy or other interventions after surgical removal of the primary lesion; these patients are currently surviving. Two hundred eighteen patients were tested for the *MYCN* gene, which was positive in 22 patients (9.7%) and was associated with a higher risk of death from the disease (7/22), compared with infants who did not exhibit *MYCN* amplification (11/196, $P < 0.001$). The median follow-up duration was 22.0 months (range, 0–121.0 months), 9 patients in this group were lost to follow-up, 19 patients died (Table 2). The mortality rate was significantly higher in the high-risk NB group (13/39) than in the low-risk NB group (15/227, $P < 0.001$). The estimated 5-year OS and EFS rates were $88.0\% \pm 2.2\%$ and $81.1\% \pm 2.7\%$, respectively (Figures 2 and 3).

Hepatoblastoma

In total, 133 patients (14.2%; 81 boys and 52 girls) were diagnosed with HB, which was the third most common disease in this study. The median age of onset was 7.0 months (range, 0–12.0 months). Five patients were diagnosed after birth; 18 patients had early lung metastases and two died. The median follow-up duration was 32.2 months (range, 0–107.3 months), 7 patients in this group

were lost to follow-up, and 11 patients (8.3%) died, of which two died of tumor rupture and bleeding within 1 week of treatment. The estimated 5-year OS and EFS rates were $83.8\% \pm 3.5\%$ and $70.2\% \pm 9.9\%$, respectively (Figures 2 and 3).

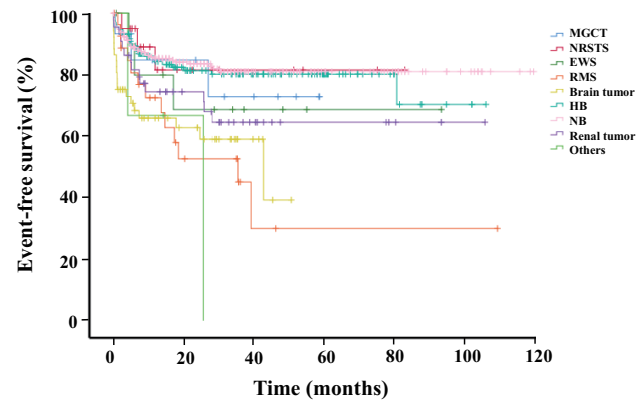


FIGURE 3 Kaplan–Meier event-free survival curves by various type of tumor. MGCT, malignant germ cell tumor; NRSTS, non-rhabdomyosarcoma soft tissue sarcoma; EWS, Ewing’s sarcoma; RMS, rhabdomyosarcoma; HB, hepatoblastoma; NB, neuroblastoma.

Central nervous system tumors

Fifty-two children (36 boys and 16 girls) were diagnosed with central nervous system tumors. One patient had spinal cord tumors, 46 patients had supratentorial tumors, and five patients had infratentorial tumors. Although there were only 52 patients in this group, there were more than 10 pathological types. In addition, seven patients (13.4%) were not treated after imaging due to the high risk involved in surgery. The median follow-up duration was 16.4 months (range, 0–88.7 months), two patients in this group were lost to follow-up, and 17 patients died (Table

TABLE 2 Demographic and clinical data of specific cancer type of infantile solid tumors

Items	Retinoblastoma (<i>n</i> = 366)	Neuroblastoma (<i>n</i> = 266)	Hepatoblastoma (<i>n</i> = 133)	Central nervous system tumors (<i>n</i> = 52)	Renal tumors (<i>n</i> = 44)	Rhabdomyosarcoma (<i>n</i> = 28)	Ewing’s sarcoma (<i>n</i> = 11)	Extracranial malignant germ cell tumors (<i>n</i> = 15)	Non-rhabdomyosarcoma soft tissue sarcoma (<i>n</i> = 20)
Male/Female	198/168	143/123	81/52	36/16	24/20	15/13	8/3	9/6	14/6
Age of onset (months)	5.0 (0–12.0)	6.1 (0–12.0)	7.0 (0–12.0)	6.1 (0–12.0)	6.8 (3.0–12.0)	5.2 (0–12.0)	8.1 (0.2–12.0)	4.7 (2.4–12.0)	3.9 (0–10.9)
Follow-up duration (months)	58.4 (2.0–124.6)	22.0 (0–121.0)	32.2 (0–107.3)	16.4 (0–88.7)	27.0 (0–107.0)	20.2 (0.2–110.6)	29.2 (0.8–94.5)	23.6 (0.4–59.5)	15.0 (2.8–83.9)
Diagnosed after birth	0	23	5	0	0	3	0	0	2
Lost to follow-up	0	9	7	2	0	2	0	0	0
Family history	14	2	0	0	5	2	0	1	0
Died	37	19	11	17	11	7	5	3	0

Data was shown as *n*, or median (range).

2). The estimated 5-year OS and EFS rates were 0 and $39.3\% \pm 16.8\%$, respectively (Figures 2 and 3).

Renal tumors

In total, 44 patients (24 boys and 20 girls) were diagnosed with renal malignant tumors. The median age of onset was 6.8 months (range, 3.0–12.0 months). Eleven patients (25.0%) died, of which two were diagnosed with renal clear cell sarcoma and nine were diagnosed with rhabdoid renal tumors; notably, all patients with rhabdoid renal tumors died. The estimated 5-year OS and EFS rates were $73.9\% \pm 7.4\%$ and $64.4\% \pm 7.9\%$, respectively (Figures 2 and 3).

Rhabdomyosarcoma

In total, 28 patients (15 boys and 13 girls) were diagnosed with rhabdomyosarcoma. The median age of onset was 5.2 months (range, 0–12.0 months). Tumors were detected in three patients after birth, two patients of which had a family history of malignant tumors. The patients with rhabdomyosarcoma had a young age of onset and did not receive radiotherapy at the initial diagnosis. Two patients underwent radiotherapy (i.e., particle implantation and external irradiation) after relapse, but both died. Totally seven patients died and two patients were lost to follow-up (Table 2). The estimated 5-year OS and EFS rates were $42.3\% \pm 1.7\%$ and $30.1\% \pm 14.5\%$, respectively (Figures 2 and 3).

Ewing's sarcoma

Eleven patients (eight boys and three girls) were diagnosed with Ewing's sarcoma. There was neither a family history of tumor nor a patient who developed disease immediately after birth. Three patients were tested for the *EWSR1* gene and only one demonstrated positive findings; one patient with negative findings died, while another patient underwent follow-up after treatment. No patients underwent radiotherapy; the median follow-up duration was 29.2 months (range, 0.8–94.5 months) and five patients died. The estimated 5-year OS and EFS rates were $54.5\% \pm 1.5\%$ and $68.6\% \pm 15.1\%$, respectively (Figures 2 and 3).

Extracranial malignant germ cell tumors

Fifteen patients (nine boys and six girls) were diagnosed with extracranial malignant germ cell tumors. The median age of onset was 4.7 months (range, 2.4–12.0 months). One patient in this group had a family history of tumors, and none had onset after birth. The primary tumor originated from the gonads in one patient. In all other patients, primary tumors originated from outside the gonads. The median follow-up duration for this group of patients was 23.6 months (range, 0.4–59.5 months) and three patients died. The estimated 5-year OS and EFS rates were $64.0\% \pm 2.0\%$ and $72.7\% \pm 14.1\%$, respectively

(Figures 2 and 3).

Non-rhabdomyosarcoma soft tissue sarcoma

Among 20 patients (14 boys and six girls) with non-striated soft tissue sarcoma and rare tumors, 17 were diagnosed with infantile fibrosarcomas, while the remaining three were diagnosed with other sarcomas. The median age of onset was 3.95 months (range, 0–10.9 months). Two patients developed disease immediately after birth. All patients are survival until the latest follow-up. The estimated 5-year OS and EFS rates were 100.0% and $81.6\% \pm 9.8\%$, respectively (Figures 2 and 3).

DISCUSSION

Epidemiology

In the absence of tumor registration, six tertiary Grade A hospitals in Beijing jointly conducted a retrospective analysis of infants with solid tumors who were admitted in the past decade. From a regional perspective, the patients covered 31 provinces in China; however, 50% of patients were mainly from Beijing and surrounding areas (e.g., Hebei, Shandong, Henan, and Shanxi). The median onset age for all 938 patients was 6.0 months; the male to female ratio was 1.3:1. The most common types of tumors were RB, NB, HB, and other embryonic tumors, which occupied 81.7%, consistent with previous reports regarding infantile tumors (mainly embryonic tumors and germ cell tumors).^{7,8} Their early onset and predominantly embryonal nature suggest a pre-natal origin and genetic factors may be important. SEER reported the most commonly diagnosed malignant tumors in American infants: NB was the most common (26%), followed by leukemia (16%), RB (15%), central nervous system tumors (11%), germ cell tumors (9%), Wilms tumor and soft tissue sarcoma (7%), and liver tumors (5%).² In our study, 28.4% of the patients were diagnosed with NB, which was consistent with that in SEER reports. However, RB and HB had frequency of 39.0% and 14.2% in this cohort, respectively, both of which were higher than the SEER reports. Only 5.5% of the patients in this population with central nervous system tumors, which was lower than that of SEER.

More importantly, solid tumors in children require a multidisciplinary joint diagnosis and treatment model; accordingly, the six hospitals in this group included hospitals that are well-known for ophthalmology and pediatric surgery expertise in China, which enhanced convenience and facilitated both diagnosis and treatment of patients. However, this also contributed to the high proportion of RB and HB in this group of patients. Hubbard et al⁹ evaluating 25 years of cancer incidence in children showed that the incidence of NB was increasing, while the incidence of germ cell tumors was declining. The occurrence of tumors also differed among ethnicities.

In addition, Hung et al¹⁰ found that the incidence of HB in China was 2–5-fold greater than that of US, France, the North of England, and Japan. Considering that genetic variation may be a risk factor for HB in Han Chinese populations, this may have contributed to the high incidence of HB. Moreover, some parents refused further diagnosis and treatment after imaging diagnosis of their infants with malignant central nervous system tumor, which was the main reason for the relatively small number of central nervous system tumors.

Infant malignant solid tumor spectra, diagnosis, and treatment of single disease

The proportion of bilaterally affected eyes in infant patients with RB (56.4%) increased significantly, which was much higher than the rate of patients with RB treated in our hospital (36.5%) during the same period.¹¹ In addition, 3.8% of patients had a family history of RB. Notably, patients who had family histories did not exhibit advanced disease, and the average diagnosis time was approximately at 5 months. Therefore, patients with a family history should be supported during the mother's pregnancy and followed-up after birth, thereby facilitating early diagnosis and treatment, which can improve prognosis and quality of life.

In smaller infants with NB, spontaneous tumor regression has been observed.⁷ Moreover, NB was the predominant type of disease after birth in our study. Twenty-three (8.6%) of the patients with NB had their primary lesions surgically removed without further chemotherapy or other interventions; these patients are currently surviving. There is a need to avoid overtreatment of infants with NB, especially those diagnosed after birth, to avoid unnecessary damage to patients.

The largest number of central nervous system tumors was choroid plexus papilloma, followed by low-grade glioma, similar to previous reports. However, the prognosis of patients with central nervous system tumors was markedly different in our study. Toescu et al¹² reported that choroid plexus papilloma occurred within 1 year of age, followed by low-grade glioma with a mortality rate of 0%, which required multiple operations. Intracranial primitive neuroectodermal tumors had a 5-year survival rate of 0%. Notably, only two patients underwent surgical resection in Beijing Tiantan Hospital in the past 10 years. Overall, 1.4%–8.45% of children's brain tumors occur before 1 year of age. Therefore, further investigations are needed to aid in understanding and treatment of central nervous system tumors.

For patients with soft tissue sarcoma, rhabdomyosarcoma was the most common type, followed by infantile fibrosarcoma, which was similar to the findings of previous reports.⁷ However, patients with rhabdomyosarcoma were not administered first-line radiotherapy because of age

and treatment toxicity. Children's Oncology Group (COG) recommends that for local treatment of rhabdomyosarcoma in small infants, individualized local treatment can be used, which comprises delayed radiotherapy.¹³ However, delayed radiotherapy impacts local treatment; local recurrence is the main reason for failure, and is more common in patients receiving individualized local treatment. COG suggests that, due to concerns regarding treatment toxicity, the degradation of effective treatment should be carefully considered and adherence to protocol-specified therapy is recommended.

Ewing-like sarcoma/undifferentiated round cell sarcoma rarely occurs in infancy or even in older children. Ewing-like sarcoma/undifferentiated round cell sarcoma is a "small round cell" sarcoma, which has many features of Ewing's sarcoma; however, it lacks rearrangement of the *EWSR1* gene (a key feature of Ewing's sarcoma). Ewing-like sarcoma/undifferentiated round cell sarcoma is typically more aggressive than Ewing's sarcoma. It is currently presumed to be related to the fusion genes *BCOR-CCNB3* and *CIC-DUX4*.¹⁴ Notably, one patient with Ewing-like sarcoma in this study died of tumor progression during chemotherapy. Therefore, greater attention is needed regarding patients with Ewing's sarcoma who are negative for *EWSR1* rearrangement.

For various types of soft tissue tumors, there is a lack of tumor marker assistance and monitoring during diagnosis and treatment; misdiagnosis or delayed diagnosis often occurs. At present, in-depth genetic research is ongoing internationally regarding various types of soft tissue sarcoma, in the context of the molecular diagnosis era. Many new specific fusion genes are found frequently,¹⁵ which will aid in precise diagnosis and grouping, as well as precise treatment. It is essential to understand the etiology of tumor, determine the best treatment approaches, and improve survival and quality of life for infant patients.

Deficiencies and improvements

Our summary also shows that the diagnosis and treatment of solid tumors in children can reflect the comprehensive strength of a specialized hospital. Beijing Children's Hospital has many departments (e.g., oncology surgery, thoracic surgery, ophthalmology, and head and neck surgery) and domestic first-class surgical treatment experts. These characteristics lead to experience with the largest numbers of patients and widest array of diseases; patients can thus choose the best hospital and receive optimal treatment. However, during the data collection process, we found repeated enrollment of patients in participating hospitals, suggesting patient mobility, as well as loosely connected hospitals that lacked communication. We hope to establish a registration system for various tumors in the near future to meet clinical research and better serve patients.

This analysis also found that the multidisciplinary combined diagnosis and treatment model in various hospitals is currently receiving increasing support; there remain absences of unified and standardized chemotherapy regimens, methods for the prevention and treatment of toxic and side effects of drugs and complications, and as efficacy evaluation indexes. In addition, systematic management of tumor therapy is insufficient; follow-up management focuses on tumor stability alone. In the retrospective analysis, there was a lack of information regarding chemotherapy drug toxicity, growth and development disorders, and long-term organ functions, which should be further summarized for each type of disease. Fortunately, in 2019, the National Health Commission of the People's Republic of China issued a series of measures to strengthen the diagnosis and treatment of children's tumors,¹⁶ and issued a number of guidelines for the diagnosis and treatment of children's tumors (e.g., NB, RB, Wilms tumor, and HB). The National Children's Tumor Detection Center has been established to monitor tumors in children nationwide by means of hospital registration, which may have a profound impact on the prevention and control of solid tumors in infants.

CONFLICT OF INTEREST

There are no conflicts of interest.

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