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CASE REPORT

Cardiac granulocytic sarcoma diagnosed by intracardiac echocardiography-guided biopsy

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Abstract A 52-year-old man presented with clinical and echocardiographic signs of cardiac tamponade. A transthoracic echocardiogram revealed a large right atrial mass that obstructed the superior vena cava flow. Cardiac magnetic resonance imaging and computed tomography demonstrated extracardiac tumour invasion of the free atrial wall extending to the right pulmonary hilus. Intracardiac echocardiography-guided biopsy of the tumour revealed the tissue diagnosis—granulocytic sarcoma of the heart. The patient was effectively treated with radiotherapy, chemotherapy and allogeneic haematopoietic stem cell transplantation. He has remained free of the disease for 12 months after treatment.

Keywords Intracardiac echocardiography · Cardiac granulocytic sarcoma

1 Introduction

Granulocytic sarcoma is a localised tumour composed of immature myeloid blast cells at extramedullary sites. It usually occurs at or after the onset of acute myelogenous leukaemia (AML) or it occurs as nonleukaemic granulocytic sarcoma without concomitant overt signs of leukaemia [1]. Although this tumour may occur at almost any site of the body, tumour involvement of the heart is rare and scarcely reported in the literature [2–4].

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2 Case report

A 52-year-old man was referred to the hospital with clinical signs of vena cava superior obstruction. A complete blood count showed haemoglobin of 130 g/L, the white cell count of 5.9 $\times$ 10^9/L (differential white blood cell count was unremarkable).

Transthoracic echocardiography showed several hypoechogenic areas along the free wall of the right atrium, involving the interatrial septum and extending behind the aorta towards the left atrium. The mass obstructed the superior vena cava flow. The inflow through the tricuspid valve was not disturbed (Fig. 1). Cardiac magnetic resonance (MR) imaging confirmed the intracardiac tumour involvement detected by transthoracic echocardiography. The patient underwent right heart catheterisation and intracardiac echocardiography-guided tumour biopsy to obtain tissue diagnosis. Using local anaesthesia, echocardiography catheter was inserted via the right femoral vein and advanced into the right atrium. Intracardiac echocardiography clearly showed a right atrial mass that, in the upper part, nearly occluded the superior vena cava and seriously impeded blood flow through the vessel. The tumour was seen to spread towards the interatrial septum, yet it did not affect the vena cava inferior inflow. Several biopsies of the tumour were taken under close intracardiac echocardiographic guidance via the left femoral vein access (Fig. 2). There were no complications related to the procedure. The histological examination of the tissue obtained showed infiltration of the myocardial tissue by CD34, CD45, CD117 and HLA-DR positive myeloblasts, a

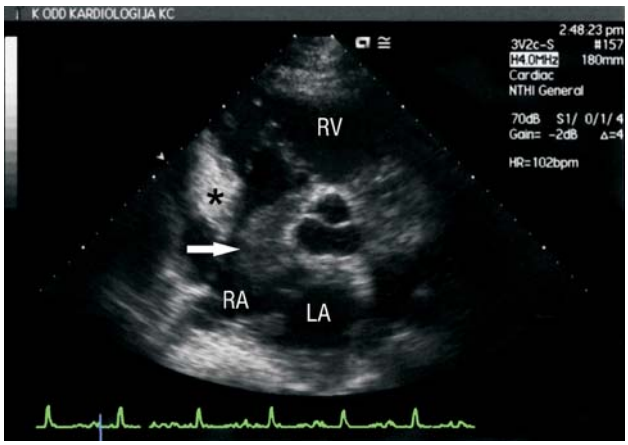

Fig. 1 A transthoracic parasternal short axis view at the aortic valve level demonstrates a large tumour of the right atrium (*RA*) free wall (*asterisk*), invading the interatrial septum and spreading behind the aorta and towards the left atrium (*LA*); *RV* right ventricle

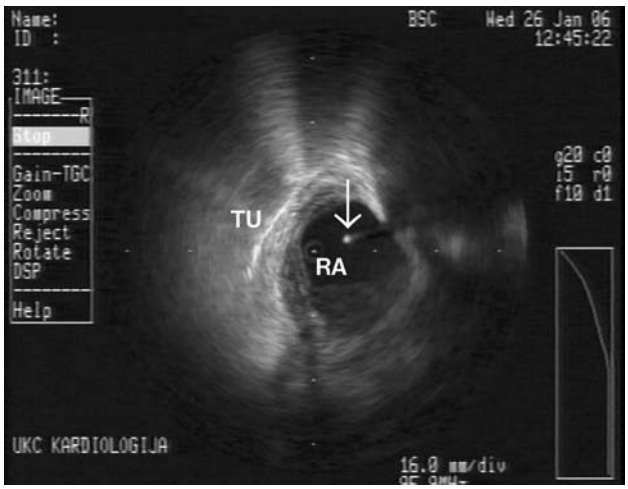

Fig. 2 An intracardiac echocardiographic view of the upper part of the right atrium shows the leftover of the right atrium chamber (*RA*) and the tumour. The *arrow* indicates the biopsy forceps

finding consistent with an immature granulocytic sarcoma of the heart. Lymphoid immunohistochemical markers (CD10, CD20, CD3, TdT) were negative. Based on immunohistochemisty, we excluded other possible intracardiac tumuor aetiology.

Bone marrow aspirate contained 3–4% of blast cells showing signs of dyserythropoiesis. Bone marrow biopsy showed hypercellular bone marrow with signs of dyserythropoiesis and dysgranulopoiesis, and less than 5% of occasionally clustered CD34+ blast cells. The patient's bone marrow kariotype studied on 17 metaphases was normal, but molecular genetic studies of the bone marrow sample disclosed AML1-ETO mRNK transcript (t(8;21)), characteristic of AML [5]. Simultaneously, some other most common fusion gene transcripts, characteristic for acute leukaemias (FLT3-ITD mutation included), were studied, but they all proved negative [6]. AML1-ETO mRNA transcript was not detached by FISH t(8;21) analysis from the same bone marrow sample. After the initial workup at diagnosis, genetic and molecular genetic studies were not repeated from existing or newly obtained bone marrow samples.

The treatment was started with irradiation of the tumour bed in the chest with a safety margin. The patient received a total dose of 15 Gy (1.5 Gy per fraction). After completion of the radiotherapy, he was placed on the MRC 10 chemotherapy protocol consisting of anthracycline and cytosine arabinoside. He received four cycles of chemotherapy according to the treatment protocol. During the entire chemotherapy, cumulative anthracyclines dosages were within recommemded noncardiotoxic ranges (cumulatively he received 300 mg/m^2 of daunorubicin and 50 mg/m^2 of mitoxantron) [7].

Because of the unusual manifestations of the disorder and in spite of its favourable cytogenetic characteristics, we decided to treat the patient with myeloablative allogeneic hematopoietic stem cell transplantation (HSCT), with the patient's HLA-identical brother as the donor. Conditioning was standard myeloablative one, with cyclophosphamide and total body irradiation (fractionated up to 12 Gy). The patient received standard cyclosporin and methotrexate-based immunosuppressive graft versus host disease (GVDH) prophylaxis. The post-transplant course was uneventful, except for localised chronic GVHD of the oral mucosa, which was treated with oral corticosteroid solution. After the transplant, AML1-ETO fusion transcript was followed from newly obtained bone marrow samples every 3 months. On each occasion, analysis proved to be negative, last check being performed 12 months after the allogeneic HSCT. All morphological characteristics of mielodysplasia, described at the time of the disease diagnosis, disappeared from bone marrow aspirate smears after the transplant. Chimerism studies were not performed. Repeat cardiac MR imaging performed 6 months after allogeneic HSCT showed no residual tumour and demonstrated normal width and patency of the caval veins.

3 Discussion

Nonleukaemic granulocytic sarcoma, especially granulocytic sarcoma of the heart, is a rare disease. To our knowledge, only three cases of nonleukaemic granulocytic sarcoma of the heart have been reported in the literature [2–4]. Our patient showed morphological signs of myelodysplasia in the bone marrow and signs of AML at a molecular level, but there was a lack of morphological

diagnostic AML criteria, but based on bone marrow characteristics, also the term "granulocytic sarcoma with myelodisplasia and molecular features of AML" would be appropriate.

A correct early histological diagnosis of the tumour was crucial for appropriate treatment of this life-threatening condition. In this particular case, intracardiac echocardiography seemed to be the most convenient tool for guiding biopsy of the right atrial mass. There have been only few reports on the use of intracardiac echocardiography-guided biopsy of cardiac tumour to obtain histological diagnosis. Biopsies of right-sided cardiac masses have been performed transvenously, mainly under fluoroscopic, transthoracic and transoesophageal echocardiographic guidance. Intracardiac echocardiography, however, provides higher resolution imaging and direct visualisation of the mass, as well as safe positioning of the bioptome associated with low complication risk. Moreover, there is no need to sedate the patient.

Otherwise, we found only one report involving granulocytic sarcoma of the neck and concurrent AML1-ETO fusion gene transcript in the available literature [8]. Despite optimal current disease status, we are aware that cardiac granulocytic sarcoma may (re)appear several years after allogeneic HSCT in patients with acute myeloblastic leukaemia and therefore close patient's follow-up is obligatory [9].

In conclusion, intracardiac echocardiograpy-guided cardiac tumour biopsy proved decisive for the diagnosis of nonleukaemic granulocytic sarcoma of the right heart, and it ensured timely, adequate and effective therapy. Our experience suggests that intarcardiac echocardiography is a useful, straightforward and safe method to guide biopsy of a right heart tumour. To our knowledge, this is the first report on the effective use of intracardiac echocardiography-guided biopsy for histological diagnosis of a very rare primary cardiac nonleukaemic granulocytic sarcoma.

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