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Case Report

Orbital rhabdomyosarcoma

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Rhabdomyosarcoma (RMS) is a malignant neoplasm related to striated muscle. RMS is the most common soft-tissue sarcoma in children and the third most common extra cranial solid tumor after neuroblastoma and Wilm's tumor.[1,2] As suggested by the term, the tumor is believed to arise from a primitive muscle cell, appearing in round, strap, racquet, and spider forms.[3] In general, RMS and other soft tissue sarcoma are often called "small round cell tumors".[2,4,5]

The incidence of RMS is very rare, in the USA it is 4-7 cases per million per year in children younger than 15 years.[2,6] The ratio of overall RMS between male and female is 1.2-1.4:1 and that of orbital RMS is 0.88:1. About 75% percent of orbital RMS occur at <10 years of age. In Indonesia there was no available data about the incidence of orbital RMS. Tjitrasari[7] in RSCM reported one case of urinary bladder RMS in a 4 year-old boy. As with most tumors of childhood, the cause of RMS is unknown, several genetic syndromes and environmental factors are associated with increased incidence of RMS.[1,2,8]

The histologic classification of rhabdomyosarcoma is based on tissue patterns. There are four histologic categories: embryonal, botryoid, alveolar, and pleomorphic rhabdomyosarcoma. This classification was first suggested by Horn and Enterline in 1958 and adopted by the World Health Organization Classification of Soft Tissue Tumors in 1969 (quoted from 9). The new classification schemes that might have prognostic significance are under consideration by the Intergroup Rhabdomyosarcoma Study (IRS) committee.[1,10]

The RMS is believed to arise from primitive muscle cells, tumors can occur anywhere in the body. The most common site are the head and neck (28%), extremities (24%), genitourinary tract (18%), the trunk (11%), orbital (7%) and retroperitoneum (6%).[2] Orbital RMS is the most common primary orbital malignancy of childhood. The classical clinical picture is sudden onset and rapid unilateral proptosis. A mass may be palpable, particularly in the superonasal quadrant of the eyelid.[3,11] If an orbital RMS is suspected, the case should be processed on an urgent basis. CT scanning or MRI can be used to define the location and extent of the tumor. A biopsy must be done immediately, usually via anterior orbitotomy. There are three modalities mostly used in the management of orbital RMS, which are surgical removal, irradiation, and chemotherapy. Most tumors arising in the orbit are embryonal, localized, and have a high rate of cure.[2,12]

Here, we report a case of orbital rhabdomyosarcoma in a 2.5 year-old female child.

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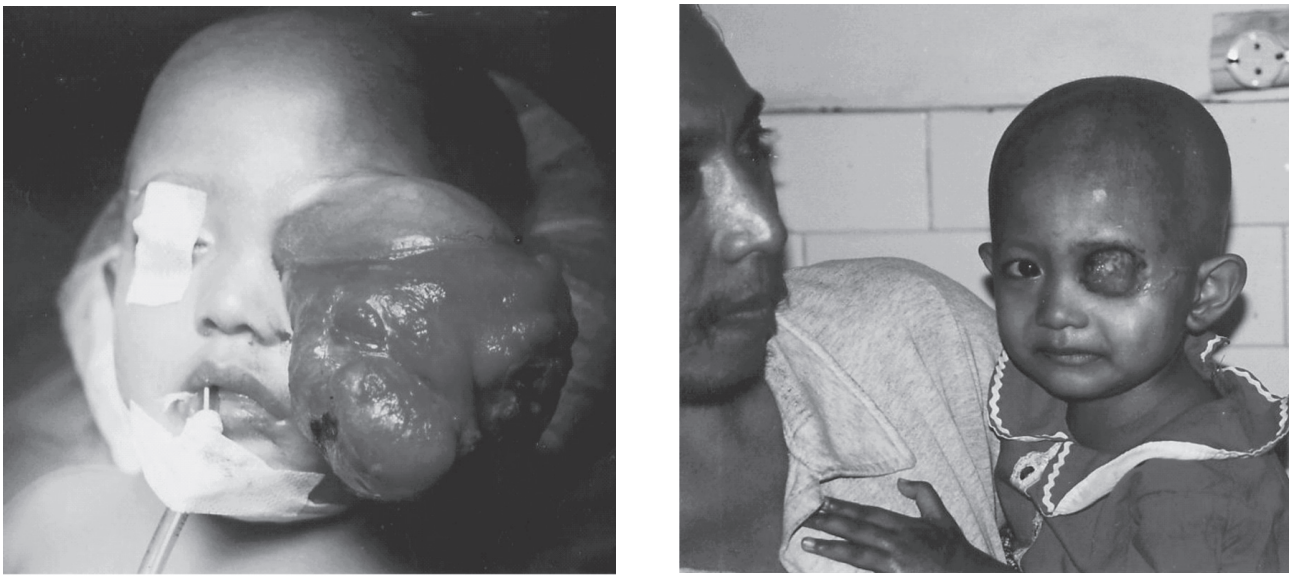
The Case

DA, a 2.5 year-old girl was admitted to the Department of Ophthalmology, Sanglah Hospital on November 28th, 2000, referred by an ophthalmologist who suspected a recurrent retinoblastoma tumor of the left eye. The history was taken from her father. These symptoms started since 3 months before admission. The diameter of the retro-orbital mass was 8-10 cm, the left eyes was rapidly protruded and painful. Daily activities were decreased. She was given medicine from her ophthalmologist, but there was no improvement. There was no history of trauma or other illnesses. She was born spontaneously, vigorously, in Tabanan Hospital, the birth weight was 3000 gram. The growth and developments were normal.

On August 1st, 2000, she was hospitalized at Ophthalmology Department of Sanglah Hospital due to tumor on the conjunctiva of the left palpebra superior. The tumor had a diameter of 3-4 cm, was hyperemic, soft, with proptosis of the left eye. The visus was difficult to evaluate. On August 8th, 2000, extirpation of the tumor was done and the result of histopathological examination was myxoid sarcoma. CT scan examination (first CT scan) showed a retro-orbital tumor. Unfortunately, at this time the parents refused a surgical therapy.

On the second admission, her physical examination revealed a normal general appearance, she was still alert, the pulse rate was 84 times/minute, regular, blood pressure was 110/70 mmHg, respiratory rate was 24 times/minute, axillary temperature was 36.5^{o}C, the body height was 82 cm, body weight was 11 kg, well-nourished (z score was 0 SD), and the body surface area was 0.47 m^{2}. The head circumference was normal. On examination of the right eye, the conjunctiva was not pale or icteric, pupil reflex was positive; on the left eye, a mass was found with a diameter of 8-10 cm, hyperemic, and without capsule. The mass arises from the orbit area of the left eye. Neck stiffness was negative. On palpation, we found no enlargement of lymph nodes either on the neck or the axilla. The chest was symmetrical on both sides. The breath sound was normal and there were no abnormalities of heart sounds on auscultation. The abdomen was not distended, liver and spleen were not palpable, and the bowel sounds were normal on all quadrants. Extremities showed no cyanosis, were warm and well-perfused.

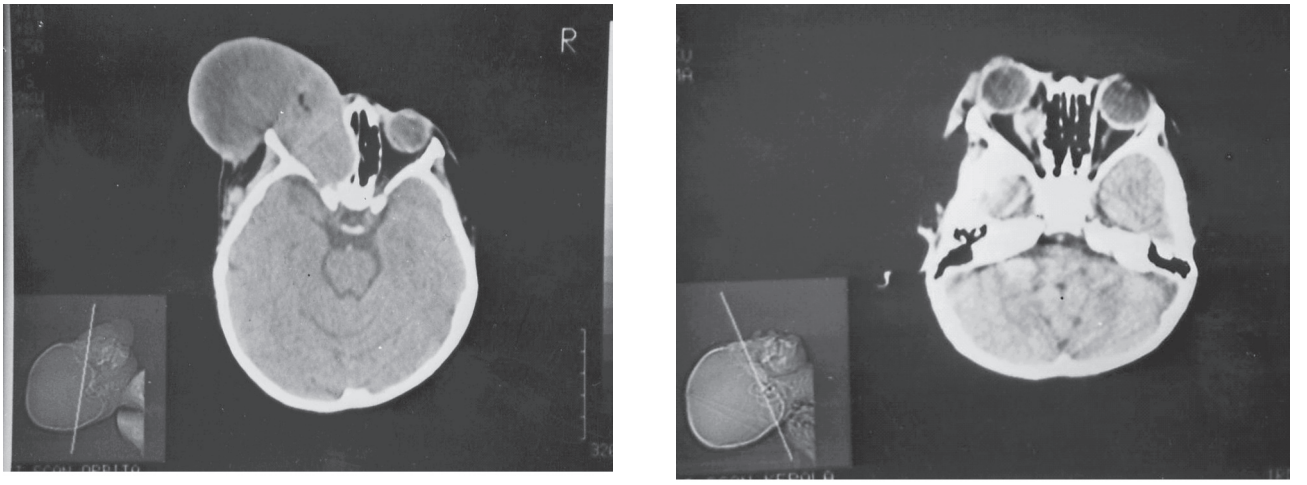
The results of the laboratory investigations were as follows: the white blood cell was 5.4 K/uL, hemoglobin was 13.6 g/dL, hematocrite was 39.4 %, platelet was 289K/uL. The bleeding time and clotting time was normal.



A. Before surgery operation

B. After exenteration of oculi sinistra

Figure 1. Mass of tumor: orbital rhabdomyosarcoma



A. First CT scan on August, 2000

Second CT scan on December 4th,2000

Figure 2. Head CT scan of orbital rhabdomyosarcoma

Based on the clinical manifestations, the differential diagnosis was rhabdomyosarcoma and retinoblastoma. The head CT scan examination (second CT scan) showed that the soft tissue tumor was united with the left bulbous occuli in the orbita. There was no destruction of the cavum orbita and no intracranial tumor. Chest x-ray was in normal limits.

Based on clinical manifestations, head and orbital CT scan, we diagnosed the tumor as orbital myosarcoma.

The patient was referred to the Department of Neurosurgery for further consultation. On December 7th 2000, when the Karnofsky performance was 80%, the excision of the tumor and exenteration of the bulbi oculi sinistra in toto was done under general anesthesia. After surgery, the patient was alert and in good condition.

Histopathological examination was performed and the result showed a tumor without capsule, with squamous epithel, consisting of a round, small, and hyperchromic malignant cells with embryonal mesenteric tissue. The features confirmed the diagnosis of embryonal rhabdomyosarcoma.

Ten days after surgery, the patient was consulted to the Department of Child Health for chemotherapy and radiotherapy. While waiting for the chemotherapy and radiotherapy schedules, supportive therapy to improve general condition was given. The laboratory examination was done and revealed that liver and renal function tests were in normal limit. On routine blood examination: the WBC was 12.9 K/UL, hemoglobin level was 13.3 g/dl, hematocrit was 39.7%, and platelet count was 205 K/UL.

Chemotherapy was started on December 19, 2000, the treatment with VAC protocol included Vincristine, Actinomycin-D, Cyclophosphamide with addition of Adriamycin. The dose of vincristin was 1.5 mg/m^2/day or 0.7 mg was given intravenously one day per week every 3 weeks for 6 cycles. Dosis of Actinomycin-D was 15 ug/kg/day 1-5 (150 ug/days) and Cyclophosphamide 300 mg/m^2/days/p.o (140 mg) was given 5 days every 6 weeks until 4 cycles and Adriamycin 60 mg/m^2 day 1 (28 mg/day) in fourth and

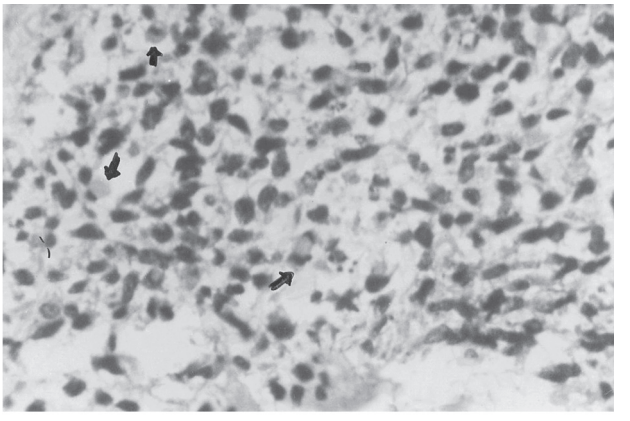


Figure 3. Histologic appearance: primitive, round to spindle cells with rhabdomyoblast cell.(No. PB: 0785/PA/2000; Hematoxylin and eosin; x 100)

tenth week. The radiotherapy was started on January 9th, 2001 and finished on March 21st, 2001, the radiation was given 5 days for 2 cycle, the total radiation was 4000 rads (**Figure 4**).

The patient was discharge from the hospital on April 18, 2001 in good condition, laboratory examinations were normal. She was further observed in the outpatient clinic. On August 12, 2002, the patient was still in good condition, recurrence of the tumor was not found, laboratory parameters, growth, and development were normal.

Discussion

Rhabdomyosarcoma (RMS) is a malignant tumor thought to arise from the same embryonic mesenchyme as striated skeletal muscle. Common sites of primary disease include the head and neck region, genitourinary tract, and extremities.[1,13] Orbital rhabdomyosarcoma is the most common primary malignancy of the orbita in children. There are four recognized histologic subtypes of RMS. The embryonal type, the most common type, accounts for 60% of all RMS and occur predominantly in the head and neck including the orbita region. The botryoid type is a variant of the embryonal form, accounts for 6% of the total RMS and commonly seen in the vagina, uterus, bladder. The alveolar type, accounts for 20% of the cases and found most often in the trunk and extremities usually with the poorest prognosis. The pleomorphic type (adult form) is rare in childhood account for 1% of the cases.[2,4,14]

The diagnosis of rhabdomyosarcoma is based on both clinical and pathologic findings. Clinical signs of orbital RMS often have a sudden onset, the rapid evolution of unilateral proptosis. Most parents first noticed as a droopy eyelid (ptosis) and the eye is more prominent (proptosis) or there was a tumor under the conjunctiva. The tumor is usually found in the superonasal orbit (that is under the upper lid near the nose). The computed axial tomography (CT-Scan) and magnetic resonance imaging (MRI) typically show a mass attached to one of the ocular or orbital muscles. CT is particularly helpful because it shows the invasion to the orbital bones.[2,15,16]

The characteristic cellular element of rhabdomyosarcoma is the rhabdomyoblast, a primitive skeletal muscle cell with eosinophilic cytoplasm and cross striations or longitudinal myofibrils. They have been described as round cells, spindle cells and tadpole or racquet cell spider web cell, and multinucleated giant cells.[17,18]

In our case, clinical findings were rapid onset of unilateral proptosis, retro-orbital mass, and bulbi oculi sinistra united with the tumor. On CT scan examination, we found retro-orbital mass, no destruction of the cavum orbita, and no tumor intracranially. On histological examination we found a mass of tumor consisted of round, small and hyperchromic malignant cells with embryonal mesenteric tissue. The features confirmed the diagnosis of embryonal rhabdomyosarcoma.

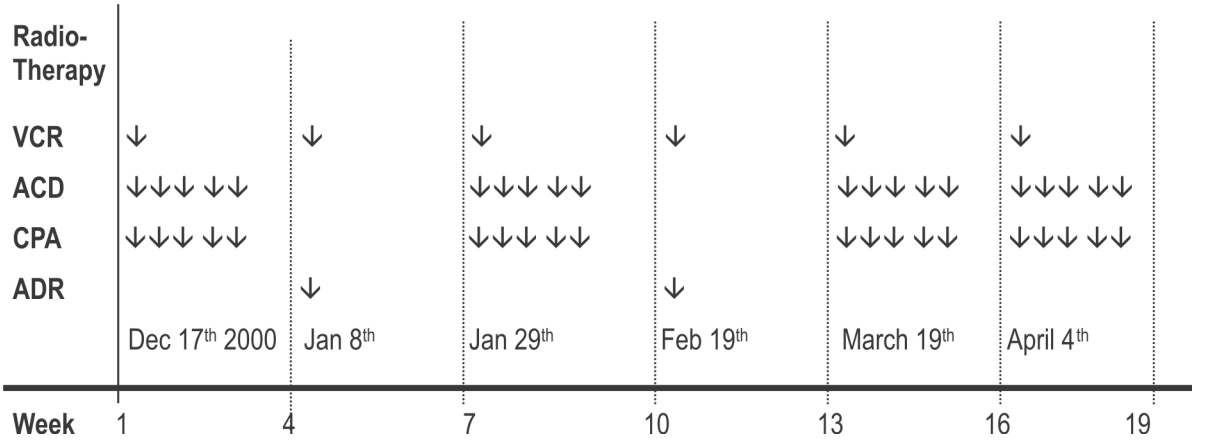


Figure 4. Chemotherapy and radiotherapy regiment of rhabdomyosarcoma patient

TABLE 1. CLINICAL GROUP STAGE SYSTEM FOR RHABDOMYOSARCOMA.[2]

Group	Extent of disease/surgical result
I	A. Localized tumor, confined to site of origin, completely resected.
	B. Localized tumor, infiltrating beyond site of origin, completely resected
II	A. Localized tumor, gross total resection, but with microscopic residual disease
	B. Locally extensive tumor (spread to regional lymph nodes), completely resected
	C. Locally extensive tumor (spread to regional lymph nodes), gross total resection, but microscopic residual disease
III	A. Localized or locally extensive tumor, gross residual disease after biopsy only.
	B. Localized or locally extensive tumor, gross residual disease after major resection (> 50% debulking)
IV	A. Any size primary tumor, with or without regional lymph node involvement, which distant metastasis, irrespective of surgical approach to primary tumor

TABLE 2. TNM STAGING SYSTEM OF RHABDOMYOSARCOMA[2]

Tumor	
T_1	extends beyond the site of origin:
T_2	A: ≤ 5 cm in diameter, B; > 5 cm in diameter
Node	
N_0	No regional node involvement
N_1	regional node involvement
N_x	Nodes unknown
Metastasis	no metastasis metastases present at diagnosis
M_0	
M_1	

Accurate staging at the time of diagnosis is critically important, as a guide to therapy and significant determinant of prognosis. The most widely used surgicopathologic staging system has been the clinical grouping (CG) system developed by the IRS (Intergroup Rhabdomyosarcoma Study) in 1972 (**Table 1**). A pretreatment tumor-nodes-metastasis (TNM) staging system modified for evaluation of site of primary tumor, local extension, size, regional nodal involvement, and the presence or absence of metastatic disease. This system recognizes four categories of disease based on the amount of tumor remaining after initial surgery and the degree of tumor spread at the time of diagnosis.[1,2]

Staging system of RMS is:[2,3] stage 1, orbit, head/neck (not parameningeal), and GU tract (not baldder/prostate); stage 2, other locations, NO or NX; stage 3, other locations, N1 if tumor less than 5 cm, NO or NX (if tumor >5cm); stage 4, any site with distant metastases.

In our patient, the staging of the tumor was stage I, the tumor was confined to site of origin that was in anatomic site origin of orbita, no regional node involvement, and no metastasis of tumor in the brain. Staging of surgicopathologic was group I (completely removed of the tumor).

The treatment of RMS depends on number of factors including general health, the size and position of the tumor. There are three modalities mostly used in patients with RMS involving a combination of surgery, chemotherapy and radiotherapy.[2,4] The goal of these multidisciplinary program is the cure of the patient by complete eradication of the tumor. The basic principle of primary surgical approach is wide resection of primary tumor with adequate margin of normal tissue. The surgical approach usually is exenteration. This method is favored in the United State. Exenteration is performed after the diagnosis has been established by incisional resection of the tumor. Radiation therapy plays an important role in the treatment of RMS. In sites such as the head and neck or pelvis, the tumor often cannot be completely removed by surgery. Radiation therapy can eradicate residual tumor cells. General radiation therapy guidelines have evolved with sequential intergroup studies with a dose of 4000-4500 rad. Chemotherapy is usually administered as a supplement to surgery and radiotherapy. Prior to combination therapy, surgery alone results in a survival rate of less than 20%. The development of adjuvant therapy has increased survival to approximately 60%. All these agents have potent systemic side effects. Several groups of chemotherapy agents are alkylating agent, antimetabolite, antitumor antibiotic include Vincristine (V), Actinomycin D (A), Cyclophospamide (C). VAC has been the gold standard for combination chemotherapy in the treatment of most cases of RMS.[19,20]

In our case we did combination therapy, surgical, chemotherapy, and radiotherapy. The surgical approach in this case was exenteration of the bulbi oculi sinistra and continued with chemo-

therapy one week after surgery. The chemotherapy regimen was Vincristine, Actinomycin-D, cyclophospamide (VAC) until 6 cycles every 3 weeks. Radiotherapy was given 2 weeks after surgery and the total dose of radiotherapy is 4000 rads.

The prognosis of rhabdomyosarcoma depends on 5 major factors: 1] age; 2] primary site; 3] histologic type; 4] stage of disease and 5] treatment. Children between the ages of 1-7 years had a better prognosis than those above these ages. Sarcomas arising in locations that produce early symptoms (e.g.orbita) are associated with a better prognosis than those that arise in a deep area (e.g. retroperitoneum). The best survival rate is associated with embryonal sarcoma and the poorest prognosis is associated with alveolar RMS. Localized (group I) and regional resectable (group II) tumors are frequently curable and have a good prognosis).[2,6,18] Mannor *et al*,[19] reported that more than 90% of children with orbital RMS respond to combination therapy. Crist *et al*,[20] reported estimated survival at 5 year from the start of treatment was 65-75% in IRS-I (localized disease, completely resected). Wharam *et al*[21] found that in 89 children who had sub total resection or biopsy only, the local control rate with radiotherapy and chemotherapy was 94%. In our case, based on age, primary site (in the orbita), histologic type (embryonal RMS), and surgicopathologic stage (stage I), the prognosis was good (superior).

Summary

We report a case of orbital rhabdomyosarcoma in a 2.5 year-old female child. The definitive diagnosis was established by clinical and histopathological findings. The treatment includes supportive therapy, surgery, radiotherapy, and chemotherapy. The patient was discharged in a good condition and on observation in the outpatient clinic, the condition was still good.

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