RECOVERY FROM MULTI-ORGAN FAILURE IN A PATIENT WITH A CONTINUOUS-FLOW LEFT VENTRICULAR ASSIST DEVICE

To the Editor:

We report a case of recovery from multi-organ failure after implantation of a Jarvik 2000 FlowMaker axial-flow left ventricular assist device (LVAD; Jarvik Heart, Inc., New York, NY). The patient, a 52-year-old man, was admitted to our hospital with acute decompensation related to chronic heart failure. His past medical history was remarkable for non-ischemic dilated cardiomyopathy and chronic renal failure.

On admission, the patient was hypotensive, with signs and symptoms of fluid overload and hypoperfusion. Pulmonary artery catheterization revealed a cardiac index of 1.6, pulmonary artery pressure of 68/31 mm Hg and pulmonary capillary wedge pressure of 30 mm Hg. An intra-aortic balloon pump was inserted, and diuretic and inotropic therapy was started. Because the patient's status did not improve, a Jarvik 2000 FlowMaker LVAD was implanted 10 days after admission.

During the early post-operative period, the patient required vasopressive and inotropic medications. On the second post-operative day, bleeding complications necessitated mediastinal exploration. The patient rapidly developed multi-organ failure with acute renal failure, inability to be weaned from the ventilator, and elevated bilirubin levels, both total and direct. At 3 weeks after LVAD implantation, his bilirubin level had risen to 68 mg/dl and he underwent a cholecystectomy for chronic cholecystitis. A liver biopsy showed centrilobular necrosis and cholestasis secondary to heart failure.

Post-operatively, the patient required continuous venovenous hemodialysis and intermittent hemodialysis for anuric renal failure. Between 2 and 3 months after LVAD implantation, his liver and renal function returned to normal, so he was weaned from renal ultrafiltration. He started to participate in cardiac rehabilitation and intensive physiotherapy. After 5 months of intensive treatment, he was discharged home in good condition. Since then he has been able to carry out daily activities with minimal symptoms. He continues to be followed up regularly in our outpatient clinic.

Multi-organ failure occurs in up to 32% of LVAD recipients and entails a mortality of 71%.[1] Our patient's remarkable recovery confirms that axial-flow left ventricular assistance can reverse multi-organ failure even after prolonged periods.

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MINUTE PULMONARY MENINGOTHELIAL-LIKE NODULES IN THE TRANSBRONCHIAL BIOPSY OF A LUNG TRANSPLANT RECIPIENT

To the Editor:

Minute pulmonary meningothelial-like nodules (MPMN) are small (100 μm–few mm) asymptomatic nodules, often identified as incidental findings in microscopic studies of lung samples. MPMNs have been found in subjects ranging in age from 12 to 91 years (up to 85% women)[1,2] and more frequently in the right lung. The lesions consist of whorls/nests of moderately sized cells with eosinophilic cytoplasms. The cells are spindle or elongated. The nuclei are oval with finely granulated chromatin and small or absent nucleoli. These lesions have been initially called "minute pulmonary tumors representing chemodectomas."[1]

Later functional and immunophenotypic studies demonstrated a meningothelial differentiation rather than neuroendocrine nature of the MPMN cells. In fact, MPMN cells positively immunostained with anti-vimentin and anti-epithelial membrane antigen (EMA) antibodies but did not react with anti-cytokeratin, anti-actin, S100, and neuron-specific enolase (NSE) antibodies.[1–3] Single lesions were defined as MPMN, whereas multiple nodules were termed MPMN–omatosis.[1,4] Despite a further study that suggested a myogenic rather than meningothelial origin (MPMN cells were reported to be EMA-negative, and vimentin- and myosin-positive) the currently supported histogenesis is meningothelial.

From the clinical point of view, single lesions are usually asymptomatic, whereas MPMN–omatosis may be associated with functional impairment.[1–4] Therefore, in most cases, MPMN is a clinically meaningless curiosity finding whose correct diagnosis prevents clinical misinterpretations, such as metastatic lesions,[5] and

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unnecessary alarms or imaging and may lead to dedicated TBB monitoring programs to differentiate lung function impairment due to allergenic reactions or infection from the rare clinical progression of MPMN.[2,5]

We describe a single MPMN that was identified in a transbronchial biopsy (TBB) specimen of a lung transplant (LTx) recipient. It was proven to be primary by the absence of imaging and autopsy findings of central meningiomas in the donor and high-resolution imaging in the recipient.

PRE-TRANSPLANT CLINICAL HISTORY

The patient is a 56-year-old man who underwent double LTx for end-stage severe respiratory failure due to bullous emphysema. His family history was negative for respiratory diseases; his clinical history before LTx was characterized by progressive loss of lung function and finally by chronic lung and right heart failure because of severe secondary pulmonary hypertension.

DONOR STUDY

The donor was a 35-year-old man who died from cerebral hemorrhage. Computed tomography (CT) and magnetic resonance image (MRI) scans documented the hemorrhagic event. Meningeal and cerebral masses were absent. The autopsy study confirmed the devastating cerebral hemorrhage and the absence of brain and meningothelial tumors.

RECIPIENT POST-TRANSPLANT STUDY

The patient was treated with a standard immunosuppressive regimen (cyclosporine A, azathioprine, and steroids) and received rabbit anti-thymocyte antibodies as induction therapy. He was then regularly monitored by a clinical, functional, and endoscopic follow-up schedule, including TBB at the post-operative time points of 1, 3, 6, and 12 months, and when clinically relevant.

His first-month TBB did not show acute rejection in any of the 6 lung samples; in one, a non-reactive human cytomegalovirus (HCMV) localization involving 2 cells was diagnosed with anti-immediate-early antigen HCMV antibodies. A corresponding high HCMV load in bronchoalveolar lavage fluid ($>2 \times 10^5$ genome equivalents/ml) led to a pre-emptive treatment with intravenous ganciclovir for 3 weeks.

In the third-month TBB, a MPMN was found in 1 of 6 lung samples at all of the 120 serially cut sections that are routine for post-transplant TBB studies (Figure 1a–c). The nodules stained negative with anti-cytokeratins (CAM5.2, CK7, AE1/E3), S-100, desmin, alpha smooth muscle-actin, HHF35, myosin, h-caldesmon, CD34, synaptophysin, NSE, chromogranin, and estrogen and progesterone receptors. MPMN was specifically stained with anti-vimentin and anti-EMA antibodies. The anti-EMA immunostain was specific but weaker than that of alveolar pneumocytes (Figure 1c–e).

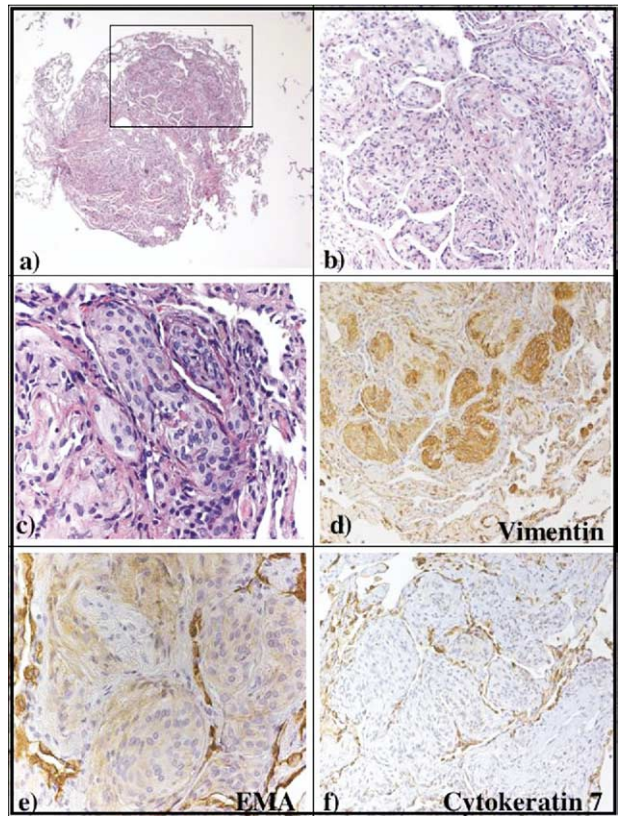

Figure 1. Panel a: low-power view of the transbronchial biopsy sample with the small nodule (square). Panels b and c: higher-power view of the minute pulmonary meningothelial-like nodules (MPMN) shows the typical morphology of the meningothelial cells (a–c: hematoxylin-eosin stain). Panel d: immunostain with anti-vimentin antibodies shows the specific reaction of the MPMN cells. Panel e: anti-epithelial membrane antigen anti-body reaction shows the weaker but specific stain of the MPMN and the stronger stain of epithelial alveolar cells. Panel f: negative immunostain of MPMN cells with anti-cytokeratin 7 anti-bodies and internal positive control of epithelial alveolar cells (d–e: immunoperoxidase stains). a) ×5; b,d,f) ×20; c,e) ×40

At this time, graft function was good and the patient reached his best post-transplant forced expiratory volume in 1 second value (3.87 liters). The patient was still functionally stable at the 7-month follow-up.

A high-resolution cerebral CT (HRCT) scan (the patient refused MRI because of claustrophobia) documented the absence of intracranial lesions. The diagnosis of primary MPMN was definitely formulated. Lung HRCT scan did not detect nodules in the lung parenchyma; accordingly, either the lesion was unique or other lesions (if any) did not reach the detection threshold of HRCT. Therefore, the MPMN was an occasional histopathologic diagnosis in the monitoring TBB specimen. Specimens from a further TBB per-

formed 1 month after the former did not show other MPMNs.

We believe this is the first report describing a MPMN in a TBB biopsy specimen of a LTx recipient: 2 additional cases in have been reported in the lungs of transplant recipients at autopsy.[4]

We excluded the origin from a central meningioma in the donor with MRI and CT and in the recipient with CT; therefore, the observed lesion was primary. Whether MPMN was present in the donor lung at the time of transplantation or arose after the procedure cannot be established. Independently of the time of onset, however, the lesion requires surveillance as, exceptionally, it may influence lung dysfunction and must be distinguished from all allogenic, infectious and adult respiratory distress syndrome-related features that may coexist in the lung allograft.

Surveillance TBB is therefore essential, not only for diagnosis and monitoring of acute and chronic rejection, allograft infections, and other conditions such as ARDS, but also for the detection of rare and unexpected conditions such as MPMN.

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