**Original Research Article**

**Children with solid tumors treated in our centre**

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Received: 06 September 2020
Accepted: 09 October 2020

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**ABSTRACT**

**Background:** General characteristics and responses to treatment of patients with solid tumors were investigated.

**Methods:** Patients treated with a diagnosis of solid tumors in the pediatric hematology and oncology clinic between March 2019 and June 2020 were included in the study. The gender, age, diagnosis, age of diagnosis, risk status, stage, treatment details, and treatment complications of the patients were evaluated. The risk status of the patients was determined according to the stage of each diagnosis, metastasis status and treatment protocol. It was noted whether the patients had undergone surgery or not, and patients who were in-operable were specified. Patients receiving radiotherapy were specified. The chemotherapeutic drugs given to the patients according to the treatment protocols were indicated one by one. Treatment complications or morbidity states were recorded.

**Results:** Out of the 31 patients evaluated, 10 (32%) were female and 21 (68%) were male. The mean±SD age was 6.3±5.16 years. The youngest patient was 3 months old, and the oldest patient was 18 years old. The central nervous system was the most commonly affected area and 7 (22%) of the patients had various CNS tumors. The second most common malignancy is neuroblastoma; 4 patients (12%). Rhabdomyosarcoma and retinoblastoma were the third most common malignancy with 3 patients each. Surgical resection was performed in 19 (61%) patients. Radiotherapy was applied to 13 of the patients (41%).

**Conclusions:** Early diagnosis and detection of the disease at low stage, complete tumor resection are important for the success of treatment.

**Keywords:** Solid tumors, Children, Chemotherapy, Radiotherapy, Autologous-HSCT

**INTRODUCTION**

Childhood cancers are one of the major causes of death in children and adolescents.¹ Childhood cancer is the fourth most common cause of death in developing countries such as Turkey, but is the second most common cause of death after accidents in developed countries. Cancers seen in childhood are important because of the long life expectancy in childhood and high treatment success rates in these cancers. In parallel with the improvements in treatment options in recent years, there have been significant improvements in the survival rates of childhood cancers.² Although there are differences in the distribution by age, according to the data of various pediatric cancer groups and associations, central nervous system tumors are the most common after leukemia/lymphomas in our country in childhood.³ When examining the distribution of cancer by age, embryonal primitive tumors in which neuroblastoma, retinoblastoma and nephroblastoma are prominent in the first year, leukemias between the ages of 1-4 years and leukemia/lymphoma between the ages of 5-14 years and central nervous system tumors constitute the majority of cases.⁴-⁷ Solid tumors have different clinical features and diversity
of cellular origins in children and adolescents according to the adults.8 Malignant solid tumors account for approximately 30% of childhood cancers.9 The predominant histology of specific solid tumors varies significantly with age.10 In current article, general characteristics and response to treatment of patients with solid tumors who were treated in clinic were investigated.

METHODS

Patients treated with a diagnosis of solid tumors in the pediatric hematology and oncology clinic between March 2019 and June 2020 were included in the study. Epicrisis, laboratory results, radiological imaging results, and consultation notes of the patients were evaluated retrospectively. The gender, age, diagnosis, age of diagnosis, risk status, stage, treatment details, and treatment complications of the patients were evaluated. The risk status of the patients was determined according to the stage of each diagnosis, metastasis status and treatment protocol. It was noted whether the patients had undergone surgery or not, and patients who were inoperable were specified. Patients receiving radiotherapy were specified. The chemotherapeutic drugs given to the patients according to the treatment protocols were indicated one by one. Treatment complications (severe myelosuppression, cardiotoxicity, kidney failure, etc.) or morbidity states (nephrectomy, splenectomy, metastatic lung, etc.) were recorded. Clinical course and response to treatment; was classified as complete response, partial response, stable disease, progressive disease, death. After evaluating the extracted data, patients’ risk status, surgical treatment results, complications and morbidity status, and treatment success results were evaluated and compared.

Statistical analysis

Standard statistical methods were used for statistical analysis. Case characteristics were described using diagnosis, age, and gender. Percentages of genders and mean±SD of age was calculated. All analyses were conducted with the use of statistical product and service solutions (SPSS 22.0) software.

RESULTS

Out of 31 patients evaluated, 10 (32%) were female and 21 (68%) were male. The mean±SD age was 6.3±5.16 years. The youngest patient was 3 months old, and the oldest patient was 18 years old. The general characteristics and treatment details of the patients are shown in (Table 1). The central nervous system was the most commonly affected area and 7 (22%) of the patients had various CNS tumors. The second most common malignancy was neuroblastoma 4 patients (12%). Rhabdomyosarcoma and retinoblastoma were the third most common malignancy with 3 patients each. Surgical resection was performed in 19 (61%) patients in our hospital or an external centre. Radiotherapy was applied to 13 of the patients (41%). During radiotherapy, 12 out of 13 patients had no major complications. A patient diagnosed with glioblastoma multiforme with progressive course and high post operative morbidity died while radiotherapy was continuing. Autologous hematopoietic stem cell transplantation (HSCT) was applied to 2 patients with a diagnosis of neuroblastoma. Allogeneic HSCT was performed after salvage chemotherapy in a patient who had previously undergone autologous HSCT with the diagnosis of treatment-resistant non-Hodgkin lymphoma. 8 (25%) of the patients are followed in complete response after treatment. While a complete response is observed in 4 of the patients whose treatment continues, 8 patients have a partial response or stable disease. Spontaneous regression occurred in a 3 month old patient who was followed up with a diagnosis of neuroblastoma and his follow-up continues. Seven patients (22%) died due to progressive disease.

DISCUSSION

Cancer is the second most common cause of childhood death in the developed world, accounting for 10%-12.3% of all childhood deaths.9 Although the majority of childhood cancers are acute leukemias, solid tumors have a special importance with the increasing life expectancy with a multidisciplinary approach in recent years. Central nervous system tumors in children are the most common childhood solid tumors after hematological malignancies.3,11 Similar to the literature, central nervous system tumors constituted the majority of our patients. Since our centre is a centre where more difficult to treat cases are referred, most of our patients consisted of inoperable or difficult to surgery cases. Our patients who are followed up for pons glioma are followed up with a partial reduction in tumor size or a stable course with radiotherapy, weekly vincristine treatment simultaneously with radiotherapy and then monthly temozolamide treatment. Two patients with high grade glioma, who had major operations in an external centre due to the tumor location, died during treatment due to disease progression. One of the our patient diagnosed with ependymoblastoma, which is very rare in pediatric patients in the literature, is ongoing chemotherapy after surgery and radiotherapy, and no residual recurrent mass was found in control imaging.12 Abdominal masses of infants and children may be caused by congenital anomalies, trauma, infection, organ enlargement, and tumors. Patient age and location of the mass significantly influence the differential diagnosis.13,14 Nine (29%) of our patients had a primary abdominal mass. The majority of these patients were patients with neuroblastoma. Neuroblastoma is the most common non-CNS solid tumor in children, and the most common malignancy in infants, with an incidence of approximately 1 per 100,000 children per year. Approximately one-half of neuroblastomas are adrenal gland origin.13,14 Two of our patients with diagnosis of neuroblastoma were with stage IV common disease. These patients who had undergone chemotherapy, surgery, radiotherapy and autologous HSCT were followed up for complete response.
Table 1: General characteristics of patients.

| Diagnosis                          | Age  | Gender | Diagnosis age | Stage/ risk group | Surgery | Radio-therapy | Chemo-therapy | Morbidity                        | Result |
|------------------------------------|------|--------|---------------|------------------|---------|---------------|---------------|----------------------------------|--------|
| Rhabdomyosarcoma                   | 5 y  | Male   | 5 y           | Stage I, group II| Yes     | -             | VCR-ACT-CPM  | -                                | CR     |
| Wilms tumor                        | 4 y  | Female | 4 y           | Stage I          | Yes     | -             | VCR-ACT      | Nephrectomy                      | TC/CR  |
| Ewing sarcoma                      | 8 y  | Male   | 7 y           | High risk group  | -       | Yes           | VCR-DOX-IFO-ETO-ACT-CPM          | -      | TC/PR                           |
| Neuroblastoma                      | 3 y  | Male   | 2 y           | Stage IV         | Yes     | Yes           | VCR-DOX-IFO-ETO-DAC-CPM, Autologous-HSCT | Pulmoner-HT | CR     |
| Retinoblastoma                     | 8 m  | Male   | 2 m           | High risk group  | -       | -             | VCR-CARBO-ETO | -                                | TC/PR  |
| Ependymoblastoma                   | 7 y  | Female | 6 y           | -                | Yes     | Yes           | VCR-CPM-CSP-ETO-CARBO            | -      | TC/PR                           |
| Pons glioma                        | 7 y  | Male   | 6 y           | Inoperable       | Yes     | -             | Temozolamide | -                                | TC/PR  |
| Ependymoma                         | 3 y  | Male   | 2 y           | Refractory       | Yes     | Planned       | VCR-CARBO-CPM-ETO                | Ventriculo-peritoneal shunt, hydrocephalus | TC/CR  |
| Sacrococcygeal teratoma/yolk salk tumor | 2 y  | Female | 1 y           | Recurrent        | Yes     | -             | IFO-CARBO-ETO | Recurrent surgery                 | TC/CR  |
| Retinoblastoma                     | 3 y  | Female | 3 y           | Low risk group   | -       | -             | Intraartery-el Methylalan-Toxotocan | -      | TC/PR                           |
| Retinoblastoma                     | 6 m  | Female | 2 m           | High risk group  | Yes     | -             | VCR-CARBO-ETO | -                                | CR     |
| Rhabdomyosarcoma                   | 15 y | Male   | 15 y          | Stage III, group III | Planned | Planned | VCR-ACT-CPM | Hypertension, increased intraocular pressure, exophthalmiae | TC/PR  |
| Rhabdomyosarcoma                   | 4 y  | Male   | 3 y           | Recurrent        | Stage III, group III | Yes     | Yes           | IFO-DOX-ETO-VCR-Irinotecan | Peripheral facial paralysis. | TC/PR  |
| Neuroblastoma                      | 3 y  | Male   | 2 y           | Stage IV         | Yes     | Yes           | VCR-DOX-IFO-ETO-DAC-CPM, Autologous HSCT | Massive mass in the abdomen, nephrectomy. | CR     |

Continued.
| Diagnosis                        | Age  | Gender | Diagnosis age | Stage/ risk group | Surgery | Radiotherapy | Chemotherapy | Morbidity                              | Result                          |
|---------------------------------|------|--------|---------------|-------------------|---------|--------------|--------------|----------------------------------------|--------------------------------|
| **Peripheral T cell NHL**       | 3 y  | Male   | 2 y           | Stage IV          | -       | Yes          | VCR-DOX-   | CNS involvement, reactive airway       | CR                             |
|                                 |      |        |               |                   |         |              | LASP-ARAC-IFO-ETO-MTX-Steroid           | disease.                        |
| **Osteosarcoma**                | 16 y | Female | 15 y          | Metastatic        | -       | Yes          | MTX-DOX-   | Respiratory distress due to pulmonary  | Progresive disease/death       |
|                                 |      |        |               |                   |         |              | CSP-ETO-IPO | metastasis.                            |                                |
| **Pons glioma**                 | 6 y  | Male   | 5 y           | Inoperable        | Yes     | VCR-           | Temozolami- | Severe neurologic findings, increased  | TC/PR                           |
|                                 |      |        |               |                   |         | Temozolami-de | -           | intracranial pressure.                 |                                |
| **Pleomorphic xanthoastrocytoma**| 14 y | Male   | 14 y          | Yes               | Yes     | Temozolami-   | -           | Severe neurologic findings, increased  | TC/CR                           |
|                                 |      |        |               |                   |         | Temozolami-de | -           | intracranial pressure.                 |                                |
| **Glioblastoma multiforme**     | 12 y | Female | 12 y          | Yes               | Yes     | -            | Temozolami- | Severe neurologic findings, increased  | Progresive disease/death       |
|                                 |      |        |               |                   |         | Temozolami-de | Bevacizumab- | intracranial pressure.                 |                                |
|                                 |      |        |               |                   |         |              | and irinotecan |                                              |                                |
| **Oligodendroglioma**           | 10 y | Female | 9 y           | Yes               | Yes     | Rituximab-    | IFO-ETO-CARBO | Recurrence after autologous HSCT.       | Death after HSCT.               |
| **Diffuse B cell NHL**          | 18 y | Female | 16 y          | Recurrence        | -       | -            | CSP-         | Tracheostomy, diffuse local disease,    | Progresive disease/death       |
|                                 |      |        |               |                   |         |              | DOXO-    | major pharyngeal bleeding.             |                                |
|                                 |      |        |               |                   |         |              | CARBO     |                                          |                                |
| **Nasopharyngeal carcinoma**    | 2 y  | Male   | 2 y           | Stage IV          | -       | MTX-CSP-      | -           | Treatment-resistant disease,          | CR                             |
|                                 |      |        |               |                   |         | SFU          |             | massive abdominal mass, respiratory    |                                |
|                                 |      |        |               |                   |         |              |             | distress due to metastasis.            |                                |
| **Hepatoblastoma**              | 2 y  | Male   | 2 y           | Metastatic        | Yes     | CSP-DOX-      | -           | CR                                     |
|                                 |      |        |               |                   |         | DOXO-CARBO   |             | Treatment-resistant disease,          |                                |
| **Wilms tumor**                 | 3 y  | Male   | 3 y           | -                 | Yes     | VCR-ACT      | -           | CR                                     |
| **Hepatoblastoma**              | 3 y  | Male   | 2 y           | Metastatic        | -       | VCR-irinotecan  | -           | Treatment-resistant disease,          | CR                             |
|                                 |      |        |               |                   |         |              |             | massive abdominal mass, respiratory    |                                |
|                                 |      |        |               |                   |         |              |             | distress due to metastasis.            |                                |
| **Ewing sarcoma**               | 6 y  | Male   | 6 y           | High risk         | Yes     | VCR-DOX-IFO- | -           | CR                                     |
|                                 |      |        |               |                   |         | ETO-ACT-CPM  |             | Treatment-resistant disease,          |                                |
|                                 |      |        |               |                   |         |              |             | massive abdominal mass, respiratory    |                                |
|                                 |      |        |               |                   |         |              |             | distress due to metastasis.            |                                |

*Continued.*
| Diagnosis                  | Age | Gender | Diagnosis age | Stage/ risk group | Surgery | Radiotherapy | Chemo-therapy | Morbidity                                                                 | Result       |
|---------------------------|-----|--------|---------------|-------------------|---------|--------------|---------------|---------------------------------------------------------------------------|--------------|
| Synovial sarcoma          | 17  | Male   | 15 y          | Metastatic        | Yes     | -            | IFO-ETO-CARBO VCR-irinotecan | Respiratory distress due to metastatic lesions, renal failure.             | TC/Progressive disease |
| Infantile fibrosarcoma    | 2   | Female | 1 y           | Recurrent         | Yes     | -            | IFO-ETO-DOX     | Massive abdominal mass, splenectomy, nephrectomy, multiple abdominal surgery. | Recurrent disease |
| Neuroblastoma             | 3 m | Male   | 1 m           | Stage I           | -       | -            | -             | End stage renal disease, dialysis, recurrent abdominal surgery.           | TC/Progressive disease |
| Congenital mesoblastic nephroma | 2  | Male   | 1 y           | Recurrent         | Yes     | -            | VCR-irinotecan | Nephrectomy, bone marrow infiltration, severe myelosuppression            | TC/Progressive disease |
| Neuroblastoma             | 7   | Male   | 5 y           | Recurrent         | Yes     | Yes          | IFO-CARBO-ETO  | Progresive disease /death                                                 |              |

y: years, m: months, CR: complete response, PR: partial response, TC: treatment continues, VCR: vincristine, ACT: actinomycin, CPM: cyclophosphamide, DOXO: doxorubicin, IFO: ifosfamide, ETO: etoposide, CARBO: carboplatin, HSCT: hematopoietic stem cell transplant, CSP: cisplatin, MTX: methotrexate, 5FU: 5-fluorouracil, LASP: L-asparaginase.

Another stage IV patient, who presented to us due to recurrent disease, died due to progressive disease in his treatment duration. Considering the risk of recurrence of the disease especially in patients with neuroblastoma in the high risk group, we think that progress in the autologous HSCT arm is more appropriate. Localized adrenal masses without other associated findings, detected in the perinatal period may not require any therapy; although careful follow up is very important. Adrenal mass regression was observed in the follow up of the patient who was referred to us after birth incidental adrenal mass.

More than 95% of all renal tumors in the pediatric age group are Wilms tumor (WT), the second most common intraabdominal cancer of childhood, with about 650 new cases diagnosed in the United States each year. Renal tumors other than WT are infrequent in children, representing less than 1% of childhood cancer. The most common non Wilms renal tumors are clear cell sarcoma of the kidney, rhabdoid tumor of the kidney (RTK), renal cell carcinoma, and congenital mesoblastic nephroma (CMN). Two patients were diagnosed with WT and surgery and chemotherapy applied. One of the patient with a diagnosis of congenital mesoblastic nephroma, who was sent from an external centre for further treatment, has a progressive course due to severe morbidity.

Hepatoblastoma occurs in children younger than 4 years of age and hepatocellular carcinoma occurs in older children and adolescents. Surgical resection is the mainstays of the therapy for hepatoblastoma, but only one-third to one-half of newly diagnosed patients have resectable disease at presentation. The use of cisplatin-based chemotherapy combined with surgery has
improved survival.\textsuperscript{17,18} Two of our patients with hepatoblastoma had massive abdominal mass and lung metastases when they presented to our centre. The patient, whose treatment was started in an external center and resistant to standard chemotherapy, died with a progressive course. Our other patient responded well to the cisplatin-based regimen. Tumor resection was performed after neo-adjuvant chemotherapy. Lung metastases disappeared completely after chemotherapy.

Rhabdomyosarcoma is the most common soft tissue sarcoma of childhood and constitutes 5-8\% of all sarcomas. The most common primary sites are the head-neck, genitourinary system, and the neighborhood of visceral organs such as the retroperitoneum, pelvis and abdomen, and the extremities. Local spread and recurrence is an important problem in rhabdomyosarcomas as in all soft tissue sarcomas.\textsuperscript{19} Treatment of 3 patients with embryonal rhabdomyosarcoma, one of which is relapse, continues and tumor control has been achieved. We have 2 patients with non-rhabdomyosarcoma soft tissue tumors diagnosed with synovial sarcoma and infantile fibrosarcoma. Infantile fibrosarcoma is most commonly seen in the first 4 years of life, constitutes 25-30\% of soft tissue tumors under one year old and is considered infantile type in this age group. Although the distal of the extremities is seen in deep soft tissue, it may be located in the trunk, head-neck, retroperitoneum and mesentery.\textsuperscript{19} Our patient diagnosed with infantile fibrosarcoma was with a poor general condition due to repeated operations and additional comorbid conditions. Although chemotherapy and tumor excision were completely cleared of tumor elements, a recurrent mass lesion was detected in the 4th month after treatment. Synovial sarcoma shows different epithelial differentiation, it is the third most common cause after rhabdomyosarcoma and Ewing sarcoma in children and adolescents. Although they are aggressive and high grade malignant tumors, their metastases are frequently seen in the lungs after 10-20 years.\textsuperscript{20} Our patient was referred after surgical excision of the primary lesion in the extremity. Lung metastases progressed under chemotherapy.

CONCLUSION

In conclusion, childhood cancers are one of the important causes of childhood mortality that should be treated in multidisciplinary centres. Especially early diagnosis and detection of the disease at low stage, complete tumor resection are important for the success of treatment. Neoadjuvant, adjuvant chemotherapy, radiotherapy and autologous HSCT are very important for controlling the tumor burden of patients, especially in cases where surgery is insufficient.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Sarbay H, Okumus M, Sertbas I, Hacisalihoglu UP, Atay A, Malbora B. Children with solid tumors treated in our centre. Int J Contemp Pediatr 2020;7:2260-6.