Native lung pneumonectomy for post-transplantation lymphoproliferative disorder refractory to rituximab following contralateral lung transplantation

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Abstract

Post-transplantation lymphoproliferative disorder (PTLD) is a life-threatening complication following lung transplantation. We report a PTLD case of high-grade, B-cell lymphoma following contralateral single-lung transplantation. The disease involved the liver, right kidney and right native lung. While the PTLD affecting the abdominal organs regressed with rituximab chemotherapy, the native lung disease progressed and was treated surgically (right pneumonectomy). Some aspects are unique in this case: (i) different response to medical treatment between lung and abdominal organs; (ii) absolute absence of involvement of the native lung and (iii) surgical treatment with a pneumonectomy, still very rarely described in the literature. We hypothesized that a different morphotype of the disease involved the abdominal organs or the penetrance of rituximab, and chemotherapy could have been impaired by the presence of pulmonary fibrosis.

Keywords: Lung transplantation • Post-transplantation lymphoproliferative disease • Pneumonectomy • Rituximab • Native Lung

BACKGROUND

Post-transplantation lymphoproliferative disorder (PTLD) is one of the most serious life-threatening complications following lung transplantation [1], with multiple risk factors including: Epstein-Barr virus (EBV) infection in naive patients [2], high levels of immunosuppression, cystic fibrosis, Cytomegalovirus (CMV) infection or old recipient age. In the majority of the cases, EBV infection leads to a transformation of B cells in conjunction with decreased levels of cytotoxic T cells, impaired natural killer cells, decreased colony-stimulating factor (CSF-1) and anti-apoptosis pathways [3]. The incidence of PTLD varies between 3 and 5% in recent reports [4], and the majority of the cases are diagnosed under a year following lung transplantation.

The paradigm of PTLD treatment has evolved during the last decade, targeting the risk factors such as EBV naive status, early diagnosis and immunosuppressant modulation [5], while surgery is reserved for tumour debulking. The reported mortality ranges between 50 and 75%, despite the current treatment options.

We report one case of PTLD high-grade, B-cell lymphoma in the native lung following contralateral single-lung transplantation, with concurrent liver and kidney disease. This was treated with pneumonectomy due to the resistance to rituximab and chemotherapy of the lung PTLD.

CASE REPORT

A 53-year old female underwent left single-lung transplantation from a donor after cardiac death for bilateral pulmonary fibrosis in January 2014. Past medical history included osteopenia, steroid-induced diabetes mellitus and diverticulitis. The donor was reported positive for EBV.

In the 6-month post-transplantation, the patient had multiple episodes of A2–A3 rejection, treated with high doses of methylprednisolone and anti-thymocyte globulin, following which the patient presented acutely with pain and diarrhoea. A computed tomographic (CT) scan of the chest, abdomen and pelvis identified multiple low-density lesions in the liver, bilateral kidneys, pancreas and right lung.

The biopsy of the liver was attempted, but due to an iatrogenic right haemothorax, the procedure was abandoned. According to the presentation and imaging, PTLD was suspected. The immunosuppressive treatment was reduced, additionally to the chemotherapy regime: cyclophosphamide, vincristine, prednisolone and...
rituximab (R-CVP). The CMV reactivation was diagnosed and treated with valganciclovir. The 2-month interval CT scan showed radiological complete remission of the PTLD in the liver, kidneys and pancreas. Progression of the disease in the right lung consisted of diffusely thickened interstitial spaces and multiple confluent consolidation areas, with the biggest increasing in size from 2.47 to 4.80 cm (Fig. 1). CT-guided biopsy of the right lung revealed monomorphic high-grade, B-cell lymphoma, positive for EBV-encoded RNA (EBER), with the diagnosis of Ann Arbor stage IV. The EBV viral load was measured at 20,000 copies/ml at diagnosis and it decreased with time, whereas the lactate dehydrogenase concentration was 2000 U/l. Further chemotherapy was initiated with cyclophosphamide, doxorubicin hydrochloride, vincristine, prednisolone and rituximab (R-CHOP) with further disease progression limited to the native lung.

After multidisciplinary discussion, the patient was left with three options for the refractory PTLD in the right lung: (i) further third-line, high-dose chemotherapy which would herald high mortality (30–40%); (ii) surgery with curative intent by performing a right pneumonectomy and (iii) palliative treatment with less than 6-month life expectancy.

In the context of the patient’s young age, relatively preserved lung function, no additional comorbidity, high risks associated with chemotherapy, the patient was offered a high-risk right pneumonectomy. The risk was stratified based on the patient receiving high-dosage steroids, immunosuppressive treatment and chemotherapy preoperatively.

An intrapericardial right pneumonectomy was performed. Histology confirmed EBER-positive, high-grade, B-cell lymphoma in the explant. The lymphoid cells were positive for CD20, with mixed CD3- and CD5-positive T cells present in the background. The patient was discharged home on Day 7 without complications. In the 6 months following surgery, the patient was readmitted with neutropenic sepsis, from which she recovered well. Interval clinical and imaging surveillance were continued for early recurrence detection, and no relapse was diagnosed during the first year of follow-up.

**DISCUSSION**

We reported a case of native lung PTLD B-cell lymphoma refractory to rituximab and chemotherapy following contralateral lung transplantation, treated by pneumonectomy. Similarly to existing evidence, this patient was diagnosed in the first year following transplantation and was subjected to recognized risk factors as high immunosuppressive treatment, EBV infection and CMV infection [3].

Some aspects are unique in this case: (i) the different response to medical treatment between lung and abdominal organs; (ii) the absence of involvement of the transplanted lung and (iii) the final surgical treatment with pneumonectomy, still rarely described in the literature.

This case intrigues due to the presentation and evolution of PTLD despite optimal medical management. The native lung was affected by the disease, whereas the transplanted lung was disease free. The PTLD affecting the abdominal organs regressed with rituximab and chemotherapy, whereas the lung disease progressed. One explanation could be the different morphotype of the disease involving the abdominal organs when compared with the lung disease. The morphotype and tumour histology could not be compared due to the lack of the liver biopsy. Alternatively,
the penetrance of rituximab and chemotherapy could have been impaired by the peribronchovascular interstitial thickening secondary to pulmonary fibrosis in the native lung.

Conflict of interest: none declared.

REFERENCES


