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Pelvic myeloid sarcoma: a multidisciplinary approach

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Summary

Myeloid sarcoma (MS) is a rare tumor mass derived from the extramedullary proliferation of blasts of one or more of myeloid lineages. It usually occurs at an anatomical site other than the bone marrow (BM). Among the anatomical site which may be involved, female genital tract is a rare localization. When MS follows a previous history of myeloid pathology it is usually associated to a poor prognosis. To date this disease was managed with exploratory laparotomy or with surgical debulking. The authors report a case of laparoscopic diagnosis of a pelvic myeloid sarcoma in a patient previously affected by acute myeloid leukemia, evidencing the importance of minimally invasive diagnosis and subsequent multidisciplinary management.

Key words: Myeloid sarcoma; Laparoscopy; Multidisciplinary approach; Pelvic mass; Extramedullary sarcoma.

Introduction

Myeloid sarcoma (MS) is a rare tumor mass derived from the extramedullary proliferation of blasts of one or more of myeloid lineages that occurs at an anatomical site other than the bone marrow (BM). It is a rare disease which usually occurs in patients with a previous history of acute myeloid leukemia (AML) or in association with an antecedent myeloproliferative disorder or myelodysplastic syndrome. However, it may appear as an isolated extramedullary leukemic tumor [1]. The gynecological tract is rarely affected and in these cases it is usually asymptomatic for a long time [1, 2], while sometimes an ureteral obstruction is reported as presenting symptom associated to cervical involvement [3]. Some authors report MS in 5% to 12% of patients previously submitted to allogenic hematopoietic stem cell transplantation (alloSCT) [4]. These cases usually show isolated sites of relapse or in combination with bone marrow involvement. The reported prognosis is poor. Indeed, post-alloSCT extramedullary relapse has a potential importance as a determinant of outcomes. However the incidence, risk factors, and treatment options are still not well understood [5]. Moreover it seems that patients with MS relapse are more likely to have had acute or chronic graft-versus-host disease (GVHD) [4]. MS should be considered in the differential diagnosis of pelvic mass, especially if there is a coexisting or previous history of hematological disorder. Diagnosis of abdominal MS frequently follows an exploratory laparotomy. It allows careful abdomino-pelvic evaluation, biopsy execution, and possible surgical disease removal. Here, the authors analyze a case of a pelvic myeloid sarcoma as a relapse of AML diagnosed by laparoscopy. The potential advantages of this approach include not only an improved magnification associated to a higher confidence in the diagnosis process, but also the avoidance of an inappropriate laparotomy incision in cases with an inoperable malignant tumor. Moreover laparoscopy is associated with less surgical trauma and postoperative pain, leading to a shorter hospitalization [5].

Case Report

A 59-years-old post-menopausal woman was diagnosed with acute myeloid leukaemia secondary to chronic myeloproliferative neoplasm with normal karyotype. Induction chemotherapy regimen consisted of cytarabine (360 mg/die) by continuous infusion for seven days and idarubicin (18 mg/die) on days 1-3 ("7+3"). At the beginning chemotherapy induced cytological remission. In the following two months the patient underwent a consolidation chemotherapy (cytarabine and idarubicin 7+3 and then 7+1) achieving complete remission (CR). A bone marrow biopsy performed one month after CR, showed a significant number of blasts that, from flow cytometry, were defined as presenting an immunophenotype compatible with a myeloid origin. Considering the lack of response to medical treatment and in presence of an HLA-matched sibling donor, patient was submitted to allogenic hematopoietic stem cell transplantation. The post-transplant period was complicated with GVHD.

One year after alloSCT the patient complained of abdominal and lumbar pain associated with urinary dysfunction. CT of the

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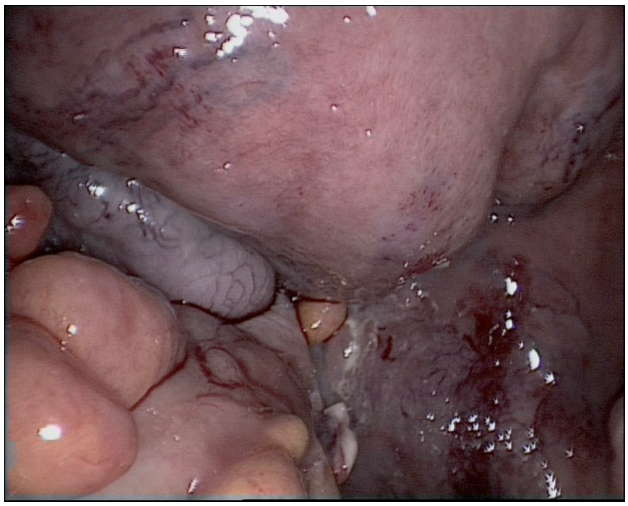

Figure 1. — Diagnostic laparoscopic findings. Of note is that both uterus and ovaries' anatomy are not identified.

abdomen showed voluminous bilateral adnexal masses in close adhesion to the bladder. Moreover the abdominal multislice CT evidenced the presence of some enlarged pelvic and para-aortic lymph nodes associated to right hydronephrosis and hydroureter, and a suspect of ovarian malignancy was placed. A pelvic transvaginal and transabdominal ultrasound revealed two large and irregular pelvic masses localized posteriorly and laterally to the uterus, measuring respectively 90×66 mm (the right one) and 56×43 mm (the left one). These masses presented high vascularization at power Doppler investigation (color score 3 out of 4). The potential uterine or adnexal origin of the masses was not clear. The patient presented oliguria and laboratory studies revealed elevated serum creatinine (5.78 mg/dl) and elevated oncological markers (CA 19.9: 168 U/ml, CA 15-3: 39 U/ml, CA 125: 52 U/ml). Retrograde pyelogram showed bilateral ureteral obstruction, therefore a ureteral stenting was performed.

In consideration of the unknown origin and nature of the masses, the patient underwent diagnostic laparoscopy (Figure 1). Intraoperative identification of pelvic structures was difficult because of the severe adhesions causing a complete obliteration of the Douglas pouch. The ovaries and the tubes were not recognizable and the uterine sierosa was irregular. It was not possible to identify cleavage planes among the masses, uterus, and rectum. The omentum showed an irregular surface and an increased thickness. The other abdominal organs and the peritoneum were macroscopically regular. Biopsy specimens were taken from the pelvic masses, from the omentum and from the rectal sierosa. To conclude, a diagnostic hysteroscopy was performed, but no signs of endocavitary pathology were found. Pathologic assessment of the ovarian biopsy revealed diffuse infiltration by a monomorphic population of blasts with scant cytoplasm and round-oval nuclei with finely dispersed chromatin and minute but distinct nucleoli (Figure 2a). On immunohistochemistry neoplastic cells strongly expressed myeloperoxidase (Figure 2b) with a partial positivity for CD34 (Figure 2c); the macrophage-restricted marker

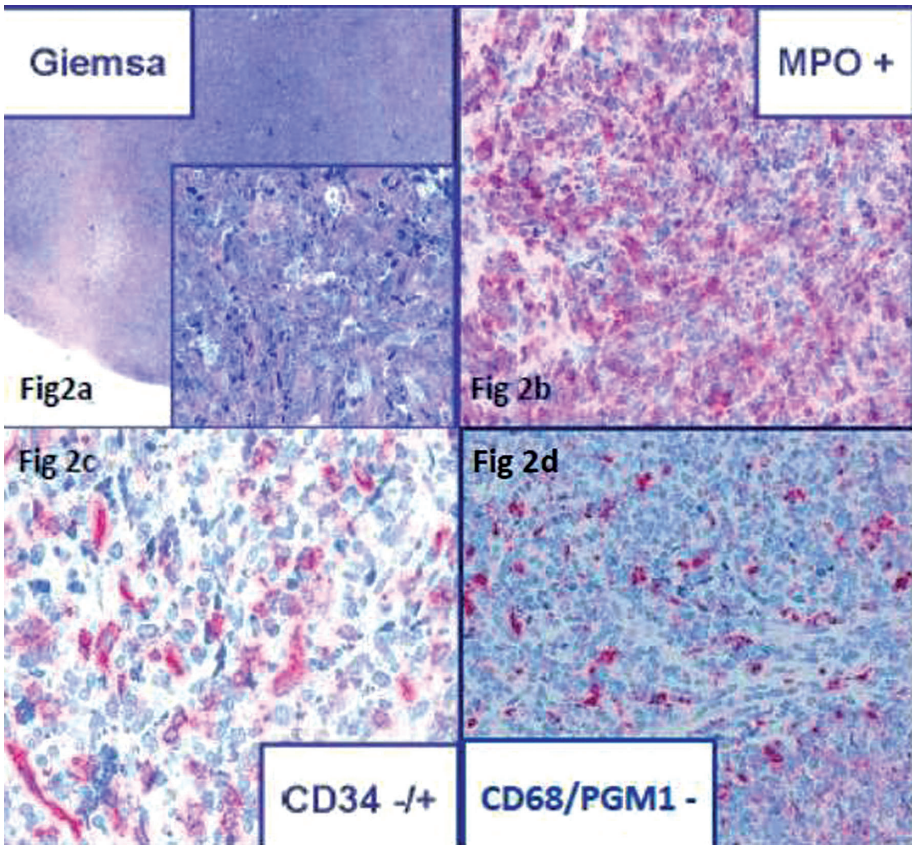

Figure 2. — Histological features of the ovarian biopsies: Figure 2a (GIEMSA ×2 magnification and ×40 magnification in the box) shows diffuse infiltration by blasts with scant cytoplasm and round-oval nuclei; Figure 2b) (×40 magnification) partial positivity for CD34; Figure 2c (×20 magnification) strong expression of myeloperoxidase; Figure 2d (×20 magnification) CD68/PGM1 negativity.

CD68/PGM1 was negative (Figure 2d), ruling out a monocytic differentiation; expression of nucleophosmin (NPM) was regularly restricted to the nucleus. The case was discussed in a multidisciplinary meeting involving oncologic gynecologists, haematologists, radiotherapists, oncologists, and anatomical pathologists specialized in gynecological histopathology. In consideration of the advanced stage of disease, the multiorgan involvement and the patient's severely compromised health condition, the patient was directly addressed to chemotherapy. After an initial reduction of the size of the masses, the patient developed bacterial and fungal infection and sepsis with progressive multiple organs failure. Death occurred one month later.

Discussion

Extramedullary relapse of AML following alloSCT is poorly understood and is usually associated with a poor prognosis [6]. Because recent improvements in supportive care and GVHD prophylaxis regimens have reduced treatment-related mortality, disease relapse has now emerged as the principle cause of treatment failure after alloSCT [7]. Frequently MS may involve multiple locations or infiltrates diffusely due to the delayed diagnosis [4]. In the present case patient presented with clinical and laboratory signs of renal failure. The preoperative ultrasound and radiologic examination were not able to establish which organ the mass originate from. Indeed, the discrimination between MS and other pelvic masses is not always accurate by using imaging [8]. The present authors performed laparoscopy evidencing a multiple sites involvement by MS: the ovaries, the intestinal sierosa, and the omentum. They may confirm that diagnostic laparoscopy is a safe technique allowing the exploration of the abdominopelvic cavity and the execution of multiple biopsies for histological, histochemical, and immunohistochemical stains [9]. Immunohistochemistry and immunophenotyping are crucial for the accurate diagnosis of MS [10]. Moreover a diagnostic laparoscopy offers the advantages of avoiding unnecessary open laparotomic exploration, permitting a shorter hospitalization. This minimally invasive procedure permits a prompt chemotherapy beginning when it is indicated. In the present Tertiary Care University Hospital, gynecologic oncologic cases are discussed during a weekly multidisciplinary meeting. This approach guarantees the proper management of each patient based on the current guidelines. In the present case, patient's age, advanced stage of disease, and the multiple organ involvement were considered exclusion criteria for surgical management. Even if there is no consensus on the treatment of MS, the current recommended treatment regimen is conventional chemotherapeutic protocols [10]. However, prognosis of these patients remains poor. A review considering 11 cases of myeloid sarcoma involving gynecologic tract showed a short time survival (1-17 months in case of involvement of at least two female genital organs) [1]. The present case reflects the evolution of multiple organs involvement, previously described in few cases in literature. The principle cause of death is usually represented by the development of sepsis and multiple organ failure.

Conclusion

In cases of pelvic mass, diagnostic laparoscopy is an adequate procedure to orientate the diagnosis. Moreover, the possibility to have a biopsy specimen is crucial to characterize the mass. Diagnostic imaging assessment may not be adequate to distinguish between myeloid sarcoma and others pelvic disease. Minimally invasive procedure associated with a shorter hospitalization make possible a prompt chemotherapy start, avoiding a more aggressive approach such as an exploratory laparotomy or surgical debulking.

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