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# Exploring the prognosis of neuroblastoma in adolescents and adults: a case series and literature review

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Neuroblastoma (NB) is one of the most common extracranial malignant solid tumors in childhood, and over 90% of NBs are diagnosed in children under the age of 10 years old. For patients between 14 and 18 years old or older than 18 years, due to the rarity of NB, few studies have been performed in this population. Defined "adolescent cases" as individuals in 14-18 years old and "adult cases" as older than 18 years old, we reported five NB cases of adolescents and adults in our hospital. 137 cases presented a review of published literature on this topic. Clinicopathological factors and treatment modalities used of the 142 patients were assessed for their prognostic value. Better outcomes were found in adolescent patients rather than adult patients (p=0.012). Patients diagnosed with neuroblastoma or ganglioneuroblastoma (nodular type) (p=0.006) and with distant metastasis (p<0.001) were characterized by poor outcomes. Distant metastasis was an independent adverse influencing factor for overall survival in adolescent and adult NB patients. Regarding treatment modalities, complete surgical resection was a significant factor improving the survival for such patients (p<0.001). For patients with distant metastasis, a significantly longer progression-free survival with chemotherapy than without chemotherapy (p=0.038), whereas chemotherapy did not show an advantage on patients with localized disease (p=0.039). The prognosis of NB in adolescent and adult patients was worse than that in children. These two groups also showed heterogeneity in clinical factors, genetic factors, and treatment tolerance. The rarity of adolescent and adult NB can lead to misdiagnosis and incorrect management. Further optimization of chemotherapy regimens and dosage for adolescent and adult NB patients is needed. The anti-GD2 immunotherapy may be an effective approach for treatment.

*Key words: neuroblastoma, adolescent and adult, outcome, heterogeneity, treatment*

Neuroblastoma (NB), an embryonic tumor originating from the sympathetic nervous system, is one of the most common extracranial malignant solid tumors in childhood and accounts for 7% of all childhood malignancies [1]. As a typical tumor of early childhood, over 90% of NB are diagnosed in children under the age of 10 years old [2]. The current risk classification of NB is based on the Children's Oncology Group (COG) guidelines [3]. It takes into account the patient's age at initial diagnosis, tumor stage, pathological characteristics, and genetic alterations, such as amplification of MYCN (encoding the transcription factor N-MYC). It is well known that older children suffer from more aggressive tumors and have a worse prognosis than younger children do. However, the prognosis of NB in adolescents and adults has not been sufficiently explored.

After the first case of adult NB was reported in 1905 [4], only over 400 cases of adolescent and adult NB had been reported. According to the review of the Surveillance, Epidemiology, and End Results (SEER) data which included cases coded as neuroblastoma and ganglioneuroblastoma diagnosed from 1973 to 2002, the 5-year overall survival (OS) rate was 85% for infants, whereas it was only 36% for adults [5]. It is evident that the overall outcome of the adult group is much worse than that of children with NB. Due to the rarity of NB in adolescents and adults, little is known about its natural history, and there are not yet systematic clinical trials aiming at this population. Therefore, in order to improve the prognosis of adolescent and adult patients with NB, it is necessary to understand the characteristics of this special age compared to that of pediatric NB.

Against this backdrop, we defined "adolescents" as individuals 14–18 years old and "adults" as older than 18 years old. We reported five NB cases of adolescents and adults in our hospital and presented a review of published literature on

this topic. The aim of this study is to explore the clinical outcomes of NB in adolescents and adults while taking into account various clinical features of the disease.

## Patients and methods

**Patients.** This report described five patients with NB who were older than 14 at diagnosis and presented to the Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine. The diagnosis of NB was confirmed by histopathology in the Department of Pathology of our hospital. Disease status was assessed using computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography-computed tomography (PET-CT). Bone marrow was evaluated by histochemical examination of biopsy specimens and aspirates. In addition, MYCN status and heterozygosity at 1p and 11q were assessed by fluorescence in situ hybridization analysis. Tumor staging was performed using the International Neuroblastoma Staging System and grouped based on COG classification. All patients were treated according to the Chinese Children Cancer Group-NB-2014 (CCCG-NB-2014) protocol [6]. The cut-off date for follow-up was conducted on December 31, 2020. The study procedures were approved by the Ethics Committee of Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, and informed consent was obtained from all patients.

**Literature review.** A comprehensive literature search was performed in MEDLINE on PubMed (www.ncbi.nlm.nih.gov/pubmed) with the following terms: "adult" or "adolescent" or "young adult" combined with "neuroblastoma". Only articles on patients diagnosed with neuroblastoma who were older than 14 years old were included. Articles were limited to full papers in the English language, and the search ended on December 31, 2020. Patients with intracranial primary NB were excluded from the study. Studies with no accurate clinical information or survival data were also excluded.

**Statistical analysis.** Statistical analyses were performed using the SPSS software version 23.0. OS and progression-free survival (PFS) were analyzed using the Kaplan-Meier method. Multivariate analysis of OS was performed using Cox regression analysis. Statistical significance was set at p-value <0.05.

## Results

**Five adolescent and adult NB patients in our hospital.** The characteristics and treatment details of the five patients in Xin Hua Hospital are shown in Table 1. The onset age of the patients (3 males and 2 females) ranged from 15 to 25 years old (median, 15 years old). Abdominal pain was the primary complaint in four patients, and fever was the first symptom in one patient. At the time of diagnosis, patients were grouped stage I (n=1), stage III (n=1), or stage IV (n=3). Four patients were classified into the high-risk group, and one patient was divided into the low-risk group. The primary tumor site was the retroperitoneum in two patients and the adrenal gland in three cases. MYCN was normal in 3 of the 4 patients tested (Case 1 was not tested). Two patients had a loss of heterozygosity at 1p, and one had a loss of heterozygosity at 11q. All cases commenced therapy according to the CCCG-NB-2014 protocol. Case 1 received radiation and chemotherapy, but she did not respond to chemotherapy and died after 28 months of follow-up. Case 2 was treated with upfront surgery followed by adjuvant chemotherapy and had a complete response. The treatment of case 3 was surgery combined with chemoradiotherapy and bone marrow transplantation. Case 4 received surgery and chemotherapy. Case 3 and 4

**Table 1. Clinicopathological and therapeutic data of five cases of neuroblastoma managed in our hospital.**

| Case NO. | Age (y) | Sex | Initial Symptoms | Histology | Stage | Risk | Primary sites | Metastases | MYCN | 1p | 11q | Therapy | Out-come | Follow-up (m) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 20 | F | Fever | NB, poorly differentiated | IV | High | Retro-perito-neal | Bone, Bone mor-row | NA | NA | NA | Chemo+ RT | DOD | 28 |
| 2 | 25 | F | Left side abdominal pain | NB, poorly differentiated | I | Low | Adrenal | | N | N | NA | S+ Chemo | ADF | 19 |
| 3 | 15 | M | Low back pain and abdomi-nal pain | NB, poorly differentiated | IV | High | Adrenal | Bone, distant lymph | Amp | Deleted | N | Chemo+ S+ RT+ BM T | AWD | 15 |
| 4 | 15 | F | Left upper abdominal pain | NB, poorly differentiated | IV | High | Adrenal | Bone mor-row, distant lymph | N | N | Deleted | Chemo +S | AWD | 8 |
| 5 | 15 | M | Left side abdominal pain | NB, poorly differentiated | III | High | Retro-perito-neal | | N | Deleted | N | Chemo | AWD | 2 |

ADF: alive disease free; Amp: Amplified; AWD: alive with disease; BM T: bone marrow transplantation; Chemo: chemotherapy; DOD: die of disease; N: normal; NA: not available; NB: neuroblastoma; RT: radiotherapy; S: surgery

were evaluated as partial remission and were still receiving chemotherapy as planned. Case 5 had currently received two courses of chemotherapy and remained on therapy.

**Prognostic factors of adolescent and adult NB patients.** Data of 142 adolescent and adult NB patients, including the 5 new cases (Table 1) and 137 cases from 68 literature reports [7–74], were extracted and reviewed carefully. The patient population comprised 62 males and 80 females. The age at diagnosis of 142 cases ranged from 15 to 86 years old, and the median age was 26.5 years old. The duration of follow-up varied dramatically (0.3–480 months), with a median follow-up of 21.5 months. Of the 142 NB patients, there were 124 cases of NB, 3 of ganglioneuroblastoma, nodular type (GNBn), 13 of ganglioneuroblastoma (GNB), and 2 of ganglioneuroma (GN). At the time of diagnosis, 82 (57.8%) patients had a primary tumor located in the abdomen, 2 (1.4%) in the neck, 27 (19.1%) in the thorax, 22 (15.5%) in the pelvis, 7 (4.9%) in the bones, and 2 (1.4%) at other sites. Sixty-seven (47.2%) patients had metastases at distant sites. Only six out of the 36 patients tested for MYCN status were amplification. Chromosome 1p deletions were reported in 4 out of 16 patients tested (Table 2).

We analyzed the relationship between various clinicopathological variables, including sex, age, pathological diagnosis, metastasis at diagnosis, MYCN status, loss of heterozygosity at 1p, and prognosis. The results are presented in Table 3. The patients who were diagnosed with NB and GNBn had poor clinical outcomes (p=0.006). Adolescent and adult NB patients with distant metastasis showed a significantly worse prognosis compared to those without metastasis (p<0.001). The prognosis was better for adolescents than for adults (p=0.012). Finally, a multivariate analysis explored the correlation between certain known factors and their relationship with patient survival. Distant metastasis at diagnosis was an independent influencing factor for OS in adolescent and adult NB patients. The 5-year OS rate was only 15.7% for patients with distant metastasis compared to 64.4% for patients with localized disease (Figure 1).

**Treatment and outcomes.** One hundred and thirty-nine patients underwent therapeutic procedures and three refused any treatment. One hundred and two (71.8%) cases were treated surgically to remove the tumor. Adjuvant therapy was administered in 115 (81.0%) cases and included chemotherapy in 103 (72.5%), radiotherapy in 59 (41.5%), and both procedures in 47 (33.1%) cases. Ten patients received a combination of bone marrow transplantation and conventional treatment. Three patients received targeted therapy, including two cases with GD2 antibody immunotherapy and one with crizotinib as a targeted therapy for Anaplastic Lymphoma Kinase (ALK). Ultimately, patients receiving anti-GD2 immunotherapy survived, whereas a patient with crizotinib died due to disease progression [9, 10, 25]. Notably, two patients only received palliative radiotherapy and both died (Table 4). The 5-year OS of NB patients who underwent different treatment modalities is shown in Table 4. The OS rate of all patients was 41.6%. Despite the survival rate differing by different treatments, patients who suffered surgery with radiotherapy were characterized by the highest survival rate.

Furthermore, we evaluated various therapeutic interventions that may influence NB prognosis. Surgical resection and chemotherapy are two major therapeutic modalities in clinical cancer treatment. As shown in Figure 2A, combined treatment with surgery and chemotherapy demonstrated superior

**Table 2.** Characteristics of the enrolled 142 adolescent and adult NB patients.

| Characteristics | | N (%) |
|---|---|---|
| Gender | Male | 62 (43.6) |
| | Female | 80 (56.4) |
| Age at diagnosis (y) | 15–29 | 82 (57.8) |
| | 30–44 | 38 (26.8) |
| | 45–59 | 13 (9.1) |
| | ≥60 | 9 (6.3) |
| Pathological subtype | NB | 124 (89.4) |
| | GNBn | 3 (2.1) |
| | GNB | 13 (9.2) |
| | GN | 2 (1.4) |
| Primary site | Neck | 2 (1.4) |
| | Thorax | 27 (19.1) |
| | Abdomen | 82 (57.8) |
| | Pelvis | 22 (15.5) |
| | Bone | 7 (4.9) |
| | Others | 2 (1.4) |
| Metastases | Yes | 67 (47.2) |
| | No | 75 (52.8) |
| MYCN status (36 tested) | Normal | 30 (21.2) |
| | Amplified | 6 (4.2) |
| Chromosome 1p (16 tested) | Normal | 12 (8.4) |
| | Deleted | 4 (2.8) |

Abbreviations: NB-neuroblastoma; GNBn-ganglioneuroblastoma, nodular type; GNB-ganglioneuroblastoma; GN-ganglioneuroma

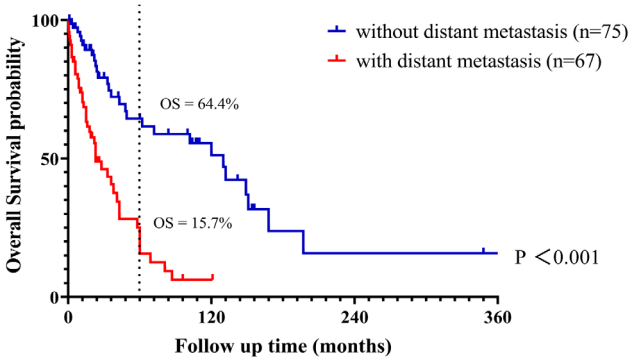


**Figure 1. Kaplan-Meier analysis of the overall survival (OS) in adolescent and adult NB patients. The 5-year OS rate was only 15.7% for patients with distant metastasis compared to 64.4% for patients with localized disease (p<0.001).**

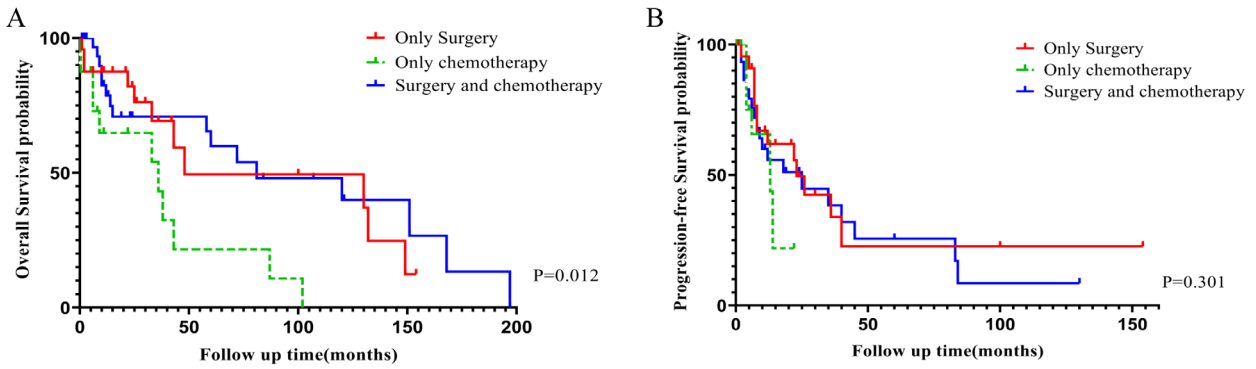


**Figure 2. Effects of different treatment modalities on the prognosis of adolescent and adult NB patients. A) Kaplan-Meier estimated of OS classified by only surgery, only chemotherapy, and combination therapy with surgery and chemotherapy (p=0.012). B) Kaplan-Meier survival curves for patients treated with only surgery, only chemotherapy, and combination therapy with surgery and chemotherapy (p=0.301).**

**Table 3. Univariate and multivariate analyses of the overall survival in 142 NB patients.**

| Characteristics | | | Univariate analysis | Multivariable analysis | | |
|---|---|---|---|---|---|---|
| | | | p-value | p-value | HR | 95% CI |
| Gender | Male (n=62) | Female (n=80) | 0.310 | | | |
| Age at diagnosis | 14–18 years old (n=16) | ≥18 years old (n=126) | 0.012 | 0.137 | 0.574 | 0.276–1.194 |
| Pathological subtype | NB, GNBn (n=127) | GNB, GN (n=15) | 0.006 | 0.054 | 0.363 | 0.130–1.017 |
| Metastases | Yes (n=67) | No (n=75) | 0.000 | 0.000 | 3.220 | 1.862–5.568 |
| MYCN status (36 tested) | Normal (n=30) | Amplified (n=6) | 0.132 | | | |
| Chromosome 1p (16 tested) | Normal (n=12) | Deleted (n=4) | 0.660 | | | |

Abbreviations: NB-neuroblastoma; GNBn-ganglioneuroblastoma, nodular type; GNB-ganglioneuroblastoma; GN-ganglioneuroma

**Table 4. Survival of neuroblastoma patients who received different treatment modalities.**

| Treatment modalities | No. of cases | Death | 5-year overall survival (%) |
|---|---|---|---|
| Without any therapy | 3 | 2 | 0.0 |
| Only surgery | 24 | 11 | 49.5 |
| Only chemotherapy | 16 | 11 | 21.6 |
| Only radiotherapy | 2 | 2 | 0.0 |
| Surgery and chemotherapy | 34 | 16 | 60.1 |
| Surgery and radiotherapy | 10 | 2 | 67.5 |
| Radiotherapy and chemotherapy | 14 | 11 | 0.0 |
| Surgery, chemotherapy, and radiotherapy | 26 | 11 | 51.0 |
| Combination treatment of conventional treatment and bone marrow transplantation | 11 | 5 | 35.0 |
| Combination treatment of conventional treatment and targeted therapy | 3 | 1 | 50.0 |
| Overall | 142 | 72 | 41.6 |

therapeutic efficacy in OS to either chemotherapy alone or surgery alone (p=0.012) whereas combined therapy did not show an advantage on PFS (p=0.301, Figure 2B). Moreover, the patients were grouped for further analysis. As shown in Figure 3A, patients who underwent surgery (n=102) with or without adjuvant treatment had significantly longer survival rates than that of patients who were not operated on (n=37, median survival time: 72 months vs. 22 months, p<0.001). No significance in survival was noted between those with or without chemotherapy (median survival time: 41 months vs. 130 months, p=0.063, Figure 3B). To assess the role of chemotherapy on the prognosis of adolescent and adult NB cases, patients were divided into two groups according to their metastatic status. For patients with metastatic disease at presentation, no differences were observed between patients with or without chemotherapy (median survival time of patients with chemotherapy vs. without chemotherapy: 28 months [n=56] vs. 19 months [n=9], p=0.162, Figure 4A). A significantly longer PFS with chemotherapy than without chemotherapy in patients with distant metastasis (median PFS of patients with chemotherapy vs. without chemotherapy: 13 months [n=54] vs. 4 months [n=8], p=0.038, Figure 4B). However, the results for patients with a localized disease revealed an opposite trend. There was no statistical benefit in OS with chemotherapy (median survival time of patients with chemotherapy vs. without chemotherapy: 102 months [n=47] vs. 132 months [n=27], p=0.194, Figure 4C). Unexpectedly, patients' concomitant chemotherapy group had significantly shorter PFS than patients without chemotherapy (median PFS of patients with chemotherapy vs. without chemotherapy: 12 months [n=44] vs. 36 months [n=26], p=0.039, Figure 4D).

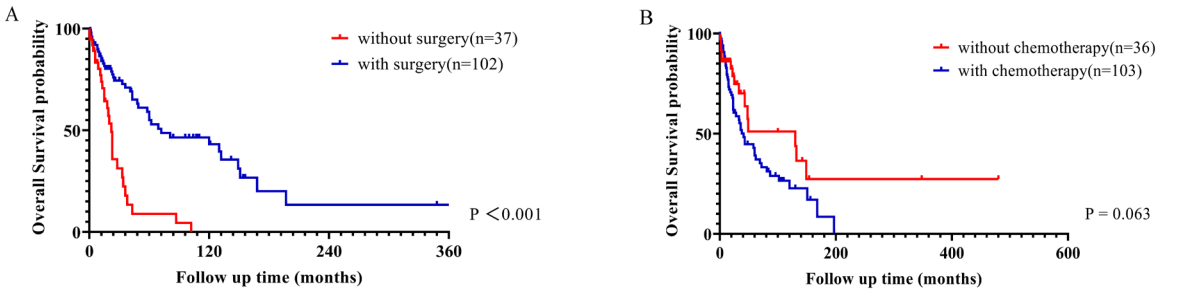


**Figure 3. Effects of different treatment modalities on the prognosis of adolescent and adult NB patients. A) Patients who had a surgery demonstrated a longer median survival time than that of patients who were not operated on (72 months vs. 22 months, p<0.001). B) There was no significant difference in the median survival time between patients with chemotherapy and those without chemotherapy (41 months vs. 130 months, p=0.063).**

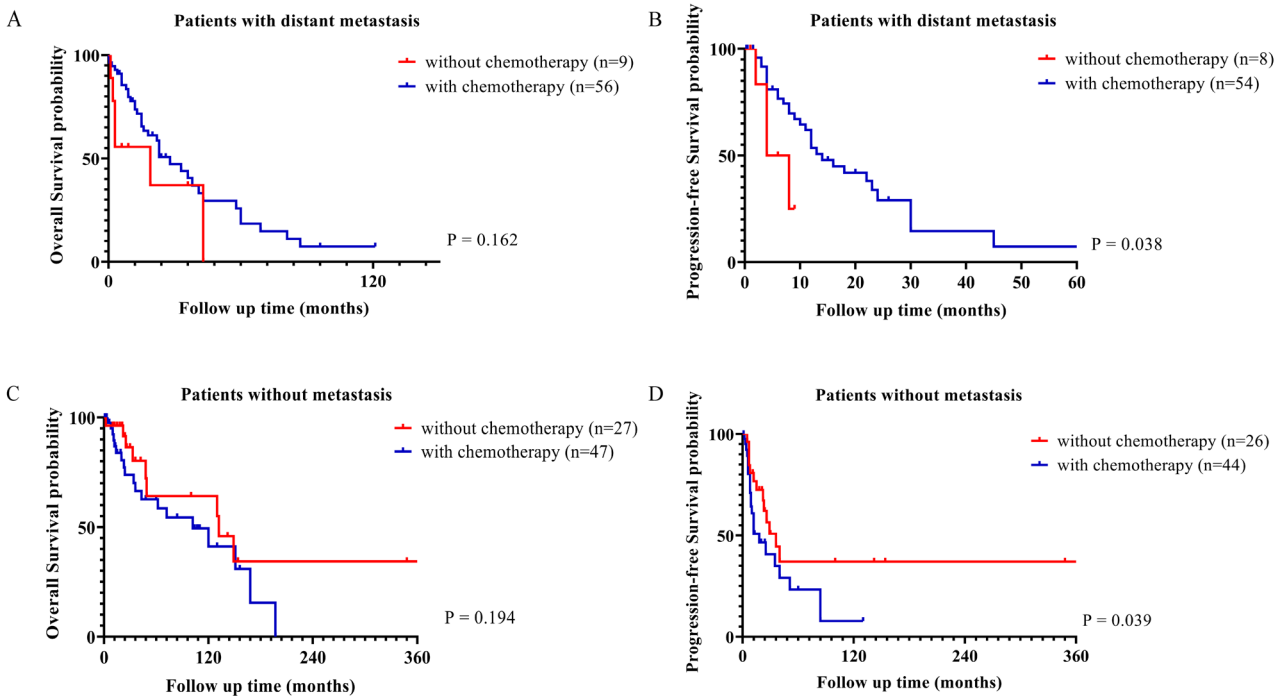


**Figure 4. Prognostic relevance of chemotherapy and long-term survival in adolescents and adults according to NB metastasis. A) OS curves of patients with metastasis (median survival time of patients with chemotherapy vs. without chemotherapy: 28 months vs. 19 months, p=0.162). B) PFS curves of patients with metastasis (median PFS of patients with chemotherapy vs. without chemotherapy: 13 months vs. 4 months, p=0.038). C) OS curves of patients without metastasis (median survival time of patients with chemotherapy vs. without chemotherapy: 102 months vs. 132 months, p=0.194). D) PFS curves of patients without metastasis (median PFS of patients with chemotherapy vs. without chemotherapy: 12 months vs. 36 months, p=0.039).**

## Discussion

The occurrence of NB is closely related to the development of the neural crest, which mainly occurs in the adrenal glands and sympathetic ganglion. To the best of our knowledge, NB rarely occurs in adolescents and adults. Its incidence is approximately 1 case/100,000 children per year, whereas it is less than 0.3 cases/million people each year in adults [5, 75, 76]. Patients who are diagnosed with NB at over 20 years old account for only 6% of all NB cases [77]. For pediatric NB, the 5-year OS in the low-risk group, intermediate-risk group, and high-risk group is over 90%, 60–85%, and less than 50%, respectively [2]. However, in adolescent and adult NB patients, the 5-year OS rate is only 15.7% for those with distant metastasis compared to 64.4% for cases with localized disease. The survival rate of adolescent and adult NB patients is significantly lower than that of the pediatric NB population. Further study is needed to reveal some contributors to such differences in prognosis.

Compared with pediatric NB, adult NB is characterized by large clinical heterogeneity and tolerance to treatment. The signs and symptoms of NB are highly variable and depend

on the site of the primary tumor as well as the presence or absence of metastatic disease. The locations of NB in adolescents and adults are similar to those in pediatric patients, with the abdomen being the most common area of NB occurrence. However, owing to its rarity, 16% of adult NB cases are misdiagnosed initially and are managed incorrectly [78]. In fact, 25 of the 142 patients were misdiagnosed before operation due to non-specific signs and symptoms. In cases with a lack of pathological evidence, patients were commonly misdiagnosed with pheochromocytoma. Small round blue cells and rosette-forming cells are typical manifestations of NB, but it should be differentiated from lymphoma and primitive neuroectodermal tumor, which report similar clinicopathological features [72]. The interval between the onset of symptoms and clinical diagnosis was longer in adolescents and adults than that of children. In pediatric NB, approximately 38% of cases were classified as stage IV disease [79]. Similar to previous studies that reported high rates of metastasis, of the 142 adolescent and adult NB patients, we found that approximately 47.2% presented with metastatic disease, and correlated with poor prognosis. This may be associated with an indolent clinical course of the disease in adolescent and adult population [80].

Elevated levels of serum neuron-specific enolase (NSE) and urine catecholamine metabolites (such as vanillylmandelic acid and homovanillic acid) are seen in 90% of pediatric NB cases and are used as tumor biomarkers for children with NB; however, they are rarely elevated in adolescents and adults [73]. Among the analyzed cases, these biomarkers were abnormal only in 19 out of 31 patients, accounting for difficulties in diagnosis. Compared with 20–25% prevalence of MYCN amplification in children, which is associated with an aggressive phenotype, only 9% of adolescent and adult NB patients have been reported to have MYCN amplification [81]. Whereas, 16.7% of cases had MYCN amplification in our case series. We speculate that this may be due to the absence of MYCN status in most literature reviewed. Conversely, ALK and ATRX Chromatin Remodeler (ATRX) mutations are far more common in adults, which suggests that the drivers of tumorigenesis in adult NB maybe differ from those in children, and may be related to slower growth phenotypes [78, 82]. Compared with children, NB diagnosis in adults is more dependent on the pathological evidence. In addition, tumor cells often express CD56, chromogranin A, synaptophysin, neurofilament, and NSE. Recently, paired like homeobox 2B (PHOX2B), a master regulator of neural crest development, has been detected in NB as a new, sensitive, and specific marker [83].

The rarity of NB in adults has resulted in a lack of systematic clinical trials for chemotherapeutic agents or targeted therapy aiming at this population. Therefore, the treatment of adult patients with NB generally depends on the regimens used for pediatric NB. Comprehensive treatment is an important means of increasing the survival of children with NB [80]. Based on our findings, compared with surgery or chemotherapy only, the long-term survival had improved significantly by combination therapies but no longer progression-free survival for adolescent and adult NB patients. Results also showed that complete surgical resection was a significant factor for improving the survival of this population whereas chemotherapy did not improve the long-term prognosis. This may be related to the fact that adults have a poorer tolerance to chemotherapy compared to that of children [80]. Side effects of chemotherapy, including hair loss, vomiting, and myelosuppression, were observed in five patients treated in our institution. Two patients were insensitive to chemotherapy. We found that 55 of 73 cases reported in reviewed literature also received chemotherapy. It is worth mentioning that 5 of 55 patients (9.1%) died from chemotherapy-related complications. This suggests that more effective regimens of chemotherapy for adolescent and adult NB cases should be considered to overcome limitations. When the analyses were performed in two groups according to metastasis, there was a trend toward a worse prognosis in patients without metastasis who received chemotherapy. For adolescent and adult NB patients, combination treatment was more effective than individual treatments. Early complete surgical resection combined with appropriate chemotherapy is recommended to improve the outcome in this population, radical surgical management is particularly important to reduce recurrence. Chemotherapy plays a key role in the treatment of children with NB, but the current regimen may not be suitable for adolescents and adults. The details of the chemotherapy regimens and doses will need to be investigated further.

GD2, a disialoganglioside, is a surface antigen overexpressed on NB cells surface but limited to neurons, melanocytes, and peripheral pain fibers in normal tissue. GD2 facilitates the attachment of tumor cells to the extracellular matrix and persists on NB cell membrane post-therapy [84]. Furthermore, GD2 is associated with proliferation, invasion, and motility. These properties make it a suitable target for immunotherapy. With the development of immunotherapy, clinical trials with anti-GD2 monoclonal Abs (mAb) have shown promising results in pediatric NB. Immunotherapy with anti-GD2 mAb was shown in a Children's Oncology Group phase III randomized clinical trial to have superior event-free survival (2y-EFS, 66±5% vs. 46±5%) and overall survival (2y-OS, 86±4% vs. 75±5%) when compared with standard therapy with isotretinoin alone [85]. In 2015, the Food Drug Administration approved the use of dinutuximab, an anti-GD2 mAb, and incorporated it into the standard of care therapy for patients with high-risk NB [86]. For patients with refractory or relapsed NB, the use of anti-GD2 immunotherapy has led to further improvement in OS and EFS after conventional therapy [80]. Adolescent and adult NB is an insidious onset with a high rate of metastasis. Due to its rarity, the diagnosis is often difficult for this population, and easy to delay treatment. Older age onset is also a high-risk factor for NB, and nearly half of those patients

are at an advanced stage at the time of diagnosis [80]. So, it may be speculated that these patients may potentially benefit from anti-GD2 immunotherapy therapy. There is limited evidence confirming this conjecture. At the Memorial Sloan Kettering Cancer Center, 5 out of 7 adult NB patients treated with anti-GD2 immunotherapy had a complete response and showed good tolerance to the treatment [78]. In the study, we found that two cases with GD2 antibody immunotherapy all survived. Given the positive outcomes of immunotherapy in pediatric NB, there is a reason to believe that anti-GD2 immunotherapy is promising for the treatment of NB in adolescent and adult NB. Further studies are required to confirm these observations.

Previous studies have shown that adult NB has a protracted course, referred to as indolent or chronic NB [87]. The prognosis is worse in adolescent and adult patients with NB than in children. We find that distant metastasis is an independent influencing factor for the outcome of adolescent and adult patients with NB. NB is characterized by a variety of genetic abnormalities, which may explain different clinical outcomes between children and adults. Surgical resection remains the mainstay in NB treatment. Further exploration of chemotherapy regimens and dosage for adolescent and adult patients with NB is necessary. Anti-GD2 immunotherapy may be emerged as an effective approach to improve clinical outcomes.

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