Case presentation

Myeloid sarcoma presenting as a solitary skin nodule – case presentation

Sarcom mieloid cu prezentare inițială sub forma unui nodul cutanat solitar – prezentare de caz

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Abstract

Myeloid sarcoma is a rare neoplasm, that according to the WHO classification represents a tumor mass consisting of myeloid blasts with or without maturation that occurs at an anatomical site other than the bone marrow. It typically occurs in the later decades of life. It can involve practically any site of the body, however there are some anatomical sites that are more frequently involved: skin, lymph nodes, gastrointestinal tract, soft tissue, bones and testis. We describe the case of a 78-year-old male patient with unremarkable past medical history that presented with multiple skin lesion consisting of reddish, slightly elevated nodules. After biopsy and histological examination, a diagnosis of non-Hodgkin B-cell lymphoma was ensued. Specific treatment was applied that caused the skin lesions to reside and disappear. After a brief period (4 months) a solitary skin nodule with central ulceration developed on the left anterior chest wall. The patient otherwise was asymptomatic without evidence of any hematological disorder or disease involving the skin. The histological and immunohistochemical findings revealed the diagnosis of myeloid sarcoma, with later evolution to acute myeloid leukaemia (AML).

Keywords*: myeloid sarcoma, skin, acute myeloid leukemia*

Rezumat

Sarcomul mieloid este un neoplasm rar, care după OMS reprezintă o masă tumorală alcătuită din blaşti mieloizi, cu sau fără maturare, care poate să apară în orice localizare a corpului, cu excepția măduvei osoase. Tipic este caracteristic decadelor târzii de viață. Poate afecta astfel fiecare parte a corpului, dar totuşi există anumite localizări mai frecvente, precum: pielea, limfonodulii, tractul gastrointestinal, țesuturi moi, oase şi testicole. Prezentăm cazul unui bărbat în vârstă de 78 de ani fără antecedente patologice, care prezintă multiple leziuni cutanate formate din noduli uşor elevați, de culoare roşiatică. După biopsie, examenul histopatologic evidențiază un limfom non-Hodgkin cu celule B pentru care se inițiază tratament specific. Post-terapeutic leziunile cutanate dispar, pacientul devenind asimptomatic pentru o perioadă de 4 luni. Ulterior, pe fața anterioară a peretului toracic, apare un nodul solitar cutanat, ulcerat central, fără ca pacientul să prezinte alte semne de boală. Examenul histopatologic, completat cu determinări de imunohistochimie susțin diagnosticul de sarcom mieloid cu evoluție ulterioară spre leucemie acută mieloidă.

Cuvinte cheie: *sarcom mieloid, piele, leucemie mieloidă acută*

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Introduction

According to the WHO classification myeloid sarcoma represents a tumor mass consisting of myeloid blasts with or without maturation that occurs at an anatomical site other than the bone marrow. It is a tissue mass that effaces tissue architecture. It's cellular component is made up of blasts of various precursor cells, such as granulocytic, monocytic, erythroid, or megakaryocytic precursors (1). Since myeloid sarcoma represents the tissue mass form of different subtypes of acute myeloid leukemia (AML), the diagnosis is equivalent to a diagnosis of AML. It may occur de novo, may precede or coincide with AML, or may represent a blastic transformation of a preceding myelodysplastic syndrome or chronic myeloproliferative neoplasm. Myeloid sarcoma may be composed of the same cell types as AML. Various types of myeloid sarcoma are named in accordance with the type of cell that composes the sarcoma.

Myeloid sarcoma is a rare neoplasm that has a slight predilection for males (male:female ratio is 1,2-2:1). It typically occurs in the later decades of life (median age, 56 years; range, 1 month to 89 years). It can involve practically any site of the body, however there are some anatomical sites that are more frequently involved. These include the skin, lymph nodes, gastrointestinal tract, soft tissue, bones and testis (2-8). In some cases it can present at multiple anatomical sites. There have been reports of unusual localizations such as jaw bone, breast, uterine cervix, dura (9-13).

When assessing a skin tumor it is important to include into the differential diagnosis list rare tumors since a mistaken diagnosis may have drastic consequences for patient management. A case is presented of a rare tumor presenting in the skin.

Case presentation

We present the case of a 78-year-old male patient with unremarkable past medical history that presented (06.2010) with multiple skin lesion consisting of reddish, slightly elevated nodules. A biopsy was performed from one of the skin lesions and upon histological examination, a diagnosis of non-Hodgkin B-cell lymphoma was ensued. Specific treatment was applied (11 cycles of PCT, according to the CHOP scheme along with 8 applications of Mabthera) that caused the skin lesions to reside and disappear. After a brief period a solitary skin nodule with central ulceration developed on the left anterior chest wall. The patient otherwise was asymptomatic without evidence of any hematological disorder or disease involving the skin.

Pathology

Surgically a 55×28×20 mm tan mass was removed (12.2010), on cut surface with a 16 mm deep central ulceration (*Figure 1*). The histopathological findings show a dermal infiltrate of large polygonal cells with moderate amount of cytoplasm and large, irregular to folded nuclei with occasional large nucleoli (*Figure 2*). The neoplastic cells infiltrate subcutaneus fatty tissue and even muscle fibers. Upon immunohistochemical examination the neoplastic cell show marked positivity for LCA (leukocyte common antigen), MPO (myeloperoxidase) and CD68, focal positivity for CD56. They are negative for CD3, CD4, CD8, CD2, CD20, kappa-lambda light chains, CD38, CD30 and CDa1. Tumour cells do not express CD34, as this marker only highlights the endothelial cells in the specimen. Neoplastic cell are intensely positive for vimentin and have a proliferation rate (as showed by the Ki67 marker) between 60-70%. The complete panel of immunohistochemical stains and the results are presented in *Table 1* and *Figures 3-5*. The histological and immunohistochemical findings support the diagnosis of myeloid sarcoma (9.02.2011). WHO criteria and immunohistochemical findings sustained the myelomonocytic histotype. The reevaluation of initial skin biopsy was carried out. Using immunohistochemistry we could not demonstrate the expresson of myelomonocytic markers (MPO, CD68, CD34).

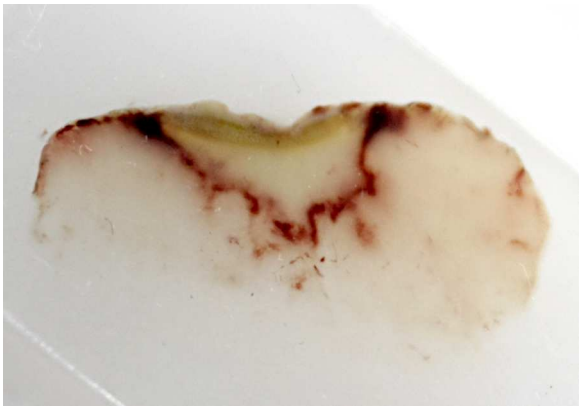

Figure 1. The gross appearance of the cut surface of the skin nodule

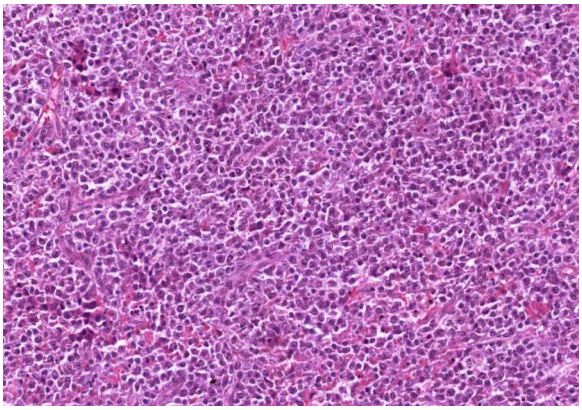

Figure 2. Histological appearance of the tumor (hematoxylin-eosin, ob. 40×)

Shortly after the histopathological diagnosis was made the patient continued treatment according to specific chemotherapy regimen. The patient regularly presented for periodical controls for treatment and evaluation. The last visit (06.2011) revealed the presence of multiple pink-bluish, non-itching non-tender skin nodules, distributed primarily on the upper and lower extremities. At this presentation the laboratory investigations showed pathological values for leukocytes 4200/ml, platellets 73000/ml, reactive C protein 45 mg/l (25.05.2011) and 93 mg/l (08.06.2011), other parameters within normal range. Urinary analysis showed normal parameters.

Table 1. Immunohistochemical findings of the skin nodule specimen

IHC stain	Tumor
MPO	positive
CD68	positive
LCA	positive
CD56	focally positive
vimentin	positive
CD20	negative
CDa1	negative
CD38	negative
CD30	negative
CD3	negative
CD4	negative
CD8	negative
kappa-lambda chains	negative
Ki67	60-70%

As laboratory and clinical data indicate, the patient developed severe secondary granulocytopenia, secondary anemia, secondary thrombocytemia. Based on hematological test results a diagnosis of acute myeloid leukaemia (AML) was ensued.

After specific and generic treatment was administered, along with antibiotics, the patient was released. Just prior submitting the article we were announced that the patient deceased at home (1 month after last medical visit).

Discussion

Myeloid sarcoma (or granulocytic sarcoma, chloroma, extramedullary myeloid tumor) is a rare solid neoplasm, composed of malignant myeloid derived cells that form an extramedullary tumor mass. Interestingly, the name 'chloroma' derives from the greenish color of this neoplasm, which also has been termed green cancer. The green pigment is primarily myeloperoxidase (verdoperoxidase). The tumor tissue fluoresces bright red under ultraviolet light.

The most common localizations are skin, lymph nodes, testis, intestine (2,14,15). The tumor may arise synchronously with a known myeloid leukemia, moreover it can be the first clinical manifestation of AML (13). It may also precede the development of leukemia by months or years (10,16), in our case the patient had no abnormal haematological clinical record at first presentation. In the comprehensive study by Pileri et al. as much as 40% of the de novo myeloid sarcoma cases had been submitted in consultation with a misdiagnosis (17). These included Diffuse Large B-cell Lymphoma (DLBCL), Small Lymphocytic Lymphoma (SLL), peripheral T-cell lymphoma, T-cell precursor (lymphoblastic) lymphoma and myeloid metaplasia. These cases emphasize the difficulty of making a diagnosis of myeloid sarcoma, especially when presenting in an uncommon location or when no previous clinical data exists suggestive for AML or myelodysplastic syndrome.

This neoplasm presents grossly as a yellow-tan-white fleshy lesion (that sometimes may have the classic greenish color), with or without necrosis, haemorrhage and fibrosis. The cellular infiltrate is represented by myeloblasts that may posses features of promyelocytic or neutrophilic maturation. Rarely they may display myelomonocytic or pure monoblastic morphology. Microscopical examination reveals diffuse or interstitial infiltrate composed of medium to large sized monotonous cells that usually efface normal tissue architecture. In our case the tumor cells infiltrated the subcutaneous fatty tissue and even muscle fiber. Moreover, our case also presented with a large area of tumor necrosis. The cytoplasm is moderate or reduced in amount, with basophilic or amphophilic staining, sometimes with vacuoles. The nuclei may be round or oval with indentations. The nuclei have dispersed chromatin with small prominent nucleoli. Three morphological variants have been described: well differentiated, poorly differentiated and blastic form. Well differentiated variant is characterized by myeloid differentiation and the presence of cytoplasmic granules. The poorly differentiated form consists of primitive cells with scarce cytoplasmic granules. In the blastic forms one sees no myeloid differentiation, rather monoblastic and monocytic differentiation.

Diagnosis of myeloid sarcoma may at times be difficult if one does not think of it as a differential diagnosis entity, especially presenting as a skin manifestation. Cutaneous manifestations in leukaemia can be non-specific (without the presence of leukemic cells), such as generalized pruritus, panniculitis or specific (myeloid sarcoma or leukaemia cutis, with the presence of leukemic cells). Non-specific lesions are more frequent (up to 30%) than leukaemia cutis (18).

Immunohistochemical stains in this regard are very helpful. Tumor cells usually do not express B- and T-cell markers (CD20, CD19, CD3, CD2), however it may sometimes express CD45. Blasts may express CD34, and monocytic cell may be positive for CD33. In variants that show monoblastic or monocytic differentiation CD68 may be expressed, and occasionally CD15, as a granulocytic marker. Moreover, CD117 and CD99 may also be expressed in myeloid sarcomas. Expression have been noted also for CD56. Some details worth mentioning about the expression of CD56, since it may cause diagnostic problems. CD56 is a non-myeloid antigen, also referred to as neural cell adhesion molecule (NCAM) represents a cell membrane protein involved in adhesion of neural cells. CD56 is expression is observed on NK cells, on a subset of peripheral CD8+ T-cells, on neural or neuroendocrine cells, and on peripheral blood monocytes. Non-hematopoetic CD56+ tumours that may involve the skin include: Merkel cell carcinomas and metastases from other primary neuroendocrine carcinomas (19). The Cutaneous Lymphoma Task Force of the European Organisation for Research and Treatment of Cancer reviewed cases of CD56 positive hematological neoplasms presenting in the skin. Among others it recognizes a subtype described as skin infiltration by CD56 positive acute myelogenous leukemia (myeloid sarcoma) (20). The report published by Pileri et al. also highlights that CD56 may be expressed in as much as 13% of cases of myeloid sarcoma (17).

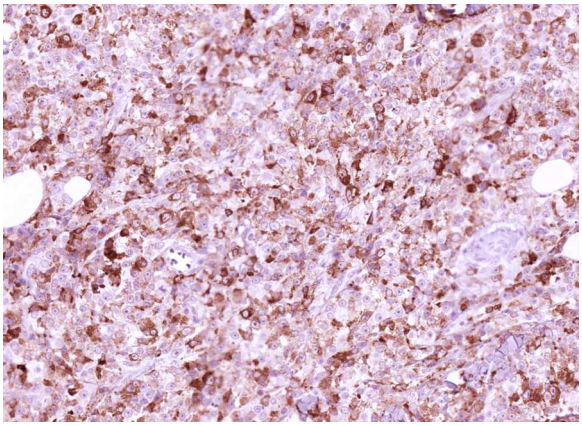

Figure 3. Immunostain for MPO (IHC stain, ob. 40×)

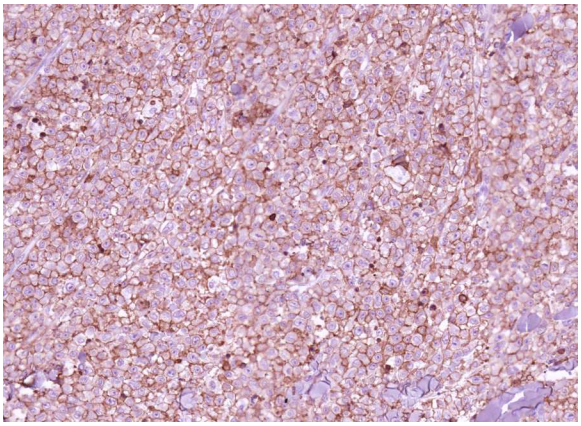

Figure 4. Immunostain for LCA (IHC stain, ob. 40×)

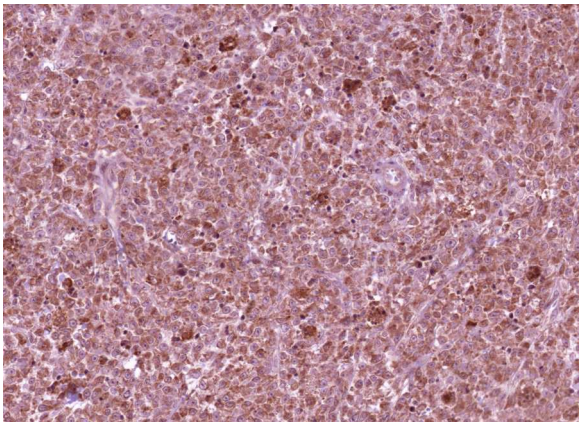

Figure 5. Immunostain for CD68 (IHC stain, ob 40×)

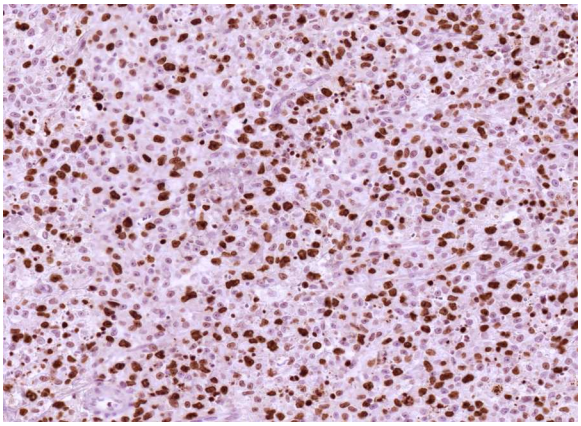

Figure 6. Immunostain for Ki67 (IHC stain, ob 40×)

The blastic form may express TdT. Myeloperoxidase is usually positive. Other markers that may be expressed however with a lower rate: lysozyme, CD61, CD30, glycophorin and CD4. Using the above mentioned markers, the WHO classification subdivides myeloid sarcomas in blastic, myeloid, myelomonocytic, monoblastic, erythroid or megakaryocytic differentiation. Of these types, blastic variant is the commonest, followed by the monoblastic and myelomonocytic types. The proliferative index (Ki67) is usually high, ranging from 50 to 95%.

The differential diagnosis of myeloid sarcoma includes lymphoblastic lymphoma, Burkitt lymphoma, small round cell tumors, blastic plasmacytoid dendritic cell neoplasm, and other non-hematological malignancies or metastatic tumors. It is important to differentiate from tissue infiltrates of acute myeloid leukemia or myeloproliferative neoplasms.

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Conflict of interests

The authors of this article declare that they have no conflict of interests.

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