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Primary Intracerebral Myeloid Sarcoma

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Keywords

Myeloid sarcoma · Granulocytic sarcoma · Chloroma · Meningioma · Extramedullary mass

Summary

Background: Myeloid sarcoma rarely presents in the absence of systemic myeloid disease. **Case Report:** In this study, we present a case of intracerebral myeloid sarcoma with no diagnosis of any hematological disease in a 22-year-old male patient in whom brain magnetic resonance image revealed a meningioma. However, biopsy showed myeloid sarcoma. No myeloid disease was determined. The mass disappeared following 8 cycles of chemotherapy. In the literature, we determined only 8 similar cases cited between 1970 and 2011. **Conclusion:** Intracerebral myeloid sarcoma has currently no standard treatment and may be confused with a primary brain disease. Chemotherapy and/or radiotherapy are the most viable and widely used treatment modalities. Potential occurrence of hematological disease should also be closely followed due to conversion risks.

Schlüsselwörter

Myeloisches Sarkom · Granulozytisches Sarkom · Chlorom · Meningiom · Extramedullärer Tumor

Zusammenfassung

Hintergrund: Das Auftreten myeloischer Sarkome ohne eine gleichzeitig bestehende systemische myeloische Erkrankung ist selten. **Fallbericht:** In dieser Studie stellen wir einen Fall von intrazerebralem myeloischen Sarkom ohne gleichzeitige Diagnose einer hämatologischen Erkrankung bei einem 22-jährigen Patienten vor, dessen magnetresonanztomographische Untersuchung des Gehirns ein Meningiom ergab. Die Gehirnbiopsie zeigte jedoch ein myeloisches Sarkom. Eine myeloische Erkrankung konnte nicht festgestellt werden. Nach 8 Zyklen Chemotherapie verschwand der Tumor. Die Literatursuche für den Zeitraum 1970–2011 ergab nur 8 weitere Fälle dieser Art. **Schlussfolgerung:** Für das intrazerebrale myeloische Sarkom existiert aktuell keine Standardbehandlung, und es ist leicht mit einer primären Gehirnerkrankung zu verwechseln. Chemotherapie und/oder Radiotherapie sind die nützlichsten und weitverbreitetsten Behandlungsmodalitäten. Auf Grund des Konversionsrisikos sollte das potentielle Auftreten hämatologischer Erkrankungen im Auge behalten werden.

Introduction

The term myeloid sarcoma (MS) is used to define an extramedullary mass composed of cells of myeloid lineage. The disease was initially referred to as 'granulocytic sarcoma' and 'chloroma', and later, in the classification of myeloid neoplasms by the 2008 World Health Organization, these terms were replaced with 'myeloid sarcoma' as a subgroup of 'acute myeloid leukemias, not otherwise categorized' [1]. MS may occur in patients with acute myeloid leukemia (AML), acute lymphocytic leukemia, myeloproliferative disease, or myelodysplasia, yet rarely presents in the absence of a myeloid disease [2, 3]. It may involve any organ system, from common involvement of the skin, bone, orbitae, and lymph nodes to rare cases involving heart, small intestines, or brain [2]. Here, we present a patient with intracerebral MS (ICMS) with no hematological disease. Radiologically, the mass had the appearance of a meningioma.

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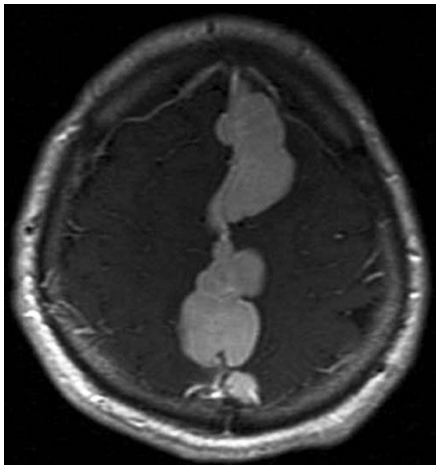

Fig. 1. Axial Gd-enhanced T1-weighted magnetic resonance image showing homogeneous enhancement in the interhemispheric region prior to chemotherapy.

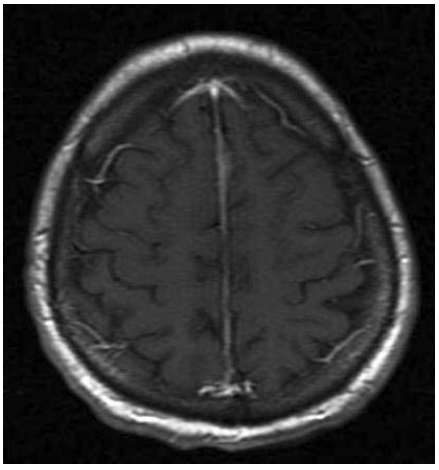

Fig. 2. Axial Gd-enhanced T1-weighted magnetic resonance image showing decreased tumor mass in the interhemispheric region after 8 cycles of chemotherapy.

Case Report

A 22-year-old male presented to our hospital with headache. Physical and neurological examination, as well as blood cell count were completely normal: hemoglobin 13.8 mg/dl, white blood cells 7,300/mm^3, 60% neutrophils, 12% eosinophils, 2% basophils, 20% lymphocytes, 6% monocytes, and platelets 324,000/mm^3. Biochemical panel and computed tomography (CT) of thorax and abdomen were also normal. Yet, a magnetic resonance image (MRI) displayed an intracerebral mass at vertex level on the parasagittal line. In the MRI, the mass resembled a meningioma. Curative surgery was carried out; however, intraoperatively the mass had no resemblance of meningioma. Therefore, biopsy was performed, and the operation ended without excision. The mass was diagnosed as MS pathologically; immunohistochemical (IHC) analysis revealed the following results: myeloperoxidase (MPO)(+), TdT(+), CD117(+), CD1a(–), S100(+). Bone marrow (BM) aspiration and biopsy showed no leukemic cell infiltration. The patient had no history of leukemia or any other malignancy in his family and had not been exposed to radiation, benzene or chemotherapy in childhood due to a malignancy. He refused chemotherapy, and was followed up without treatment. 20 months later, he returned, this time with weakness in his right side. Neurological examination revealed right hemiparesis, while the physical examination, including skin, was normal. As before, laboratory, thorax and abdomen CT findings were also normal. Cerebral MRI now showed a multiple mass resembling meningioma in the interhemispheric region (fig. 1). Cerebrospinal fluid was evaluated: 2 white blood cells, and no red blood cells and no blasts were determined. G-banding and fluorescence in situ hybridization chromosome analyses were run. BM results were as follows: t(8;21)(–), t(11q23)(–), trisomy 8(–), monosomy 8(–), t(16;16)(–), t(15;17)(–). A triweekly chemotherapy was applied (methotrexate 3.5 g/m^2, cytosine arabinoside 2×2 g/m^2, leucovorin 4×100 mg/m^2), and improvement was observed on MRI following the treatment. The right hemiparesis improved after 3 cycles of chemotherapy. A total of 8 cycles of therapy was performed, and MRI showed total disappearance of the mass (fig. 2). Autologous hematopoietic stem cell transplantation was recommended to the patient but he refused. The patient was followed up for a period of 18 months, still responding to chemotherapy.

Discussion

Generally, MS occurs in patients with AML and other related disorders [1] either before or weeks, months and even years after the hematological disease [4]. Initially, ICMS may develop in patients with no signs of hematological disease, as in our case and other cases cited here (table 1). It usually presents as an extra-axial mass, and the mechanisms responsible for the pathogenesis are believed to originate from the BM of the skull. ICMS cells may travel along the Haversian canals and reach the subperiostium and dura mater as well as perivenous adventitial tissue, and enter the subarachnoid space. Rupture of the pial/glial membrane results in invasion of the brain parenchyma [5, 6]. There are also sanctuary sites leukemic cells may enter where attacks by CD8+ and natural killer cells might be difficult due to detection problems, in which case the immune system may be ineffective in combating such cells. ICMS is not a well-known disease due to the rarity of cases. In addition to our case, 8 further cases appear to have been cited so far, including 5 females and 3 males with a mean age of 28 years [6–13]. In a small group of patients with MS, hematological disease may never appear [14]. In this review, while AML was observed in 3 cases following diagnosis, no hematological disease was observed in 4, and no reliable data regarding such a disease was obtained in the remaining case.

Radiological findings may present images similar to lymphoma, metastasis, eosinophilic granuloma, and microglioma [7, 10, 15]. The initial image in our case resembled meningioma. Capable of discriminating between myeloid and non-myeloid cells with monoclonal antibodies against MPO and lysozyme [16], IHC forms the basis of MS diagnosis [4]. Although not fully ascertained, some chromosomal abnormalities may be associated with MS. The t(8;21) translocation is the most commonly reported cytogenetic abnormality; others include t(11q23), t(9;11), del(16q), t(8;17), t(8;16), t(1;11), and (q22;q22). Molecularly, t(8;21) and inv(16) are regarded as carrying a favorable prognosis [6, 16]. In this review, genetic

translocations were studied in 1 cited case as well as in our case (table 1). Although molecular and genetic mutations are important in evaluating acute leukemia and assessing prognosis, there is limited information regarding their role in MS. A nucleophosmin gene mutation (NPM1) was found in 50% of AML patients with a favorable prognosis. NPM1 mutations were reported in 14% of MS; and FMS-related tyrosine kinase 3 gene mutations were reported in 35% of AML patients with an unfavorable prognosis [16]. There are some studies showing that in the case of an MS diagnosis, the patient usually has more than 1 manifestation. In this case, the most widely used and available approach is utilization of 18-fluorodeoxyglucose positron emission tomography/CT (18FDG-PET/CT) which can help detect intra/extracranial MS [17, 18].

Due to lack of prospective data, there is no consensus on the treatment of MS. Most treatments are based on retrospective data. Intensive chemotherapy is usually recommended. Imrie et al. [2] demonstrated that, in the treatment of isolated MS, anti-leukemia chemotherapy at the time of diagnosis significantly reduced the probability of developing AML from 71 to 41%. The median survival time also significantly increased in comparison with the group that received no therapy. The study revealed that neither radiotherapy nor surgical removal influenced survival. In 1 of the cases reviewed in our study, in whom chemotherapy was applied, leukemic transformation to AML was observed during clinical follow-up [7]. Another case received allogeneic hematopoietic stem cell transplantation, and 7 years following diagnosis the patient was reported to still be alive [6]. The systemic treatment approach can be regarded as providing long-term survival. Our patient, during a follow-up period of 18 months, is still responding to chemotherapy.

In summary, IHC as well as chromosome abnormalities and molecular methods may prove to be very helpful in the diagnosis and prognosis of MS. PET can also be used, and is one of the most effective diagnostic techniques since ICMS images may resemble other intracranial masses such as meningioma. We believe that a correct diagnosis, besides comprehension of the natural course of the disease, is very important for the right choice of therapy. If needed, emergency decompression and biopsy should be carried out for surgery. Although radiotherapy may be an effective option for local control, it may not be sufficient for systemic disease on its own. Chemotherapy retains a prime role in the treatment of the disease.

Disclosure Statement

The authors declare that they have no conflict of interest or any sponsorship or funding arrangements relating to their research.

Table 1. Cases in the literature

Case	Author [ref.]	Year	Age, years	Sex	Site	Initial histological diagnosis	Course			Treatment
							latency time to AML development	complete remission	last follow-up	
1	Wiernik et al. [7]	1970	44	F	bilateral frontal lobe-right parietal lobe, hip	eosinophilic granuloma	9 months	n.a.	deceased (17 months)	Bx+R+C (BCNU+daunomycin)
2	Liena et al. [8]	1978	37	M	cerebellum, meninges	GS	7 months	n.a.	deceased (10 months)	S+R
3	Nickels et al. [9]	1979	7	M	cerebellum	GS	no AML at autopsy	no	deceased (5 weeks)	Bx+C+R+IT C
4	Arnal-Monreal et al. [10]	1981	40	F	meninges	histiocytic lymphoma, microglioma	no determined AML or HD	n.a.	n.a	S+R+C (BCNU)
5	Takagi et al. [11]	1983	40	n.a.	frontal lobe, bone	GS	n.a.	n.a.	deceased (9 months)	Bx+C
6	Yoon et al. [12]	1987	16	F	left parietal	GS	no determined AML or HD	yes	reported to be alive at 24 months	S+R
7	Park et al. [13]	2003	3	F	right temporal lobe, bilateral renal, bone	GS	no determined AML or HD	yes	n.a.	Bx+C (BHAC+idarubicin+ 6-thioguanine+IT ARA-C)
8	Widhalm et al. [6]	2006	35	F	right parietal lobe, spine	GS	no determined AML or HD	yes	alive	Bx+C (cyclophosphamide)+ R (total body) +allo BMT
9	current case	2008	22	M	interhemispheric, parasagittal	GS	no determined AML or HD	yes	alive	Bx+C

n.a. = Not applicable; F = female; M = male; Bx = biopsy; S = surgical resection; C = chemotherapy; R = radiotherapy; Allo BMT = allogeneic bone marrow transplantation; HD = hematological disease; BHAC = N4-behenoyl-1-beta-D-arabinofuranosylcytosine; ARA-C = cytosine arabinoside; BCNU = bis-chloroethylnitrosourea.

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