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Disseminated malignancy after extracorporeal life support and left ventricular assist device, diagnosed by left ventricular apical core biopsy

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Abstract

The left ventricular apical core biopsy performed during implantation of a left ventricular assist device (VAD) is a well-known diagnostic procedure in confirming cardiomyopathies leading to end-stage heart failure. We describe a patient in whom disseminated malignancy was revealed by means of the apical core biopsy after extracorporeal life support and left ventricular assist device implantation as a bridge to transplantation. This case emphasizes the importance of thorough oncological screening before VAD implantation and the possible consequences of circulating tumour cells in this device-assisted circulation.

Keywords: Ventricular assist device • Apical core biopsy • Heart transplantation • Fibrolamellar hepatic carcinoma

CASE

After resuscitation for ST-elevated myocardial infarction-induced ventricular fibrillation, an occluded left anterior descending artery was stented in a 44-year old female without a significant history. Despite optimal inotropic support and intra-aortic balloon counterpulsation therapy, cardiogenic shock persisted. Transoesophageal echocardiography (TOE) confirmed poor biventricular function, so a venoarterial extracorporeal life support (ECLS) system was implanted. The circuit was composed of a Quadrox-D® oxygenator (Maquet Cardiopulmonary, Hirrlingen, Germany) and a Revolution® centrifugal blood pump (Sorin, Arvada, Co, USA). The patient was heparinized, with target activated partial tromboplastin time values of 70 s. Twenty-four hours later, TOE persistently showed biventricular hypokinesia and the presence of left ventricular (LV) apical thrombus. Screening investigations for heart transplantation revealed no unknown pathology, so a left ventricular assist device (LVAD), type Excor®Berlin Heart, Berlin, Germany, was implanted as a bridge to transplant after 9 days of ECLS support. The LV apical core biopsy, removed during implantation of the LVAD inflow cannula, was routinely sent for pathological examination. The specimen showed LV myocardial infarction and thrombus on the endocardial surface, surprisingly revealing tumour cells caught in fibrin, consistent with the existence of an unknown carcinoma (Fig. 1), as confirmed by immunohistochemical investigations. No previous examination had shown presence of any malignancy. While screening for the primary tumour, all tested tumour markers (alpha-foetoprotein, human choriongonadotropine, carcinoembryonal antigen, CA 15.3, CA 19.9) showed negative. Fourteen days after LVAD initiation, the patient was weaned from the ventilator. The day after, however, she showed bilateral mydriasis due to multiple cerebellar infarctions with massive cerebral herniation. Autopsy revealed the presence of a multifocal fibrolamellar hepatocellular carcinoma (FLC). Portal veins and hepatic arteries showed circulating tumour cells similar to those found in the LV apical thrombus and the FLC (Fig. 2). A patent foramen ovale of 1 cm and infarction zones due to arterial thrombi in the brain, lungs, liver, spleen, kidneys and thyroid were also found.

DISCUSSION

Pathological investigation of the LV core biopsy in LVAD placement has already proved its value in diagnosing cardiomyopathies leading to end-stage heart failure [1]. Furthermore, it can help in predicting the LV reverse remodelling capacity and the subsequent likelihood of weaning from the assist device [2–4].

The importance of pretransplant screening for comorbidities that could reduce survival after heart transplantation is obvious, but thorough screening is not always feasible in urgent settings [5]. To our knowledge, however, the detection of oncological conditions by means of the LV apical core biopsy, leading to discontinuation of therapy in a pretransplant situation, has not yet been described.

FLC is known to occur mostly in relatively young, female patients without stigmata of chronic liver disease or risk factors associated with classical hepatocellular carcinoma (HCC) [6, 7]. Blood results often show normal liver enzymes and tumour markers (alpha-foetoprotein, carcinoembryonal antigen), as seen

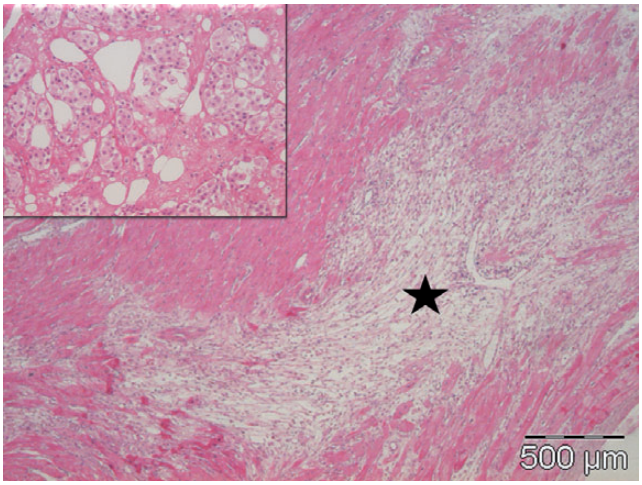

Figure 1: The left ventricular apical core biopsy showed myocardium with areas of infarction (black asterisk). Surprisingly, there was also the presence of a tumour thrombus (inset) (hematoxylin and eosin stain).

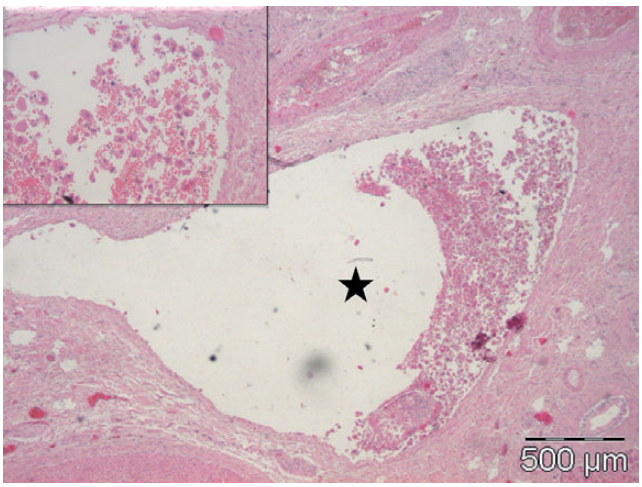

Figure 2: Large portal tract composed of an artery, bile duct and vein (black asterisk). This vein contains a lot of circulating tumour cells (inset) (hematoxylin and eosin stain).

in our patient. FLC is thought to be associated with better outcome than classical HCC, mainly due to the absence of underlying cirrhosis. However, in FLC, metastatic tumour thrombus and direct tumour invasion in the inferior caval vein or the right atrium are often detected at the time of diagnosis and predict poorer survival [6–10]. Treatment by means of resection, chemotherapy, transarterial chemoembolization and radiation has been described with varying success rates. As aggressive treatment results in prolonged survival compared with palliative care [8], the presence of a VAD should not limit the decision for surgical resection. Specific attention is needed, however, for perioperative haemodynamic management and bleeding issues due to complex coagulopathies. A review of the case imaging (pretransplant ultrasound and computed tomography) showed no consistent signs of hepatic carcinoma or caval or atrial thrombosis. The LV apical thrombus, however, was already present pre-LVAD implantation.

The explanation for the presence of thrombi and tumour cells in the different organ systems can be found in two different mechanisms: paraneoplastic hypercoagulability and seeding. The paraneoplastic presence of multiple thrombi has been described repeatedly in literature (e.g. multiple pulmonary emboli). This hypercoagulability state can also occur in heparinized patients [8, 10]. Seeding of tumour cells by the ECLS flow in the entire arterial system and in the LV, and antegrade embolization through the patent foramen ovale could explain the presence of LV tumour thrombus, as found in the apical core biopsy. Yu-Chun *et al.* [9] describe a case of RV metastasis of a HCC, possibly due to haematogenous spreading. Sung *et al.* [10] describe that isolated metastases can possibly seed through a patent foramen ovale. Retrospectively, in this case, the FLC must have been pre-existent and most probably has been disseminated by the continuous venoarterial ECLS flow. The oxygenator [Quadrox-D® (Maquet Cardiopulmonary, Hirrlingen, Germany)] used in this ECLS circuit is not capable of filtering out these tumour cells, as the stacked and crosswise-arranged fibre mats in the filter behave like a screen with a pore size of ∼150 µm (Personal communication Maquet Cardiopulmonary, Hirrlingen, Germany) while the tumour cells size ∼20 µm. No systematical analysis on this issue has yet been performed, however.

This case re-emphasizes the need for thorough screening investigations before heart transplantation even in patients that are supported by means of ECLS. As the number of patients supported by VAD, both as bridge-to-transplantation and as destination therapy, is increasing worldwide, the chance of diagnosing malignancies in these patients will also increase. Due to the assisted circulation, haematogenic seeding alter the patient status from a potentially curable to a disseminated and palliative setting, in which cardiac transplantation is no longer an option. Any heart team dealing with VAD-assisted patients should be prepared to decide whether or not to continue VAD therapy in these specific cases.

As a response to the increasing shortage of donor organs, the implantation of VAD's has become more liberal lately. Their use should, however, be very well considered in patients with end-stage heart failure, even if already supported by ECLS. Assisted circulation can cause tumour cells to disseminate throughout the body, excluding the patient from later transplantation. Furthermore, apical core biopsy specimens should always be sent for pathological examination, even if only the diagnosis of ischaemic myocardium is expected.

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