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Rhabdomyosarcoma metastases to the bone marrow of a 2-year-old male patient: A case report

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Case Report

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ABSTRACT

Rhabdomyosarcomas are the most common pediatric soft tissue sarcomas. However, rhabdomyosarcoma cases that manifest as a systemic disease or showing diffuse metastasis in the bone marrow are sporadic. The most common sites of metastasis due to rhabdomyosarcoma include lungs, lymph nodes, and bone marrow. The bone marrow involvement is seen in about 30% of cases of metastasis. We report a case of a 2-year-old boy with complaints of right eye protrusion. The result of a head CT-scan arouses suspicion of rhabdomyosarcoma. On physical examination, protrusion of the eye and swelling of the neck with a fixed and flat surface were observed. Peripheral blood examination resulted in pancytopenia (hemoglobin: 4 g/dL, leukocytes: 3,490 cells/µL, platelets: 16,000 cells/µL). The peripheral blood morphologies showed lymphoblasts and myeloblasts, whereas the bone marrow biopsy result showed infiltration of tumour cells (rosette cell form). Chest imaging examination showed suspected of skeletal metastases in bilateral scapulae and bilateral costae. Pancytopenia with tumour cells metastasis to the bone marrow was found in this case. Diagnosis of rhabdomyosarcoma with multiorgan metastasis and the presence of tumour cells in the bone marrow was based on clinical features, physical examination, laboratory examinations, and other supporting investigations.

Rhabdomyosarcoma adalah keganasan jaringan lunak yang paling umum terjadi pada anak. Keganasan ini paling sering bermetastasis ke paru-paru, limfonodi, dan sumsum tulang. Metastasis ke sumsum tulang mencakup 30% dari semua kasus dengan metastasis organ. Kami melaporkan seoran anak laki-laki berusia 2 tahun dengan keluhan mata kanan menonjol. Hasil CT scan kepala mencurigai malignancy rhabdomyosarcoma*. Pada pemeriksaan fisik didapatkan mata menonjol dan pembengkakan pada leher dengan permukaan rata, dan terfiksasi. Pada darah tepi didapatkan pansitopenia (Hemoglobin: 4 g/dL, lekosit: 3490/µL, trombosit: 16.000/µL). Morfologi darah tepi didapatkan limfoblas dan mieloblas sedangkan pada sumsum tulang didapatkan adanya infiltrasi sel-sel non hematopoietik (*rossette cell form*). Pemeriksaan pencitraan dada dicurigai metastasis pada scapula bilateral dan ossis costae bilateral. Pada kasus ini didapatkan adanya anemia dengan metastasis sel-sel nonhematopoitik pada sumsum tulang. Diagnosis rhabdomyosarcoma disertai metastasis pada organ lain serta infiltrasi sel-sel nonhematopoietik pada sumsum tulang didasarkan pada gambaran klinis, pemeriksaan fisik, pemeriksaan laboratorium, dan pemeriksaan penunjang lainnya.*

INTRODUCTION

Rhabdomyosarcoma (RMS) is the most common soft tissue malignancy in children with 3-8% of all children malignancies with an incidence of 4-5 per million children under the age of 18 each year.[1] Rhabdomyosarcoma cases that manifested as a systemic disease are sporadic, and cases that show diffuse metastasis in the bone marrow are most unusual. Rhabdomyosarcoma most commonly metastases to the lungs, lymph nodes, and bone marrow.[2] Bone marrow involvement is about 30% of all metastases cases.[3] The clinical picture of the spread of RMS in children may resemble acute blood malignancy and can cause a misdiagnosis because of its morphological resemblances to lymphoblasts and myeloblast.[4] Immunohistochemistry and microscopic examination need to be done in order to ensure that the bone marrow metastases due to rhabdomyosarcoma.[5]

CASE DESCRIPTION

A 2-year-old child was admitted to Sardjito General Hospital on the 18th of July 2018 with a worsening right eye protrusion as a chief complaint. The parent reported that the right eye had been protruding for two months before admitting to Sardjito Hospital. There were no complaints in decreasing body weight, bleeding, food appetite, and prolonged fever. He had a history of going to Ngesti Waluyo Hospital one month ago with the same complaint as his eye protruded. A computed tomography scan of his head showed suspicion of rhabdomyosarcoma. His routine blood test results were haemoglobin of 4 g/dL, white blood count of 3,490/µL, and platelets count of 16,000/µL. The patient underwent transfusion whose haemoglobin became 11 g/dL. There was no history of malignancy in the family.

On general physical examination, the child was compos mentis and well-nourished with a body height of 93 cm and a bodyweight of 11 kg. He was hemodynamically stable on room air with the blood pressure of 90/70 mmHg, respiratory rate of 26 x/minute, pulse rate of 100 x/ minute, a body temperature of 36.5°C, and zero scores of the pain scale. On eye examination, we found protrusion on bulbous oculi dextra with macular hyperpigmentation on the inferior palpebra and anisocoria pupils (4 mm/2 mm). On the neck palpation, a fixed, round mass on the submandibular dextra, Colli lateralis dextra; sized 2 mm x 2 mm, was palpated. Supporting examinations were also performed in purpose to confirm the diagnosis.

Table 1 informs the laboratory test. In peripheral blood morphology, normocytic normochromic anaemia and cells resembling lymphoblasts (5%) and cells resembling myeloblasts (1%) were seen (Figure.1).

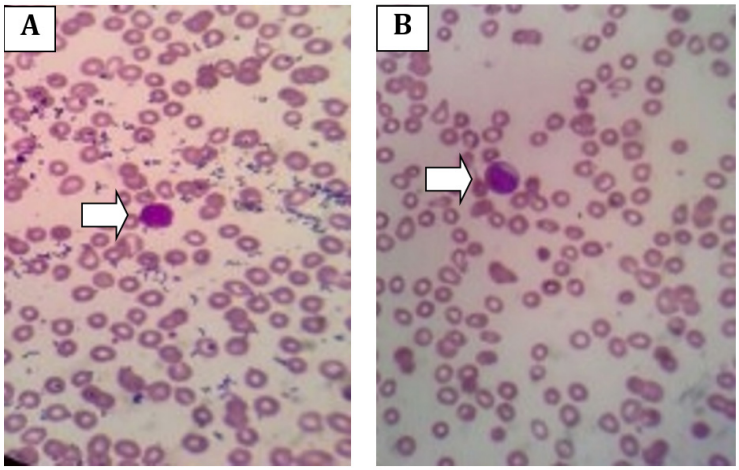

Figure 1. A. Peripheral blood morphology resembled lymphoblastic cells (arrow); B. Resembled myeloblastic cells (arrow)

Bone marrow aspiration was done and showed a hypercellular density. Moreover, we found a group of cells (cluster) as well as rosette-forming cells whose characteristics were large cells, diffuse cytoplasm, and a large nucleus. Therefore, the infiltration of non-hematopoietic cells (rosette-forming cells) was found (Figure 2). Additionally, a computed tomography (C.T.) of his abdomen reported a mass in the para-aorta and cystic nodules in the right pulmonary, which suspected to be lymphoma. In contrast, his thorax x-ray revealed nodules in the right paracardial and suspicion of skeletal metastases in bilateral scapulae and costae.

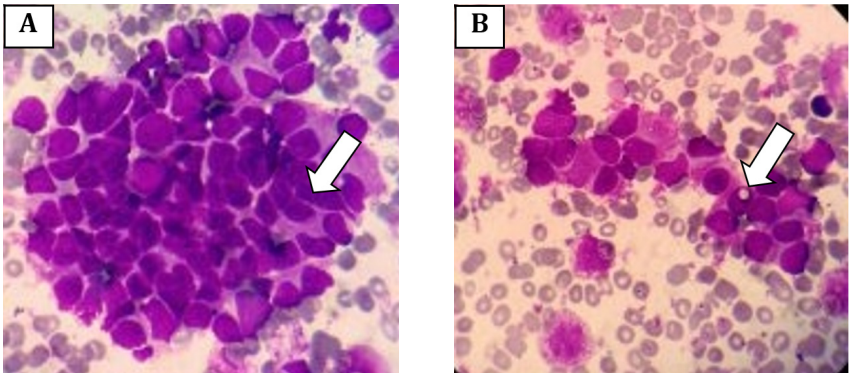

Figure 2. A. Bone marrow aspiration contained rosette-forming tumor cells (arrow); B. a cluster with a vacuolated cytoplasmic (arrow).

Table 1. Laboratory Test Result

Parameters	Value	Reference
Haemoglobin	4	9.6-15.6 g/dL
White blood cell	3,490	5.50-17.50x10^3/uL
Platelets	16	150-450 x 10^3/uL
PPT	14.3	12.3-15.3 second
APTT	26.0	27.9-37
BUN	11.90	6-20 mg/dL
Creatinine	0.34	0.7-1.2 mg/dL
Albumin	4.03	3.97-4.94 g/dL
AST	52	< 40 U/L
ALT	56	< 41 U/L
Sodium	138	136-145 mmol/L
Potassium	4.23	3.50-5.10 mmol/L
Chloride	97	98-107 mmol/L

PPT: Prothrombin Time; APTT: Activated Partial Thrombin Time; BUN: Blood Urea Nitrogen; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase

This patient was clinically diagnosed with rhabdomyosarcoma accompanied by the evidence of skeletal metastases and infiltration of tumour cells (rosette-forming cells) to the bone marrow. In patients with rhabdomyosarcoma, a complete blood count monitor was performed to investigate bone marrow failure. Examination of liver function

and kidney function to evaluate the functional impairment due to metastases should be routinely conducted. In purpose to ensure rhabdomyosarcoma metastases to bone marrow, immunohistochemistry examination is also required.

DISCUSSION

Rhabdomyosarcoma is the most common soft tissue malignancy in children, of 3-8% of all child malignancies with an incidence of 4-5 per million children under the age of 18 each year.[1] The mean age at diagnosis is 5-6 years, and 72-81% of patients are younger than ten years at first presentation, with a slight male predominance (1.3 males to 1 female).[6] Similar to this case, where the patient is a 2-year-old boy. Based on histological morphology, there are two main types of pediatric rhabdomyosarcoma, the embryonal and alveolar. The embryonal subtype (70% cases) is associated with younger age and better prognosis, while the alveolar subtype (15% cases) highly occurs in older children with poorer prognosis.[7]

Rhabdomyosarcoma often clinically manifested as a visible or palpable mass, which most commonly (36%) presents in the head and neck (includes the orbit, non-parameningeal, and meningeal areas). The orbital tumours tend to have a more precise presentation with proptosis, and therefore are detected earlier and have a better prognosis.[7] In these reported patients, the clinical manifestations are worsening protrusion of the right eye—the result from a head C.T. scan suspected to be rhabdomyosarcoma malignancy. Besides right eye protrusion, right submandibular and neck mass were observed.

A routine blood test was performed, which the result suspected to be any depression in bone marrow (pancytopenia with haemoglobin: 4 g/dL, white blood count: 3,490/µL, platelets: 16,000/µL). The peripheral blood morphology revealed a feature of lymphoblasts and myeloblasts, which haematological malignancies with either lymphoid or myeloid series can be formulated as a differential diagnosis. Solid tumour cells are rarely seen in peripheral blood smears, but this patient revealed a leuko-erythroblastic blood picture. However, circulating tumour cells have been described in cases of some malignancies, such as breast carcinoma, small cell carcinoma, ovarian carcinoma, neuroblastoma, Wilms tumour, and rhabdomyosarcoma, sometimes mimicking the clinical appearance of acute leukaemia. Fortunately, despite thrombocytopenia, this patient had no manifestations of bleeding or DIC.

Signs and symptoms at presentation will depend on the site of the primary tumour, whether there is extension into contiguous organs, and in some cases, the presence of metastatic disease.[8] About 10-20% of patients RMS present with distant metastases, most commonly to the lungs, bone, bone marrow, or lymph nodes.[7] In cases of Head and Neck Rhabdomyosarcoma in children, 33% of patients present with metastases at the time of diagnosis, 11% cases occurred in the bone marrow, 6% in cerebrospinal fluid, 6% in peritoneal fluid, 4% in lung, 2% in parietal pleura, 2% in pleural fluid and 2% in pericardial fluid.[9] By contrast with the outcome for children with localized tumours, the prognosis of those with metastatic rhabdomyosarcoma has not substantially improved during the last 20 years. Five-year survival remains between 20% and 30% for the entire group.[10] Significantprognostic factors include the characteristics of the primary tumour, such as its location, size, and resectability, and the occurrence of regional relapse or distant metastasis.[11,13]

Another possibility was due to infiltration to the bone marrow. An infiltration of tumour cells (rosette-forming cells) whose characteristics were giant cells with scanty cytoplasm and large nucleus was seen by performing a bone marrow aspiration.

Both the peripheral blood morphology and bone marrow aspiration result, whose features resembled haematological malignancies, left problems in diagnosing the disease. Massive bone marrow involvement of RMS is not unusual, but mimicking of leukaemia is a rare instance. Especially, diffuse bone marrow involvement of RMS with the unknown primary site might

be diagnosed as leukemia.[14] The picture of cells infiltrating bone marrow is very similar to lymphoblasts. This similarity causes RMS with those undergoing metastasis to the bone marrow often to be confused with acute lymphoblastic leukaemia. The beneficial thing of this patient had a specific clinical picture for RMS in the form of protrusion of the eyeball. Differentiation between acute leukaemia and bone marrow metastasis of rhabdomyosarcoma is challenging, as both of these conditions may lead to diffuse involvement of blast-like cells.[15] Thus, an immunohistochemistry examination (such as Desmin and Myogenin immunohistochemistry) was needed to confirm rhabdomyosarcoma metastases in the bone marrow. Flow cytometry (FCM) may also be useful for the detection of bone marrow metastasis due to RMS since it is commonly used in the diagnosis of haematological malignancies.[16]

CONCLUSION

Based on clinical features, physical examination, laboratory tests, and other supporting examinations, the patient was diagnosed with rhabdomyosarcoma with evidence of distant metastases in the skeletal organs and infiltration of tumour cells (rosette-forming cells) in the bone marrow. There was no further examination or any result of pathology diagnosis; therefore, we cannot exclude other diagnoses for this case, such as neuroblastoma, lymphoma, or other small round blue cell tumour.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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Not applicable.

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