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Orbito-ocular granulocytic sarcoma and posterior mediastinal sarcoma in a child

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1. Introduction

Myeloid sarcoma (MS) is a rare variant of myeloid malignancy. Condition was described first by Burns [1], named as chloroma in 1853 [2] after almost 40 years, but association between MS and leukemia was recognized by Dock and Warthin [3] and term granulocytic sarcoma was suggested by Rappaport in 1967 [4]. The World Health Organization has classified MS into 3 main types, depending on the degree of maturation; (i) blastic type, mainly composed of myeloblasts (ii) immature type, composed of myeloblasts and promyelocytes and (iii) differentiated type composed of promyelocytes and more mature myeloid cells [5]. It manifests as an extra-medullary tumor composed of myeloblasts and myeloid precursors with varying degrees of differentiation, and more commonly occurs in the pediatric population. MS is a pathological diagnosis for extramedullary proliferation of myeloid lineage blasts occurring anywhere in the body. The most common sites are the lymph nodes, skin and bones, and less often the orbita and the central nervous system. We describe a patient with AML with Auer rods (Myeloid Sarcoma according to the WHO classification) presenting with two separate MS involvements including the orbita and posterior mediastinal region.

2. Case report

A 7-year-old female was admitted to our clinic with progressive swelling in the right periorbital region over the previous 7 days. Her symptoms were fever, frontal headache and weakness. Physical examination revealed pallor and mild proptosis of the right eye with restricted eye movement. The liver was palpable 1 cm below the right costal margin and the spleen 1 cm below the left costal margin. Complete blood count revealed hemoglobin 7.3 g/dL, leukocytes 10,530/ml and platelets 62,000/ml. Peripheral blood smear revealed 30% neutrophils, 25% monocytes, 1% basophils, 34% lymphocytes and 10% blast cells with Auer rods. Chest *X*-ray showed an opacity in the posterior upper zone of the right lung. Bone marrow aspiration revealed 5% myelocytes, 3% monoblasts, 31% myeloblasts, 27% polymorphonuclear leucocytes, 21% lymphocytes, 4% normoblasts, 2% monocytes, and 5% metamyelocytes. Myeloblasts exhibited Auer rods and hypogranulation. Positive parameters of flow cytometric (FCM) analysis of the bone marrow were Cluster of Differentiation (CD) 45 (95.38%), CD45 + CD4 (95.38%), CD13 (61.25%), CD45 + CD34 (55.93%), CD38 (91.74%), CD15 + CD117 (73.45%), CD45 + HLA-DR (95.38%), cCDTdt (53.62%), and myeloperoxidase (MPO) (99.52%).

AML was diagnosed on the basis of bone marrow aspiration findings and bone marrow biopsy which showed young myeloid cell hyperplasia and myeloblasts. Immunohistochemical staining of bone marrow biopsy revealed positivity of myeloperoxidase and CD 13 monoclonal stain. Karyotype analysis revealed a 46, XX chromosome pattern. Cerebrospinal fluid analysis was negative for myeloid leukemia cells. Orbital magnetic resonance imaging (MRI) revealed a 10 × 24 mm mass lesion in the lateral rectus muscle of the right orbita (Fig. 1). Computerized tomography (CT) of the chest

Abbreviations: MS, Myeloid Sarcoma; AML, Acute myeloid leukemia; WHO, World Health Organization; CD, Cluster of Differentiation; MPO, Myeloperoxidase; OOGS, Orbito-ocular granulocytic sarcoma; CNS, Central nervous system; EM, Extramedullary.

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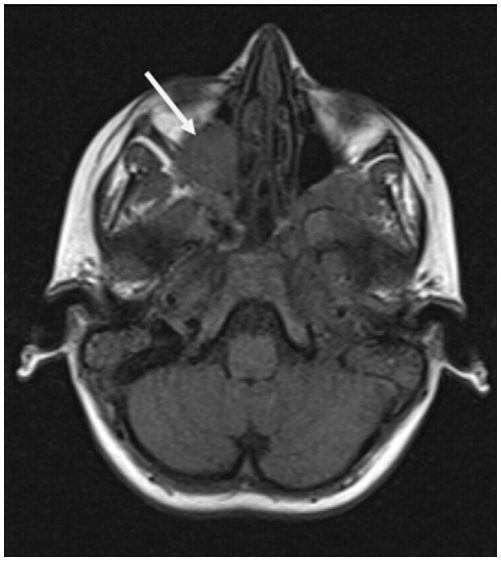

Fig. 1. Orbital MR showing a 10 × 24 mm mass lesion in the lateral rectus muscle of the right orbita.

revealed a mass lesion within the spinal canal extending from T1 to T4. At the T2 level, the lesion extended to the right paravertebral soft tissue in the form of a dumbbell tumor. Two homogenized masses were observed at the left T4-5 levels with a diameter of 19 × 5 mm and at the T7 level with a diameter of 26 × 7 mm. No destruction of the adjacent bone was observed (Fig. 2a). CT-guided tissue biopsy was performed at the site of the paravertebral lesion. Immunohistochemical staining of tumor cells revealed MPO (+), CD68 (+), CD34 (+), CD13 (+), CD56 focal (+), and lysosome (+) (Fig. 3). Based on these findings, the patient was diagnosed with MS with comorbid AML. AML BFM 2004 was administered. Induction

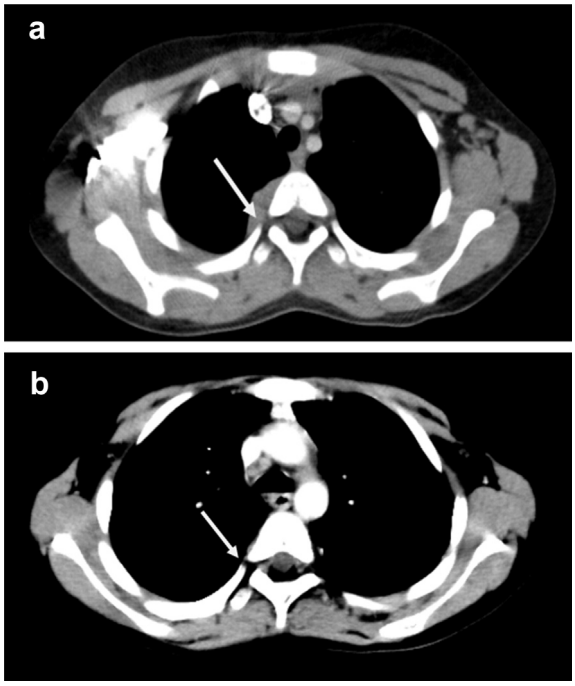

Fig. 2. a: Computerized tomography of the chest showing a mass lesion extending to the right paravertebral soft tissue in the form of a dumbbell tumor. b: Computerized tomography of the chest after treatment.

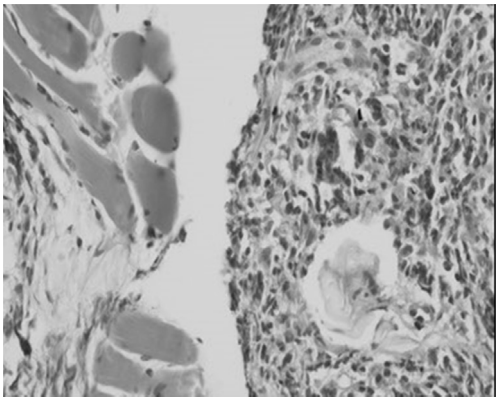

Fig. 3. Hematoxylin and eosin staining of a MS. Diffüz infiltration of round, small malignant neoplastic cells. The neoplastic cells infiltrated the skeletal muscles. Original magnification × 200).

chemotherapy included cytarabine (100 mg/m^2/d as a 48 h-ıv-infusion day 1 starting in the am until day 3 in the am), cytarabine (100 mg/m^2/d bid as a 30 min-iv-infusion, day 3 am until day 8 am, total 8 doses), idarubicin (12 mg/m^2/d iv, day 3, 5, 7, prior to cytarabine, 120 min-iv-infusion), etoposide-phosphate (150 mg/m^2/d iv, days 6–8, prior to 8.-10.-12. cytarabine dose, as a 1 h-iv-infusion), cytarabine intrathecally with age-dependent dosage on day 1 and day 8. Following the induction cycle of chemotherapy, no mass was observed in CT of the chest (Fig. 2b) and no blasts were observed on bone marrow smear. The patient is currently being monitored at another center.

3. Discussion

MS is seen in 1–5% of all AML cases. It may occur alone or concurrently with myelodysplastic syndrome, myeloproliferative disease or AML. Montoro J et al. reviewed a case in which MS preceded a diagnosis of AML by months or years [6]. Our case was compatible with blastic type MS concurrent with AML.

MS is more commonly encountered in childhood AML than in adults. Ohanian et al. reported MS in 9% of AML cases of all ages and in 40% of childhood AML cases. The signs and symptoms of MS are related to the pressure effect of the sarcoma mass on adjacent structures [7]. Orbital involvement orbito-ocular granulocytic sarcoma (OOGS) as an initial manifestation of AML is less common. Most cases present with unilateral proptosis, and only a few case reports have documented of bilateral orbital involvement as an initial manifestation of AML [8]. Patients may present with painful proptosis and restricted eye movements.

Clinical and imaging features of OOGS have been described by Bidar et al. [8] OOGS may include lacrimal gland enlargement, conjunctival mass and even uveal infiltration. Our case presented with progressive swelling in the right periorbital region.

Myeloid sarcomas are commonly located in the bone, periosteum, soft tissues of head and neck region, skin and orbita. Rarely, they may be located in the intestine, mediastinum, pleura, peritoneum, biliary tract, breast, uterus and ovaries [7]. Involvement of the central nervous system (CNS) is rare, and spinal cord compression by MS in the form of a dumbbell tumor is even rarer [9]. Our patient presented with AML with two separate MS involvements including the orbita and posterior mediastinal region. A mass in the right paraspinal soft tissue extended to the right paravertebral region, but there was no spinal cord compression. Neuroblastoma, ganglioneuroblastoma, ganglioneuroma, neurofibroma, and pheochromocytoma causing posterior mediastinal

mass should be considered as differential diagnosis of MS involving the posterior mediastinum. Our patient's urine test was negative for vanilmandelic acid and homovanillic acid. When MS occurs in the setting of previously or concurrently diagnosed AML, a tissue sample is needed for accurate diagnosis. Appropriate immunohistochemical staining in these cases is particularly essential in order to establish definitive diagnosis. Imaging investigation in our case revealed posterior mediastinal MS, which was verified by tissue biopsy. Peripheral blood and bone marrow aspirate examinations confirmed the diagnosis of AML.

Bakst et al. [10] reported that the molecular mechanisms underlying EM involvement are not well defined but recent immunophenotyping, cytogenetic, and molecular analysis are beginning to provide some understanding. A variety of chromosomal abnormalities have been reported in patients with AML with EM involvement. The t(8;21) translocation is the most commonly reported cytogenetic abnormality associated with EM involvement, both at presentation and at relapse. In children, it has been associated with orbital MS. The inv(16) is another cytogenetic abnormality with a higher incidence of EM involvement, particularly in the abdomen. Molecularly, t(8;21) and inv(16) result in the AML1/ETO44 (RUNX1/RUNX1T1) and CBF_/MYH1145 fusion genes, respectively, which carry a relatively favorable prognosis. Other reported abnormalities in MS include t(9;11), 49 del(16q), 50 t(8;17), 51 t(8;16), 52 and t(1;11). Recent systematic fluorescence in situ hybridization analysis on MS samples detected several chromosomal aberrations, including monosomy 7, trisomy 4, trisomy 8, trisomy 11, del(5q), and del(20q), among others previously mentioned [10]. We only conducted fluorescence in situ hybridization analysis of bone marrow for del 5q31, del 20q12, del 7q31, trisomy 8 because of limited analysis of cytogenetics laboratory.

It is still unclear whether MS confers a poorer prognosis in patients with AML than AML alone. Some case reports, however, have demonstrated survival rates similar to that of AML in both adult and pediatric populations, with 3- and 5-year survival rates of 30% and 21%, respectively [5,11]. Regardless of whether or not it is associated with systemic AML, MS is treated with an aggressive chemotherapy regimen similar to that employed in treating systemic AML [11]. Chemotherapy is the mainstay of treatment, but allogeneic bone marrow transplantation from a matched family donor still remains the best long-term option providing remission-free survival for most patients.

The simultaneous presence of two extramedullary involvements in both orbital and posterior mediastinal masses in childhood AML is very rare. Granulocytic sarcoma should be considered at differential diagnosis of posterior mediastinal mass in patients with or without AML because granulocytic sarcoma is not always associated with AML blast cells at bone marrow infiltration [12]. Granulocytic sarcoma should be remembered in patients with AML presenting with a mass anywhere in the body.

Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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