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Successful Multidrug Chemotherapy for Rhabdomyosarcoma in a Seven-Year-Old Girl: A Case Report

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Abstract

The most frequent soft tissue cancer in children is rhabdomyosarcoma (RMS). A diagnosis typically occurs between the ages of 5 and 6 in women. We report a seven-year-old girl was referred to Hospitals with complaints of a protruding left eye. The swelling was presented in July 2021, which was small earlier but has increased and become more prominent. An examination of the left eyelid showed a 2.5 x 2.5 x 1.5 cm solid mass with edema, erythema, and secretion in the superior and inferior affected eyelid. A Head CT scan revealed a left superolateral lacrimal duct tumour with a normal intracerebral structure. The histopathology examination found dacryoadenitis with an RMS tumour. This patient was treated using the RMS multidrug chemotherapy protocol (vincristine, actinomycin, and cyclophosphamide) for three sessions, which decreased tumour progressivity five months later. Early and appropriate treatment of this patient with chemotherapy regimens according to the protocol for RMS has a good prognosis.

Keywords: Case Report, Chemotherapy, Rhabdomyosarcoma

Abstrak

Kanker jaringan lunak yang paling sering terjadi pada anak-anak adalah rhabdomyosarcoma (RMS). Diagnosis biasanya terjadi antara usia 5 dan 6 tahun pada anak perempuan. Kami melaporkan seorang anak perempuan berusia 7 tahun dirujuk ke rumah sakit dengan keluhan mata kiri menonjol. Bengkak muncul pada Juli 2021, yang awalnya kecil tetapi membesar dan menjadi lebih menonjol. Pemeriksaan kelopak mata kiri menunjukkan massa padat berukuran 2,5 x 2,5 x 1,5 cm dengan edema, eritema, dan sekresi pada kelopak mata superior dan inferior. CT scan kepala menunjukkan tumor duktus lakrimal superolateral kiri dengan struktur intraserebral normal. Pemeriksaan histopatologi ditemukan dakrioadenitis dengan tumor RMS. Pasien ini dirawat menggunakan protokol kemoterapi multiobat RMS (vinkristin, aktinomisin, dan siklofosfamid) selama tiga sesi, yang menurunkan progresivitas tumor lima bulan kemudian. Pengobatan dini dan tepat pada pasien ini dengan regimen kemoterapi sesuai protokol RMS memiliki prognosis yang baik.

Kata kunci: Laporan Kasus, Kemoterapi, Rhabdomyosarcoma

Introduction

Rhabdomyosarcoma is the most prevalent soft tissue cancer in children, accounting for 3-8% of all pediatric cancers with an incidence rate of 4-5 per million children under the age of 18 per year. The male-to-female ratio at diagnosis is 1.5 to 1.1, and the average age is 2 to 5 years.[1,2]

Rhabdomyosarcoma is an extremely lethal tumour that primarily affects young children in their first ten years of life. Rhabdomyosarcoma (RMS) develops from immature cells that can potentially transform into skeletal muscle cells in the future. Soft tissues such as skeletal muscle, connective tissue, bone, the bladder, prostate, testicles, nose, orbits, and anus can all be the source of RMS.[3,4] Prompt diagnosis and treatment can save lives.[5,6]

Proptosis (80-10%) or ocular dislocation (80%), which typically moves downward and outward because two-thirds of these tumours are superonasal, are the most common symptoms in patients with ocular RMS. RMS rarely spreads through the eyes, but if untreated, it frequently accomplishes mostly through hematogenous spreading to the lungs, bone, and bone marrow. Locally, ocular RMS can extend intracranially and infiltrate the orbital bone.[5]

Vincristine, actinomycin D, cyclophosphamide/ifosfamide chemotherapy, radiation, and surgical tumour removal are all included in the standard treatment for RMS. While no substantial improvement was seen in patients with metastatic RMS, multidrug chemotherapy regimens dramatically improved outcomes in people with localized RMS. In both North America and Europe, vincristine, actinomycin D, and cyclophosphamide make up the conventional chemotherapy protocol for RMS (VAC).[3,7]

Several research studies have been conducted in recent years to enhance rhabdomyosarcoma treatment and prognosis. Ocular rhabdomyosarcoma has a good prognosis, according to several studies, with three-year survival rates as high as 93%. This is particularly found in patients more than six years old.[8,9] Over the past few decades, considerable advancements have been made in enhancing the treatment and prognosis of rhabdomyosarcoma. A multidisciplinary approach involving specialized medical fields such as pediatrics, ophthalmology, surgery, and imaging was employed for the management of this patient. We describe a 7-year-old girl patient with left eye rhabdomyosarcoma who got first-week multidrug chemotherapy by the protocol and underwent six days of treatment in this article.

Case Presentation

A 7-year-old girl came with the chief complaint of an enlarged right eyelid since July 2021. She felt her eyelids getting bigger so that her eyes protruded more. The patient had no complaints of fever, convulsions, coughing, vomiting, or shortness of breath. The patient did not have a history of trauma, bleeding, skin rash, weight loss, and blood transfusion. The patient had a normal prenatal and perinatal history with a growth and development pattern still in the normal category for his age.

The physical examination showed that the patient was conscious, malnourished (Body Weight/Height = 85%; Body Weight/Age = 76%) and had normal vital signs. On eye examination, the right eye appeared to be a solid extrabulbar mass covering the left superolateral lacrimal duct with a size of 1.5x1.5x0.5cm. These lesions are accompanied by edema and erythema of the superior and inferior lids accompanied by eye discharge (Figure 1). No abnormalities were found in the left eye and enlarged cervical lymph nodes. Neurological examination found no focal or local deficits.

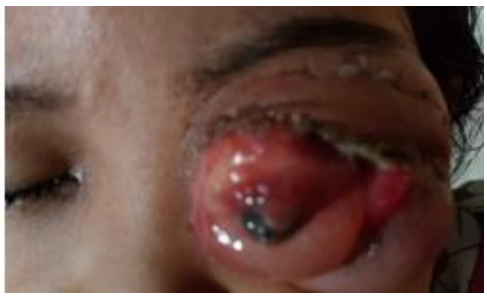

Figure 1. Initial Clinical Photograph of the Patient Showing the Progressive Eyelid Oedema

Laboratory examination results revealed mild anemia with Hb 11.3 g/dL. Serum electrolytes, kidney function, liver function, and albumin were within normal limits. Peripheral blood smear showing microcytic anemia with suspected iron deficiency anemia. Bone marrow aspiration examination found normal results. On a head CT scan, it was found that the left superolateral lacrimal duct tumour and normal intracerebral structures were found. The tumour biopsy tissue sample showed little normal lacrimal gland tissue surrounded by a large amount of tumour mass. A normal lacrimal gland had a fairly dense distribution of lymphocytic inflammatory cells. The tumour mass showed highly cellular and atypical proliferation of spindle nuclei, a high mitotic index, and a small proportion showed rhabdomyoblastic differentiation with eosinophilic cytoplasm. The tumour grows infiltratively between the connective tissue stroma, invades blood vessels (angioinvasion), and is surrounded by areas of hyalinization.

The patient was diagnosed with rhabdomyosarcoma of the left eye accompanied by mild iron deficiency anemia and nutritional marasmus. In October 2021, the patient began undergoing main therapy with a multidrug chemotherapy regimen in the first cycle consisting of Vincristine 1.12 mg/intravenously, actinomycin 270 mg/intravenously, and cyclophosphamide 225 mg/intravenously. The patient received oral iron supplementation therapy and 1,035 kcal enteral nutrition therapy with 175 ml x 8 doses of F75 milk. During the monitoring of cycle I therapy, significant problems were not found. After undergoing three cycles of chemotherapy, the patient showed a regression in tumour size in March 2022 (Figure 2).

Figure 2. Regression of the Tumour Size Following the Multidrug Chemotherapy of the Patient

Discussion

Rhabdomyosarcoma (RMS) is a malignant soft tissue sarcoma of the skeletal muscle phenotype that develops in children and is caused by progenitor mesenchymal cells. Children under the age of six are diagnosed with the majority of instances. Thirty-five of the estimated 350 new RMS cases diagnosed each year in the US are ocular RMS.. The most typical childhood malignant ocular tumour is RMS. The orbit is the tumour's main location in 10% of these RMS tumours.[10,11] These epidemiological features are consistent with the cases reported in this paper.

Clinical symptoms are the rationale for the diagnosis of RMS. The eye bulbs can develop tumours in any part of it. The retrobulbar is the most frequent site, followed by the top and bottom parts. The initial indication is typically the existence of a tumour with a rapidly expanding proptosis. In other situations, around one-third of patients have a palpable tumour with ptosis. The presence, location, and extent of the tumour must be identified using orbital ultrasonography, cranial tomography, and magnetic resonance imaging (MRI) in order to establish a conclusive diagnosis. If a rhabdomyosarcoma is suspected, a biopsy should be performed based on clinical and radiological examinations.[12] In our patient, the initial symptom found was swelling of the left eyelid, which was felt to be getting bigger, and the eye was more protruding. This solid extrabulbar mass is accompanied by edema and erythema of the lids with discharge.

Several imaging tests can be used to diagnose rhabdomyosarcoma, such as ultrasound, CT scan, MRI, and nuclear imaging. Extraconal (37–87%) or intra- and extraconal (13–47%) RMS of the eye are the common. Particularly in embryonic RMS, ocular RMS is more prevalent in superonasal sites. In contrast, alveolar RMS has a higher prevalence of inferior locations. Initially, the tumour is clearly defined, but as it advances and pseudocapsular invasion occurs, the boundaries become erratic. There may be bleeding and cyst formation from the tumour.[5] Ocular RMS presents as an isodense mass of well-defined, homogeneous soft tissue on a head CT scan. There was no evidence of bone damage in the early stages. In more severe circumstances, calcification and invasion of nearby structures actually occur. A heterogeneous appearance may arise in situations of localized hemorrhage or necrosis, and intravenous contrast therapy often improves the condition moderately to significantly.[5] In this patient, an MSCT brain examination was performed with an impression of a left superolateral

lacrimal duct tumour with normal-density intracerebral structures and no pathological lesions were seen.

Rhabdomyosarcoma is the most frequently performed malignant orbital tumour, which is very important for biopsy to establish the diagnosis and determine the prognosis. Depending on clinical and imaging findings, a biopsy can be achieved by incision or excision. However, needle aspiration is not very useful because the tissue obtained is limited, so sometimes, it is insufficient for pathological examination and diagnosis[5] In this patient, a biopsy was performed with the results of dacryoadenitis with a tumour mass of rhabdomyosarcoma.

Prior to starting therapy, patients were categorized based on their location, the size of the main tumour, the nodal status, and the presence of distant metastases. One of the most crucial prognostic criteria for predicting outcomes and determining the categorization defined by the Intergroup RMS research is the severity of the disease. The risk stratification used in the RMS therapy algorithm takes into account factors like group, stage, histology, and the time of initial diagnosis.[13]

Surgery, chemotherapy, and radiotherapy are the three currently recommended therapeutic methods for the treatment of children with rhabdomyosarcoma. The purpose of surgical resection is to remove the tumour completely. Another important objective for this pediatric population is organ preservation. Therefore, it is crucial to consider if surgery could result in positive functional outcomes.[13] Surgery can only be performed if the entire tumour is resected or has little residue. Preoperative chemotherapy tends to significantly reduce tumours and get ahold of metastatic potential, establishing the foundation for aggressive surgery. Chemotherapy after surgery is crucial in preventing tumour recurrence. It is well known that standard and efficient chemotherapy aids in the removal of cancer patients' post-surgery residual lesions and that children are more sensitive to and tolerable of chemotherapy medications than adults. As a result, chemotherapy with regular cycles and an efficient clinic plan can lower the recurrence rate.[14]

All RMS patients receive multidrug chemotherapy as part of their care. Over time, there has been a noticeable increase in the overall developmental independent survival rate. Chemotherapy's mainstays include vincristine, dactinomycin, and cyclophosphamide (VAC). Based on the findings of the intergroup RMS investigation, differences in VAC by clinical group and disease location were revealed.[13] A case report of a 9-year-old female diagnosed with stage I embryonic orbital rhabdomyosarcoma had a good response and tumour regression of 30% significantly after 13 weeks of VAC treatment 30%. Chemotherapy and radiotherapy have many advantages over surgical excision therapy, such as preserving the eyeball and vision.[15] Another case report is a 14-year-old patient diagnosed with embryonic rhabdomyosarcoma after undergoing orbital surgery aimed at complete tumour removal. Following surgery, the patient received chemotherapy (VACA (INT protocol)) consisting of vincristine 1.5 mg/m2 IV once weekly for seven weeks, actinomycin-D 0.5 mg/m2 IV on day three of the fourth week, cyclophosphamide 1200 mg/m2 IV on day one of weeks 1, 4, and 7, and doxorubicin 30 mg/m2 IV on days 1 and 2, weeks 1 and 7, for a total of 26 weeks. To achieve great survival,

3600 cGy of local radiation was given at a site-limited one cycle/week for four weeks. Blood tests performed a month after beginning cancer therapy revealed a lowered ESR (30 mm/hour), a slightly higher hematocrit (34.2%), leukocytes at a level of 3700/mm3, and no lymphocytes. The left orbit was normal on the CT scan, and the tumour had been entirely excised.[12] In our patient, chemotherapy was carried out according to the first cycle rhabdomyosarcoma protocol in the first week with a regimen of Vincristine 1.12 mg/intravenous, Actinomycin 270 mg/intravenous, Cyclophosphamide 225 mg/intravenous.

Rhabdomyosarcoma is a type of cancer that commonly affects children, and chemotherapy is an essential component of its treatment. The administration of chemotherapy and the duration of therapy varies depending on the patient's individual needs. The primary goal of therapy is to achieve the highest cure rate possible while minimizing the adverse effects of chemotherapy. Clinical studies have evaluated various approaches for treating rhabdomyosarcoma and have shown that multiagent chemotherapy regimens, which include cyclophosphamide or ifosfamide plus dactinomycin and vincristine, yield the best results. Cyclophosphamide and ifosfamide are alkylating agents that damage tumour cells by inducing DNA damage and disrupting DNA regulation. Dactinomycin is a chromopeptide that interferes with RNA transcription by binding to the DNA double helix, inhibiting cell division. Vincristine binds to the tubulin protein, which prevents tubulin dimers from polymerizing to form microtubules, resulting in cells being unable to separate their chromosomes during metaphase. This leads to the cancer cells' apoptosis or programmed cell death.[3,14]

The prognosis of RMS patients is typically determined by a variety of variables, including the histological and cytological subtype, the disease stage at diagnosis, the tumour burden, the location of the original tumour, the patient's age, the cellular ploidy, and the therapeutic response. Twenty years old, a 5 cm tumour, no local or distant disease, a surgical resection with negative margins, and a pleomorphic type are all favourable prognostic factors for survival. The five-year overall survival rate is about 70 percent in all childhood age groups with chemotherapy, radiotherapy and surgery.[8]

This case report has a major limitation in the form of a case study, so it cannot adequately ensure a good prognosis of multidrug chemotherapy in RMS. The lack of serial monitoring of tumour lesion size in patients was also a limitation of this report.

Conclusion

Rhabdomyosarcoma is the most frequently developing malignant tumour in the orbit. Diagnosis of RMS is established by history taking, physical examination, radiology examination, and histopathology. All individuals with RMS receive multidrug chemotherapy. Chemotherapy works successfully for the rhabdomyosarcoma. This patient has a favourable prognosis with early and adequate chemotherapy regimens administered following the RMS protocol.

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