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CASE REPORT

Spinal epidural granulocytic sarcoma in non-leukemic patient

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Abstract A previously healthy 24-year-old male presented with a 3-month history of progressive backache and weakness in both legs. Magnetic resonance imaging of the spine showed a large soft tissue mass infiltrating paraspinal musculature of lumbosacral area, sacral laminas, last lumbar and all sacral vertebra, protruding into the spinal canal, and with propagation into pelvis. Baseline laboratory data were normal. Decompressive laminectomy and tumor removal were performed resulting in neurological improvement. Histological examination identified granulocytic sarcoma (GS). Bone marrow biopsy showed normal findings. The patient underwent adjuvant chemotherapy and radiotherapy, resulting in the elimination of residual lesion, followed by autologous transplant. Immediate diagnosis and adequate systematic treatment are essential to achieve optimal results in patients with isolated GS. The patient is alive and free of the disease 14 months from the diagnosis.

Keywords Granulocytic sarcoma · Leukemia · Treatment · Spine · Immunohistochemistry

1 Introduction

Granulocytic sarcoma (GS), also termed myeloid sarcoma or chloroma, is a rare malignant solid tumor resulting from the extramedullary proliferation of myeloblasts or immature myeloid cells [1, 2]. GS most frequently occurs in patients with acute myeloid leukemia (AML), myeloproliferative neoplasms or myelodysplasia. GS rarely presents in the absence of systemic myeloid disease [3, 4]. Moreover, 66–88% of patients with an isolated GS will develop AML at a mean of 9–11 months after diagnosis [5]. GS may involve any organ system, from more common involvement of the skin, bone, soft tissue of the head and neck (frequently the orbits) and lymph node, to rare cases involving heart or small intestines [2, 6–8]. The involvement of the central nervous system (CNS) is rare, and spinal cord compression by GS is even rarer [1, 2]. Here we present a case of GS with lumbosacral location, with spinal cord compression and propagation into pelvis, in a patient without the evidence of systemic myeloid disease.

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2 Case report

A previously healthy 24-year-old male presented with a 3-month history of progressive backache and weakness in both legs. Magnetic resonance imaging (MRI) of the spine showed a large soft tissue mass infiltrating paraspinal musculature of lumbosacral area, sacral laminas, last lumbar and all sacral vertebra, protruding into the spinal canal, and with propagation into pelvis (Fig. 1). The patient was immediately taken to a surgery and a large part of the tumor was removed with the resolution of patient's neurological symptoms. Postoperative computed tomography (CT; not shown) scan showed residual disease and further therapy was planned. Pathological examination of the tumor tissue showed positivity for myeloid markers: myeloperoxidase, CD34, CD117, and HLA-DR, but negative for CD3, CD5, CD79 alfa, CD20,

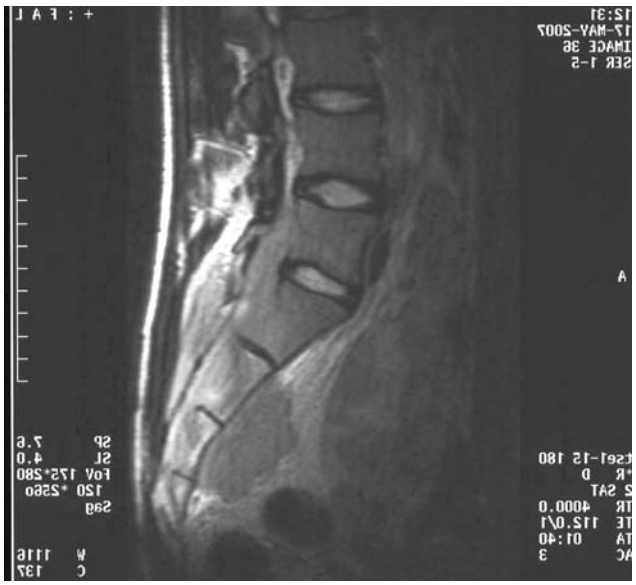

Fig. 1 Magnetic resonance imaging of the patient's spine at the time of presentation. T2 weighted magnetic resonance image showing large soft tissue mass infiltrating spinal canal at the L5–S3 levels with invasion into the pelvis

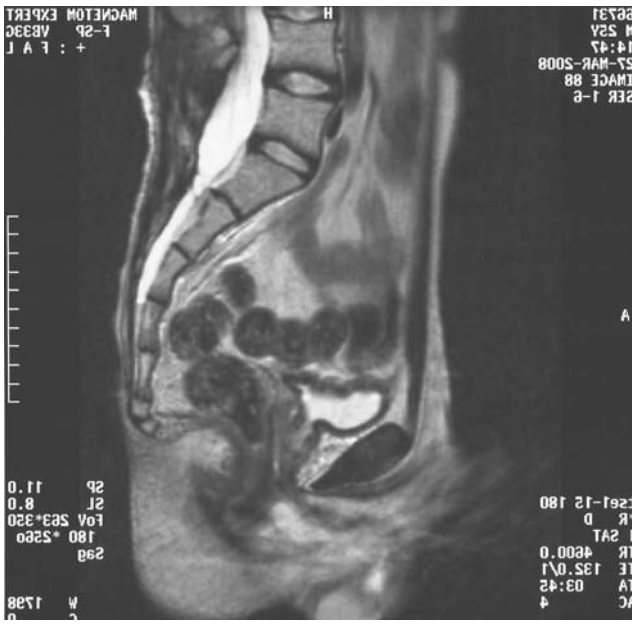

Fig. 2 Magnetic resonance imaging of the patient's spine after surgery and adjuvant chemotherapy and radiotherapy. T2 weighted magnetic resonance image after the systemic chemotherapy and radiotherapy showed normal findings

CD10, bcl2, bcl6, CD38, CD15, CD30, MUM1, CD38, CD138, CD45RO. Final histological diagnosis was GS. Patient's blood cell count was normal: hemoglobin 126 g/l, white blood cell count 4.8×10^9 per l, and platelet count 182×10^9 per l, with 50% neutrophils, 5% eosinophils, 1% basophils, 32% lymphocytes, and 12% monocytes. Complete biochemical panel was normal. CT scan of thorax and abdomen was normal. A bone marrow biopsy and aspirate, with flow cytometry testing, showed normal findings. Cytogenetic study of the bone marrow cells revealed a normal karyotype. A lumbal puncture, done after the surgery, revealed acellular fluid with normal protein and glucose values.

One month after surgery systemic induction chemotherapy was started, consisting of daunorubicin given as 45 mg/m^2 IV over one hour daily on days 1–3 and continuous infusion of cytarabine 200 mg m^{-2} day^{-1} on days 1–7. Two months after the start of chemotherapy, patient received radiotherapy in total dose of 40 Gy to the lumbosacrale spine, over 20 consecutive days. Three weeks after the conclusion of radiotherapy the patient received another cycle of the same chemotherapy. One month later MRI of the spine showed normal findings (Fig. 2). Seven months after surgery the patient received mitoxantrone IV 10 mg/m^2 daily days 1–5 plus cytarabine 1,500 mg/m^2 IV days 1–3 with the harvesting of the stem cells for autologous transplantation. Six weeks later the patient underwent autologous stem cell transplant, conditioned with oral Busulfan (4 mg/kg daily for 4 days) and Melphalan (140 mg/m^2 IV once). Patient recovered without complications and is free of the disease 14 months from the diagnosis.

3 Discussion

Granulocytic sarcoma occurs in four different clinical settings: (a) as a localized tissue manifestation in patients who already have AML; (b) as a sign of impending blast crisis in chronic myelogenous leukemia or leukemic transformation in patients with myelodysplastic syndrome; (c) as a forerunner of AML in non-leukemic patients; and (d) as an isolated neoplasm without progression to AML (least common) [9]. GS is rarely considered in the differential diagnosis of a soft tissue mass. In a review of 154 patients with GS, 47% were initially misdiagnosed. In order to prevent misdiagnosis circumstantial histological examination is obligatory. Basic histopathologic analysis with proper histochemical stains provide sufficient information for diagnosis [10].

The prognosis of patients with GS depends on the initial context in which it occurs. Most cases of GS occurring in non-leukemic patients progress to AML within months. Optimal therapy for GS has not been fully defined, in part due to a variety of different clinical presentations. Chemotherapy (both systemic and intrathecal), bone marrow transplant (BMT), radiation therapy, surgical resection, or a combination of these approaches is employed on a case by case basis. For example, in here presented case surgical

decompression of spinal cord was undertaken at presentation due to progressive neurological deficit in the patient, even before the diagnosis of GS had been made. In most cases surgical resection of GS is not needed, even in unusual cases like the GS of the heart [6].

Several reports have summarized the outcome of relatively large cohorts of patients with GS. Yamauchi and Yasuda investigated association between the therapeutic regimens and disease-free survival (DFS) in group of 74 patients with GS. DFS was significantly longer in patients treated with systemic chemotherapy (median 12 months) than in those treated with surgery (3 months) or local irradiation (6 months) [11]. Tsimberidou reported data about incidence, therapy and outcome of GS in 1,520 patients with AML, and 402 patients with high-risk MDS. GS occurred in 20 patients, of which 80% received AML-type chemotherapy. Thirteen patients (65%) achieved complete remission (CR). Median overall survival (OS) was 20 months while median DFS was 12 months [12].

Pileri with coworkers [13] reported outcome on 67 patients with GS, of which 25 (27%) presented as non-leukemic GS. Among them 47 received chemotherapy (70.1%), six allogeneic BMT (allo-BMT) (9.0%), and four autologous BMT (auto-BMT) (6.0%). At a median follow-up of 150 months, only seven are still alive (10.5%) and are in CR; six of them underwent allo-BMT. Overall, patients treated with auto- or allo-BMT had longer survival then those who received conventional therapy (OS at 48 months: 76 vs. 0%). Chevallier et al. [5] published retrospective multicenter study assessing the outcome of 51 patients with GS who underwent allo-BMT; six had isolated GS. Forty patients were in CR (from induction chemotherapy) at the time of allo-BMT. With a median follow-up of 33 months, OS and DFS were 47 and 36% at 5 years, respectively. Twenty patients (39%) relapsed at a median of 204 days after allo-BMT, with relapse being the major cause of death. In a Cox multivariate analysis, age $\geq$15 years and remission status at time of allo-BMT (CR vs. other) were associated with improved OS. Inoue et al. [14] recapitulated 26 aleukemic patients with spinal GS. Main affected site was thoracic region and major clinical finding were pain, paresis or weakness, incontinence and sensory impairment. Treatment strategies differed; most patients had surgical decompression with adjuvant systemic chemotherapy and half never showed bone marrow involvement. In patients that developed systemic disease outcome was generally poor (up to 20 months survival).

In conclusion, GS should be treated as AML even in the absence of clinically detectable leukemia. The remission rate after intensive chemotherapy in patients with GS with or without the evidence for systemic diseases (i.e. AML) does not differ [2, 9]. It seems that the performance of all-BMT (or at least auto-BMT) at the time of CR may help improve long-term outcome of these patients. Surgery is generally reserved for patients presenting with acute spinal cord compression or neurological symptoms, or when it is necessary to obtain an adequate tissue biopsy for diagnostic analysis.

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