Peritoneal Myeloid Sarcoma in a Patient Treated for a Testicular Seminoma

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Patient: Male, 46
Final Diagnosis: Myeloid sarcoma
Symptoms: —
Medication: —
Clinical Procedure: Laparoscopy • CT scan • Pet-scan
Specialty: Oncology

Objective: Rare disease
Background: Myeloid sarcoma is a rare extramedullary soft tissue neoplasm composed of myeloblastic cells, usually associated to hematologic tumor disorders and a poor prognosis. Its diagnosis is very difficult as radiological images are not specific. Histology and immunohistochemistry are necessary for an accurate diagnosis.

Case Report: We report the case of 46-year-old, Caucasian, non-smoker male, treated in 2014 by orchiectomy and systemic chemotherapy for a stage IIB testicular seminoma. Considering the rapid increase of lactate dehydrogenase (LDH) levels without any evident medical reason, a computed tomography/positron emission tomography (CT/PET) scan was performed and revealing a diffuse, nodular, peritoneal tumor infiltration associated with multiple mesenteric and mediastinal adenopathies. Laparoscopy confirmed a diffuse tumor infiltration of the peritoneum. Histology and immunohistochemistry were consistent with the diagnosis of a myeloid monoblastic sarcoma. Cytology of bone marrow documented an monocytic acute myeloid leukemia. The patient started a systemic induction chemotherapy with high dose cytarabine and idarubicin that was complicated by an infectious pneumonia and colitis, and a grade IV thrombocytopenia leading to a brain subdural hemorrhage and quickly to patient’s death.

Conclusions: We describe a rare, peritoneal, myeloid sarcoma in a young patient who had been treated by systemic chemotherapy for testicular seminoma 4 years earlier. The patient was clinically asymptomatic and presented only elevated LDH levels without any evident clinical reason. Considering the persistence of this biochemical abnormality, more investigations were performed leading to a diagnosis of peritoneal myeloid sarcoma associated with monocytic acute myeloid leukemia, probably secondary to the past chemotherapy.

MeSH Keywords: Leukemia, Myeloid, Acute • Sarcoma, Myeloid • Testicular Neoplasms

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Background

Myeloid sarcoma (MS) is a rare extramedullary soft tissue neoplasm composed of myeloblastic cells with poor prognosis [1–3]. MS can be unifocal or multifocal and it is most commonly associated with acute myeloid leukemia (AML) or chronic myeloid leukemia (CML), or other myelodysplastic syndromes. Several cases of isolated “de novo” MS in patients without leukemia have also been described, which had a rapid transformation to AML [1–3].

In the absence of hematological history, the diagnosis of MS is very difficult as radiological images are not specific [4–14]. Histology and immunohistochemistry are necessary for an accurate diagnosis [5–8]. Systemic chemotherapy is the standard treatment for MS, with radiotherapy and surgery considered only in symptomatic patients [15–22].

We report a rare, peritoneal MS in a young patient treated by systemic chemotherapy for testicular seminoma 4 years earlier. The patient was clinically asymptomatic. All the biological tests were within normal range except for lactate dehydrogenase (LDH) levels that were elevated. Considering the persistence of this biochemical abnormality without any evident clinical manifestation, more investigations were performed leading to a diagnosis of peritoneal MS associated with monocytic AML, probably secondary to past chemotherapy.

Case Report

A 46-year-old, Caucasian, non-smoker male was regularly followed for testicular seminoma, stage pT1, cN2, M0 (stage IIB). In April 2014, he underwent percutaneous biopsies of the skin and liver that led to a diagnosis of AML with FLT3 duplication and NPM1 mutation (M5 subtype according to French-American-British, FAB classification). The patient had presented with a brain arterio-venous fistula, which was treated by embolization in 2016. He had no relevant comorbidities. The patient’s history was uneventful, and he was asymptomatic. Biochemical tests and tumor markers were in the normal range except for LDH levels that were elevated at 1086 UI/mL (NV <480 UI/mL). Clinical examination was negative.

Considering the rapid increase in LDH levels to 1856 UI/mL in only 7 days and the absence of any evident medical reason justifying this biochemical abnormality, a whole-body contrast-enhanced computed tomography (CT) scan was performed revealing multiple peritoneal tumor lesions with mesenteric and mediastinal enlarged lymph nodes (Figure 1A). The positron emission tomography (PET) scan confirmed the presence of a diffuse, nodular, peritoneal tumor infiltration associated with multiple mesenteric and mediastinal adenopathies (Figure 1B). As the percutaneous cytology was not diagnostic, the patient was referred for a coelioscopic laparoscopy, which documented a diffuse tumor infiltration of the peritoneum (Figure 1C). Histology confirmed the presence of poorly differentiated tumor cells with scant cytoplasm and prominent mitotic figures (Figure 1D). Immunohistochemical staining found tumor cells positive for CD68, CD56, CD45, CD4, NPM (nuclear), and LCA (Figure 1E) and negative for AE1/AE3, EMA, calretinin, CD117, synaptophysin, chromogranin, myeloperoxidase (MPO), CD 123, and PS100, according with the diagnosis of myeloid, monocytic sarcoma. Cytology of bone marrow documented a diffuse tumor infiltration with 56% of blasts suggesting a monocytic AML without FLT3 gene duplication and NPM1 mutation (MS subtype according to French-American-British, FAB classification).

A systemic, induction chemotherapy was started with high dose cytarabine and idarubicin. This treatment was complicated by an infectious pneumonia and colitis, and a grade IV thrombocytopenia leading to a brain subdural hemorrhage and to patient’s death.

Discussion

First described by Rappaport [1], MS, also referred to as granulocytic sarcoma (GC), chloroma, myelosarcoma, and extramedullary myeloid cell tumor, is a rare extramedullary soft tissue neoplasm composed of myeloblastic cells and it has poor prognosis [1–3]. MS can occur in any extramedullary location with a higher prevalence in bone, periosteum, soft tissues, lymph nodes, and skin [2]. It can be unifocal or multifocal and it is most commonly associated with AML, CML or other myelodysplastic syndromes, an isolated “de novo” MS in patients without a leukemia is extremely rare [1–3]. In this latter case, MS predicts a short transformation to AML, 10–12 months on average, after its diagnosis [1–3].

MS is reported in 2% to 14% of cases of AML, most commonly in patients with specific cytogenetic abnormalities, e.g., t (8; 21) or inv (16) or FAB class M2 [3–5].

According to morphological classifications, MS is usually subclassified into granulocytic, monoclastic, or myelomonocytic and as immature, mature or blast type [5].

Molecular factors triggering the appearance of MS are poorly understood. The human myeloid cells, called HSM1, which can adhere to the skin stroma, are incriminated in the formation of cutaneous MS. A recent study showed that 40% of AML-treated patients overexpressing cell NCAM (natural cell adhesion molecule or CD56), developed MS [6]. Recently, a significant correlation was found between extramedullary infiltration and co-expression of chemokine MCP-1 (monocyte chemoattractant...
protein-1) and its receptor, CCR2 (chemokine receptor type 2) by AML type 4 and 5 blasts, explaining the occurrence of MS in monocytic AML [6].

Histology is necessary for an accurate diagnosis, but it should always be confirmed by immunohistochemistry, flow cytometry, fluorescence in situ hybridization, and molecular analysis [5–9].

Because MS is usually associated with a synchronous hematological malignancy, bone marrow evaluation by aspiration and/or biopsy should be performed [6–9].

MS presents with several nonspecific radiological features. Enhanced homogenous soft tissue masses at multiple sites strongly suggest the presence of MS, especially in patients with a hematological disorder [10–12]. Imaging techniques, such as magnetic resonance imaging (MRI) or CT scan, are necessary for tumor staging and a differential diagnosis with undifferentiated cancers or tumor complications, including abscesses and hematomas that are frequently observed in hematological cancer patients [10–12]. The FDG-PET scan is an optional imaging technique to study tumor localization and size, to detect multiple lesions, to planning local treatments such as radiotherapy or surgery, and finally to monitoring the treatment response [13,14].

Since primary MS is a rare entity, there are no prospective randomized studies that could validate the optimal treatment. The treatment depends on MS localization and history (initial diagnosis vs. relapse), and the patient’s performance status, age, and comorbidities. Treatments mainly include surgical resection, local radiotherapy, and systemic chemotherapy [15–22]. Only systemic chemotherapy, especially AML-type induction chemotherapy, seems to delay transformation of isolated MS to AML and improve prognosis of all patients. Early chemotherapy is associated with a better event-free and overall survival as compared to patients with an AML [15–22].

Exclusive radiotherapy is not an optimal therapy and it should be associated with systemic chemotherapy, particularly in...
symptomatic patients, in case of CNS involvement, or as a consolidation therapy [15,16].

The same considerations can be made for surgery which should be considered before chemotherapy only in patients with acute and life-threatening symptoms, such as intestinal occlusion or perforation [15,16].

There are no prospective studies about hematopoietic stem cell transplantation (HSCT) in isolated MS patients. The data about HSCT comes only from retrospective small groups, mostly MS concomitant with AML. Several data reports support HSCT to be considered for patients with isolated MS especially for relapsed patients and patients who are in their first remission [15,16].

Conclusions

In our case, the patient presented a rare, peritoneal, MS associated with synchronous monomyelocytic AML, probably secondary to past chemotherapy realized 4 years before for treatment of testicular seminoma. MS is rare, and it can be clinically and radiologically misdiagnosed, particularly in the absence of a hematological history [1–15]. It should be confirmed by histology and immunohistochemistry [6–9]. Systemic chemotherapy represents the standard treatment [15,16]. Loco-regional approaches, such as surgery and radiotherapy, should be considered only in selected patients with life-threatening symptoms, such as intestinal occlusion or perforation [15,16].

The particularity of this case relies on the rarity of MS and on the atypical clinical history, characterized by unexplained, elevated LDH levels in the absence of any clinical symptoms.

Considering the persistence of this biochemical abnormality, more investigations were performed in this case, leading to a diagnosis of a peritoneal MS associated with synchronous, secondary monocytic AML.

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Conflict of interests

None.

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