CASE REPORT

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Isolated meningeal chloroma (granulocytic sarcoma) –
a case report and review of the literature

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Abstract Isolated chloromas (granulocytic sarcomas) are rare tumors, most of them progressing to acute myeloblastic leukemia within months. There are still no conclusive treatment strategies for this entity; however, early antileukemic chemotherapy seems to lower the probability of developing systemic disease and prolong survival. We report on a patient with isolated meningeal chloroma, primarily misdiagnosed as a high-grade Non-Hodgkin’s lymphoma. Two cycles of antileukemic induction chemotherapy were administered, followed by local irradiation and intensified consolidation therapy with autologous stem cell transplantation. After 20 months, he is still in complete remission.

Key words Chloroma · Acute myeloblastic leukemia · Chemotherapy · Autologous stem cell transplantation

Introduction

Extramedullary tumors consisting of myeloid precursor cells are referred to as granulocytic sarcomas or chloromas. The latter term has been derived from the Greek word chloros (green) describing the lesion’s typical greenish appearance. The color is due to high expression of myeloperoxidase and is not always detectable because it rapidly fades after exposure to oxygen [37, 38].

Chloromas are rare tumors, presenting usually as a complication during the course of hematologic neoplasias, such as acute myeloblastic leukemia as well as myeloproliferative and myelodysplastic syndromes [5, 27, 32]. Factors such as certain chromosome abnormalities [t (8:21) and inv (16)], morphologic subtype of the underlying leukemia (FAB-type M2, M4, M5), and expression of surface markers CD 56, 2, 4, 7 are associated with a higher incidence of extramedullary myeloid tumors [4]. Chloromas may be the first sign of relapse after bone marrow transplantation [3, 14, 34, 40, 42, 43] or may precede systemic disease by up to 2 years [15, 20, 22, 28, 30]. Most but not all [4, 23] of the localized cases finally proceed to overt leukemia.

Chloromas are more common in younger patients [39] and have been described in almost every location. They are found in bone and periosteum, skin and soft tissue, lymph nodes, central nervous system, and viscera [27]. Symptoms are related to the location of the lesion, ranging from indolent or painful swellings [12, 28], neurologic compression signs [1, 10, 29, 37], obstructive jaundice [21, 34], hydronephrosis [19] or ileus [7], and gastrointestinal bleeding [36] to right ventricular failure due to cardiac muscle infiltration [9]. A retrospective analysis of 90 patients with isolated chloromas suggests an altered predilection pattern in these cases with more visceral manifestations and very rare involvement of the central nervous system [18].

Considering the high probability of patients with isolated chloromas to eventually develop systemic disease, some authors recommend early antileukemic chemotherapy [9, 18, 25]. However, there are still very few data about the kind of induction therapy to be applied and how much consolidation and maintenance treatment there should be.

Here, we report on a patient with isolated meningeal chloroma, who after two courses of induction
chemotherapy and local irradiation underwent intensified consolidation with autologous stem cell transplantation and is still in complete remission after 20 months.

Case report

A 35-year-old male patient without precedent medical history presented in February 1998 with progressive visual loss in the left eye and diplopia. No headache, dizziness, weight loss, or night sweats were reported. Physical, neurologic, and ophthalmologic examination showed no pathologic results, except paresis of the left nervus abducens and a central scotoma on the same side. All laboratory findings were within the normal range, especially serum-lactate dehydrogenase (LDH), hemoglobin, erythrocytes, thrombocytes, leukocytes, and peripheral blood smear. Magnetic resonance imaging (MRI) of the brain and orbit revealed a well-defined mass in the region of the left sphenoidal wing, entering the foramen opticum and leading to compression of the orbital nerve as well as deviation of the carotid interna. The tumor measured $3 \times 3 \times 4$ cm, was almost isointense to gray matter on T1- and T2-weighted images, and showed marked homogeneous enhancement following contrast administration.

Suspecting a meningeoma, an osteoplastic craniotomy was performed with partial resection (R2) of the tumor and decompression of the nervi opticus and oculomotorius, which were completely encased by tumor tissue. Upon histologic examination, a diffuse infiltration of the dura mater by cells with centroblastic appearance was seen expressing neither epithelial, mesenchymal, nor B-cell markers. Forty percent of the cells were positive for the proliferation marker Ki-67. A diagnosis of not further classifiable high-grade non-Hodgkin’s lymphoma was made.

To complete tumor staging, the patient was referred to the Department of Hematology/Oncology. Bone marrow cytology and histology, liquor cytology, and computed tomography of the neck, thorax and abdomen revealed no abnormality. MRI of the vertebral column showed no spinal or osseous involvement. In the course of these examinations, the tumor histology was reevaluated by the Institute of Hematopathology (German Lymphoma Node Registry), University of Kiel, Germany. Again, diffuse infiltration of the dura mater by undifferentiated centroblast-like cells without cytoplasmic granulation was described. The blasts neither expressed the B-cell antigens CD20 and 70a nor were they positive for the T-cell antigen CD3. The monocytic antigen CD68 was not detectable. Negative results were also achieved with the marker O 13, which is directed against the Ewing’s sarcoma-associated fusion protein encoded by the translocation t(11;22). Staining for neutrophilic elastase with the antibody Ki-My2 as well as for CD45 was strongly positive. Chlo- roacetate esterase staining showed positivity in approximately 15% of blasts.

In consequence of these findings, the tumor was reclassified as a granulocytic sarcoma (chloroma, Fig. 1, Fig. 2, Fig. 3) and the patient was treated with antileukemic induction chemotherapy. Two courses according to the HAM protocol [cytostine arabinoside (Ara-C) 6 g/m², days 1–3 and mitoxantrone 20 mg/m², days 3–5] were administered. Peripheral blood stem cells were harvested after the first course. MRI control scans of the brain at the end of induction showed residual enhancement in the former tumor region ($2 \times 0.3$ cm), which was subsequently irradiated with a total dose of 30 Gy. High-dose chemotherapy (busulfan 4 mg/kg, days 1–4 and cyclophosphamide 60 mg/kg, days 5–6) and autologous stem cell re-transfusion followed irradiation. Except for several episodes of fever of unknown origin that readily responded to standard antibiotics, no major complications occurred during the whole treatment phase. The patient regained full visus and ocular motility during the first cycle of

Fig. 1 Dense myeloblastic infiltrate with several mitoses and apoptoses. Hematoxylin and eosin staining, × 200

Fig. 2 Immunostaining of the same myeloblastic infiltrate shown in Fig. 1 with the myeloid antibody Ki-My2 directed against neutrophilic elastase. Strong cytoplasmic positivity in a considerable part of myeloid precursors and blasts is shown. Alkaline phosphatase-antialkaline phosphatase staining, × 100

Fig. 3 Chloroacetate esterase staining of the myeloblastic infiltrate, demonstrating strong cytoplasmic positivity in around 15% of the cells