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# Myeloid sarcoma with multiple lesions of the central nervous system in a patient without leukemia

## Case report

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✓The authors report the unusual case of a 35-year-old woman suffering from left leg numbness and radiculopathy due to multiple lesions in the central nervous system: one right parietal extracranial–intracranial lesion with invasion of the sensory cortex, and two intraspinal, intradural lesions compressing the spinal cord at T3–5 and S1–4. Biopsy sampling of the extracranial part of the parietal lesion led to a diagnosis of myeloid sarcoma. Further examination revealed no evidence of leukemic disease or myeloproliferative disorder. An aggressive multimodal approach to treatment in this patient with a combination of chemotherapy, whole-body radiotherapy, and allogeneic bone marrow transplantation was started immediately. The patient experienced full neurological recovery and complete disappearance of all lesions. At the 7-year follow-up examination, there was no evidence of disease. To the authors' knowledge, this is the first report of a myeloid sarcoma with both intracranial and intraspinal manifestations in a patient without leukemia.

**Key Words • myeloid sarcoma • chemotherapy • radiotherapy • allogeneic bone marrow transplantation • long-term remission**

Myeloid sarcoma is a rare malignant tumor composed of immature myeloid cells, or myeloblasts, which often occurs in patients with AML. This pathological entity was first described by Burns in 1811,[6] and in 1853 King[13] named it "chloroma" due to its greenish hue, a result of the presence of myeloperoxidase. Rappaport[20] coined the name "granulocytic sarcoma" in 1966, which was in use until its replacement with "myeloid sarcoma" in the 2002 World Health Organization classification of myeloid neoplasms.[26] This type of lesion may occur anywhere in the body in patients of any age, but most commonly originates in the subperiosteum of the vertebrae, sternum, orbital bones, and cranium; from there it spreads to the soft tissues. Myeloid sarcoma only rarely involves the CNS.

### Case Report

*History and Examination.* This 35-year-old woman presented with a 1-year history of severe bilateral frontal headaches and an 8-month history of radiculopathy corresponding to the S-1 dermatome on her right side. No pathological signs were evident on a computed tomography scan of her brain, but a scan of the spine revealed a mediolateral disc herniation at L5–S1 on the right side. The patient's radicular pain was treated conservatively with physical therapy and oral and intravenous pain medication. Four months prior to her second presentation, however, the patient began to experience hypesthesia in the anogenital region and along the inner femoral surface, primarily on the right side. Lumbar MR imaging studies obtained 2 weeks before her admission to our department revealed an intraspinal, intradural lesion between S-1 and S-4 in addition to the previously diagnosed disc herniation (see Fig. 2). The patient also reported a rapidly increasing subgaleal swelling in the right parietal region, which she had first noticed 6 months previously, and hemihypesthesia in her lower left leg. A 4-cm lesion, both extra- and intracranial, was revealed on MR imaging with extension into the sensory cortex on her right side (Fig. 1). Also on the right side there was another smaller and exclusively subgaleal lesion in the occipital region. After admission to our institution—7.5 months after her initial presentation—her symptoms increased, and a mild sensorimotor paraparesis from T-5 downward, along with sphincter dysfunction and urinary retention, developed in the patient. An MR imaging investigation of the cervical and thoracic regions revealed another intraspinal, intradural

*Abbreviations used in this paper:* AML = acute myelogenous leukemia; CNS = central nervous system; EC–IC = extracranial–intracranial; MR = magnetic resonance.

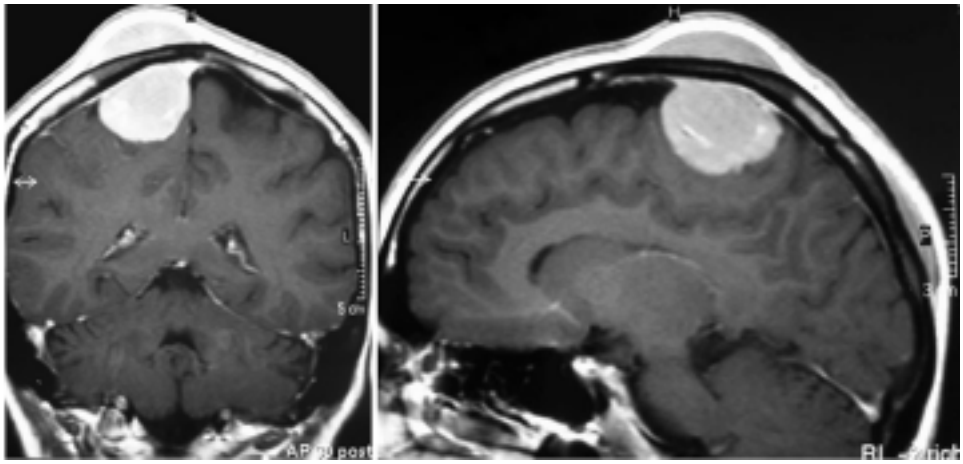

FIG. 1. Coronal *(left)* and sagittal *(right)* Gd-enhanced $T_1$-weighted MR images showing a homogeneously enhancing EC–IC right parietal mass with invasion of the sensory cortex and a small subgaleal lesion in the occipital region.

extramedullary lesion at T3–5 with significant compression of the spinal cord from the left dorsal aspect (Fig. 2).

*Operation and Pathological Studies.* The extracranial part of the EC–IC lesion was surgically removed with the patient under local anesthesia, and a sample was sent for histological examination. The intracranial part was not resected due to its sensory cortex involvement. Macroscopically the tumor mass was firm, dark red, and clearly delineated from the surrounding tissue. Microscopic investigation revealed closely packed, small- to medium-sized blastlike cells with monomorphic, round- or oval-shaped nuclei containing at least one small nucleolus, but more in some cases. The small rim of cytoplasm surrounding the nuclei stained moderately basophilic, and mitotic cells and apoptotic bodies were widespread.

The tumor cells showed intense staining for CD34, CD43, c-kit (CD117), and myeloperoxidase (Fig. 3). This immunoprofile and the histomorphology of the neoplastic cells were consistent with the diagnosis of myeloid sarcoma. Fluorescence in situ hybridization revealed a t(8;21)(q22;q22) translocation—a common finding in patients with myeloid sarcoma and AML.

*Treatment and Posttreatment Course.* After establishing the myeloid sarcoma diagnosis on the basis of biopsy sampling, peripheral blood examinations and a bone marrow biopsy were taken. However, there was no evidence of a leukemic or myeloproliferative disorder. Treatment was started with cyclophosphamide chemotherapy, followed by whole-body radiotherapy with 13.2 Gy and allogeneic bone marrow transplantation. The patient's posttransplant course was complicated by an autoimmune reaction of the skin and liver, which resolved after corticosteroid treatment and photopheresis.

Three months after treatment was initiated, the patient's neurological symptoms had disappeared and she experienced a full neurological recovery. An MR image of the neuraxis taken at that time showed a marked reduction in the size of the EC–IC parietal lesion and complete disappearance of all the other lesions. Two years postoperatively no lesions could be detected on MR imaging. Complete remission persists 7 years postoperatively with no evidence of the initial disease and no sign of leukemia or any myeloproliferative disorder.

## Discussion

Frequently, myeloid sarcoma is diagnosed simultaneously with or after the onset of AML. In patients who do not have leukemia, myeloid sarcoma usually precedes AML. In 87 to 88% of patients with no evidence of a hematological abnormality at presentation, AML develops within 10.5 to 11 months (range 1–49 months);[18,27] however, in a small group of patients with myeloid sarcoma, AML never appears.[15] This often makes diagnosis challenging for clinicians and pathologists. In the absence of an obvious hematological disorder, up to 75% of these tumors are initially misdiagnosed, most frequently as non-Hodgkin lymphoma.[15,16]

Although a t(8;21)(q22;q22) translocation was detected on fluorescence in situ hybridization, there was no evidence of leukemia or myeloproliferative disease in our patient during peripheral blood examinations and bone marrow biopsy. A t(8;21)(q22;q22) translocation in patients with AML is generally associated with a greater probability of the presence of myeloid sarcoma. Tallman and colleagues[23] reported a less favorable prognosis in patients with AML, myeloid sarcoma, and the t(8;21)(q22;q22) translocation compared to patients with AML and myeloid sarcoma but no translocation. In a recent study, however, Felice and associates[11] reported that the presence of myeloid sarcoma and a t(8;21)(q22;q22) translocation in children was not an adverse prognostic factor. The prognostic significance of this translocation in patients with myeloid sarcoma but without leukemia (as in our patient) is not yet clear.

Some authors have indicated that myeloid sarcoma is more frequently diagnosed in children, particularly under the age of 15 years.[8,14,19] Others mention a wide age range, with a common occurrence in middle-aged patients.[7,12,15,17,18,27] Nearly every part of the body may be affected by myeloid sarcoma. Multiple appearances of the lesion with involvement of more than one type of tissue, either concurrently or sequentially, have also been reported.[7,12,14,18,19,27]

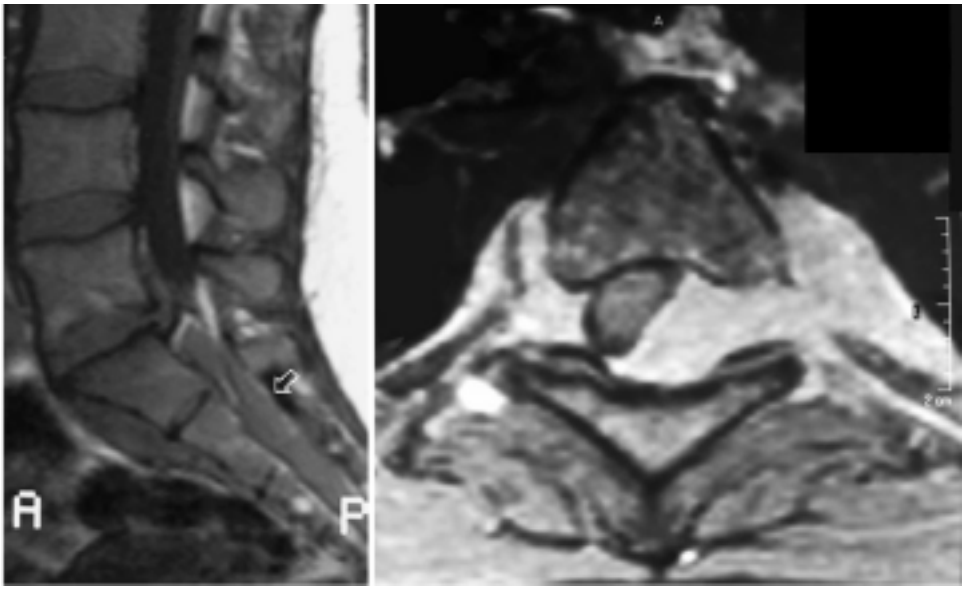


FIG. 2. *Left:* Sagittal $T_1$-weighted MR image revealing an intraspinal, intradural, isodense mass between S-1 and S-4 *(arrow)*. *Right:* Axial fat-saturation Gd-enhanced $T_1$-weighted MR image demonstrating a homogeneously enhancing intraspinal, intradural, extramedullary lesion at T3–5 with significant compression of the spinal cord from the left dorsal aspect of the lesion.

However, CNS manifestations of myeloid sarcoma are rare.[3,19] Bone involvement is most frequently seen subperiosteally and is commonly localized in the vertebrae, sternum, orbits, and cranium.[14] Intracranial myeloid sarcomas usually present as extraaxial masses and are believed to emerge from the bone marrow of the skull. These lesions may traverse the haversian canals and reach the subperiostium and dura mater as well as the perivenous adventitial tissue, and enter the subarachnoid space. Rupture of the pia mater–glial membrane results in invasion of the brain parenchyma,[2,3,19] as was observed in our patient. To our knowledge, the only other case of a patient with known AML and multiple lesions was reported in a 5-year-old child with intracranial, epidural, and two paraspinal myeloid sarcomas.[22]

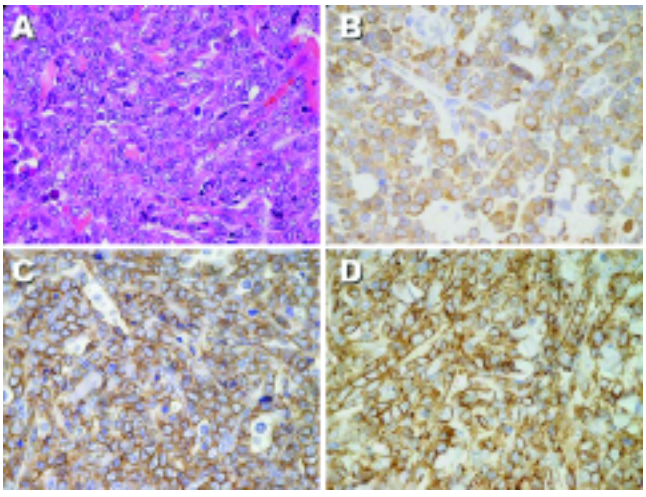


FIG. 3. Photomicrographs showing portions of tumor stained with H & E (A), myeloperoxidase (B), CD43 (C), and CD34 (D). Original magnification × 600.

In contrast to the lesion's intradural involvement of the spine in our patient, spinal myeloid sarcomas are usually located extradurally, and may in some cases cause signs and symptoms of spinal cord compression.[9] Although all spinal levels may be affected by myeloid sarcoma, the thoracic spine (73%) is most commonly involved, followed by the lumbar (34%), sacral (23%), and cervical (5%) spine. Multiple spinal lesions have been diagnosed in only 18% of patients.[17]

At present, a diagnosis relies not only on conventional histological staining, but also on immunohistochemical techniques. It has been shown that immunohistochemical staining for CD43, lysozyme, and myeloperoxidase was most sensitive for detecting myeloid sarcomas and more than 90% of such tumors stained positive.[21] In addition, positive staining for CD34 and CD68 and negative reactivity to the lymphocyte antigens CD3, CD20, and CD79a is characteristic of this type of tumor.[1,16,24] The Leder stain, a histochemical method for detecting the presence of naphthol-AS-D chloroacetate esterase, can be useful but yields positive results in only 75 to 77.7% of tumors, primarily in well-differentiated myeloid sarcomas.[18,21]

Surgical biopsy is essential for the management of myeloid sarcoma. In our patient, a biopsy specimen was obtained from the extracted extracranial parietal lesion, and a decompressive laminectomy (essential in patients with acute spinal cord compression) was not necessary.[17] Immediately after the diagnosis had been established, the patient was started on an aggressive, multimodal therapy. The treatment regimen included chemotherapy with cyclophosphamide, whole-body radiotherapy, and allogeneic bone marrow transplantation. As early as 3 months later, the size of the EC–IC lesion was markedly reduced, and all other lesions had disappeared. The authors of several studies have

concluded that systemic administration of intensive chemotherapy immediately after the initial diagnosis—the same treatment recommended for patients with AML—appears to be the most effective treatment strategy in patients with myeloid sarcomas.[10,25,27] Furthermore, Imrie, et al.,[12] have demonstrated that in the treatment of isolated myeloid sarcoma, antileukemic chemotherapy at the time of diagnosis significantly reduced the likelihood of AML from 71 to 41%. The median survival time also significantly increased in comparison with the group that received no therapy for leukemia. A multivariate analysis revealed that neither local radiotherapy nor surgical removal influenced survival.[12] Although most myeloid sarcomas respond well to local radiotherapy alone, the transition to acute leukemia cannot be influenced by this therapy.[5,27] Allogeneic or autologous bone marrow transplantation after induction therapy has been reported to reduce the risk of a subsequent occurrence of systemic disease,[4,5,12] which was confirmed by our findings.

## Conclusions

Although myeloid sarcomas of the CNS are rare, this lesion type should be included in the differential diagnosis in cases of multiple lesions even without evidence of hematological disease. Early diagnosis is essential so that an aggressive multimodal therapy can be started in a timely fashion. The latter reduces the risk of systemic disease and may lead to several years of remission or even total cure.

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