A Case of Multiple Focal Nodular Hyperplasia in the Liver Which Developed after Heart Transplantation

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Abstract

An 18-year-old woman, who had undergone cardiac allograft transplantation, developed continuous back pain two months after surgery. Abdominal computed tomography showed multiple enhanced lesions in her liver, which were not present before transplantation. One tumor bulged from the surface of the liver and compressed the stomach. Partial resection of the liver was performed and her symptoms improved. The pathological diagnosis was focal nodular hyperplasia (FNH). To our knowledge, this is the first report of multiple FNH after heart transplantation. Transplant clinicians may need to keep this possibility under consideration following heart transplantation.

Key words: heart transplantation, complications, multiple focal nodular hyperplasia

(DOI: 10.2169/internalmedicine.50.4282)

Introduction

Focal nodular hyperplasia (FNH) is a benign liver tumor, which is often seen in young women. However, multiple FNH is rare. The pathogenesis of FNH is not well understood. There are many possible complications we should be aware of following heart transplantation. Here we present the first case, to our knowledge, of development of multiple FNH after heart transplantation. The current case is instructive and indicates that we should keep this possibility under consideration if new liver lesions were detected after heart transplantation.

Case Report

An 18-year-old female cardiac allograft recipient was referred to our hospital for suspected rejection six months after transplant. She underwent transplantation in January 2008 for uncontrollable right ventricular (functional left ventricular) dysfunction due to corrected transposition of the great arteries, status post Rastelli operation, tricuspid valve replacement, and cardiac resynchronization therapy (CRT). She had been taking oral contraceptives for about two years since menarche until heart transplantation to prevent anemia that could worsen heart failure. After the transplantation surgery, she started taking oral immunosuppressant agents including prednisolone 10 mg per day, mycophenolate mofetil 500 mg per day, and cyclosporine A, the trough concentration of which was regularly monitored to be maintained in the range of 160-240 ng/mL.

In March 2008 she developed continuous back pain. Osteoporotic bone disease was excluded. Steroid pulse therapy was given on suspicion of acute rejection, but her symptom did not improve. Therefore, in July, she was referred to our hospital for further investigation.

Physical examination did not show any abnormal findings, such as eczema, rush or abdominal pain. Her blood tests, chest X-ray, electrocardiogram, and cardiac echocardiography did not suggest the cause of her symptom. Cardiac catheterization revealed almost normal hemodynamics. Her coronary arteries were intact without any vasculopathy on coronary angiography and intravascular ultrasonography. Endomyocardial biopsy did not explain her symptom either with the tissue showing minimum cellular rejection Grade 1 R by Standardized Cardiac Biopsy Grading (1).

During her evaluation, abdominal computed tomography (CT) showed multiple enhanced lesions in the liver, which had not been seen prior to heart transplantation in March 2004 (Fig. 1A, 1B). Central scars were not apparent in the
lesions. We considered magnetic resonance imaging (MRI), which is considered to be more informative for the differential diagnosis of liver tumors (2). However, as the leads of CRT-defibrillator (CRT-D) were still in her vein, MRI was not possible.

One tumor in the left lateral segment bulged from the surface of the liver and compressed the stomach (Fig. 1C, 1D). Since it was suspected to be related to her back pain and because there was fear of rupture and possible malignancy (including posttransplant lymphoproliferative disease), partial resection of the liver was performed in October 2008 (Fig. 2A, 2B). The pathological findings of the tumor included hyperplastic hepatocytes with acinar structure, ductular reaction, abnormal vessels, and central scar (Fig. 2C-F), which are typical findings of FNH. Her back discomfort improved after the surgery. In fact, even though the residual lesions are slowly enlarging, back pain remains absent about two years after surgery.

**Discussion**

There are many possible complications after heart transplantation, such as rejection, coronary vasculopathy, infection, and malignancy (3). We can never be too careful to notice any unusual symptoms or signs in transplant recipients, as they are often atypical presentations of these pathological complications. The present patient complained of continuous back pain. We considered the above possibilities and attempted to determine the cause of her complaint. In the process of her evaluation, many nodular lesions were detected in her liver, which had not been present before heart transplantation. The pathological diagnosis of the tumors was found to be FNH. After surgical resection, her back pain resolved. We presume, in the current case, FNH was related to her complaint.

FNH is one of the most common benign neoplasms of the liver, which accounts for 8% of all primary hepatic tumors. It is more commonly found in women (4). In most cases it appears solitary. Multiple FNH is extremely rare, and few reports exist in the literature (5). The pathogenesis of multiple FNH is not well understood. In the current case, the etiology of the multiple FNH cannot be definitively attributed to her prior heart transplantation. Other possible contributing factors present before and after transplantation, including the use of oral contraceptives, surgical stress, and immunosuppressant therapy.

A possible relation between FNH and oral contraceptive use has been proposed but remains controversial (6). In the current case, the recipient had been taking oral contraceptives for about two years since menarche preceding heart transplantation to prevent anemia, which may have contributed to the development of multiple FNH. Because candi-
dates for heart transplantation suffer from severe heart failure, it is not unusual to receive oral contraceptives to prevent anemia or pregnancy. The current report suggests that development of FNH should be especially considered in such patients.

There is no evidence for the relationship between immunosuppressants and FNH, but immunosuppressant agents are causally related to malignant tumors, including post-transplant lymphoproliferative disease (7). The current patient needs to continue immunosuppressant therapy. With no evidence for rejection having been seen during periodic cardiac biopsy, we have been modulating her agents carefully. In fact, the residual lesions are slowly enlarging after surgery, but surgical resection of the liver for treatment of FNH is not indicated unless the patient has symptoms related to the tumor size or location (4). Our clinical plan includes periodic abdominal CT in order to monitor the residual tumors.

In this case we diagnosed FNH by tissue pathology, but, in general, diagnosis by imaging is preferred. For non-invasive diagnosis, MRI is more useful than CT, the sensitivity and specificity of which are 70% and 98%, respectively (2). The patient, however, could not undergo MRI because CRT-D leads were still in her vein. In addition, because one tumor was suspected of causing her back pain and because of risk of rupture, we chose prompt surgical resection.

Again, the causality cannot be proven. However, this is an instructive case; the first case report, to our knowledge, of multiple FNH observed after heart transplantation, although FNH is not rare after hematopoietic stem cell transplantation (8). To the best of our knowledge, there are no case reports of FNH after solid organ transplantation. Data of Japanese patients after heart transplantation are scarce, and accumulation of such data will be clinically useful. Based on the present report, we suggest that multiple FNH should be considered if new liver lesions are detected after heart transplantation, especially if the patient had taken oral contraceptives before surgery.

The authors state that they have no Conflict of Interest (COI).

References


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