Pictorial essay

Postoperative imaging after lung transplantation

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Abstract

Lung transplantation (LT) is an established procedure for chronic end-stage lung diseases. Complications are frequent and diverse and are the consequence of the complex surgical technique, the severity of the initial pathology, and the deep state of posttransplantation immunosuppression. Complications following LT include primary graft dysfunction, rejection (hyperacute, acute, and chronic), infections, posttransplantation lymphoproliferative disease, pleural and airway complications, native lung complications, and recurrence of primary disease. An understanding of these complications, their temporal evolution, and the role of radiology and other diagnostic methods in their diagnosis and management will help reduce the morbidity and mortality associated with LT.

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1. Introduction

This pictorial review covers the spectrum of postoperative imaging of lung transplantation (LT) based on our experience of an LT program established since 1994. LT is now an established procedure for end-stage lung disease; the most frequent indications are emphysema, idiopathic pulmonary fibrosis, and cystic fibrosis (Fig. 1). A detailed knowledge of immediate and late complications, both surgical and medical, is essential for earlier detection and treatment. Complications are frequent and diverse and are due to the complex surgical technique, the severity and chronicity of the initial pathology, as well as the immunosuppressive therapy required after transplantation.

The most important complications following LT include primary graft dysfunction (PGD), rejection (hyperacute, acute, and chronic), infections, posttransplantation lymphoproliferative disease, complications involving the pleura and airways, complications of the native lung, and recurrence of primary disease.

1.1. Primary graft dysfunction

PGD is the recommended term by the International Society of Heart and Lung Transplantation [1]. It is also known as reimplantation or reperfusion edema and primary graft failure. PGD incidence varies from 11% [1] to nearly 100% [2]. Because of an increased capillary permeability and alveolar damage caused by an ischemic vascular injury to the transplanted lung, an interstitial and alveolar edema of the allograft occurs when reperfusion is initiated. It appears within the first 48–72 h and resolves within 3 weeks [2]. PGD is a diagnosis of exclusion. The most frequent radiological manifestation is air space disease occurring in the lower and middle lung zones, which may progress to total lung opacification (Fig. 2).

1.2. Hyperacute rejection

Hyperacute rejection is a rapidly fulminating syndrome occurring within hours following the completion of the vascular anastomoses. It is extremely infrequent, with only few cases reported [3]. It probably results from the interaction of preformed recipient antibodies directed against major donor allograft antigens. Chest radiograph (CXR) shows diffuse consolidation of the entire transplanted lung. Only one suspected case
of hyperacute rejection was encountered in our center. The lung allograft became grossly edematous intraoperatively, and the patient died within hours.

1.3. Acute rejection

The time frame for acute rejection extends from within the first week [4] through the first year after LT [5] but most often occurs within the first 3 to 6 months. Risk factors are still not well understood. However, acute rejection is a known risk factor for the development of bronchiolitis obliterans syndrome (BOS). Histologically, acute rejection consists of perivascular or bronchiolar mononuclear inflammation. Transbronchial lung biopsy is the gold standard for the diagnosis. The radiological findings are not specific (Fig. 3). CXR can be normal in low-grade acute rejection. In high-grade acute rejection, there are usually ground-glass opacities (localized or widespread). Absence of ground-glass opacities makes severe acute rejection unlikely [6].
1.4. Chronic rejection

Chronic rejection is the main factor limiting long-term survival after LT. It affects 45% of patients who survive 5 years or more and is responsible for 57% of the deaths occurring after the first year from LT. Chronic rejection usually begins 6 months after LT [6]. Among proven risk factors are prior episodes of acute rejection and cytomegalovirus (CMV) infection. BOS is classically defined as a manifestation of chronic lung allograft dysfunction (CLAD). At pathology, it presents as eosinophilic hyaline fibrosis in the respiratory bronchiole walls, with luminal occlusion [7], leading to airway distortion and scarring.

In the current nomenclature, chronic rejection is classified as present or absent [7]. However, because of the patchy distribution of CLAD, transbronchial lung biopsies often provide inadequate tissue samples. Recent investigators [5,8] proposed changes in the classification of chronic rejection as there are other manifestations involved. Knoop & Estenne [5] have identified four different pathologic entities: neutrophilic reversible allograft airways dysfunction, upper lobe fibrosis, exudative follicular bronchiolitis, and large airway stenosis/malacia. Sato et al. differentiates BOS from restrictive allograft syndrome (RAS) [8]. RAS presents restrictive functional changes, extensive interstitial and pleural fibrosis, in contrast to BOS, which has relatively intact peripheral lung tissue. RAS also has an adverse effect on patient survival [8]. BOS frequently shows air trapping on expiration computed tomography (CT). On follow-up, CT can show central or peripheral bronchiectasis, bronchial wall thickening, mosaic pattern on inspiration, interlobular septal thickening, and peribronchovascular infiltrates.

Fig. 3. Acute lung rejection. (A) Posteroanterior CXR of a patient with Grade 1 rejection showing nonspecific finding of a small left-sided pleural effusion 15 days post transplant; (B) Histology of acute rejection showing lymphocytic infiltration (arrows) in a perivascular distribution.

Fig. 4. Chronic lung rejection. (A) Patient with bilateral bronchiectasis giving rise to a “signet ring appearance” (white arrow), on inspiratory noncontrast chest CT; (B) Air trapping (white arrow) on expiratory noncontrast chest CT, in another patient; small bilateral bronchiectasis are also seen; (C) Histology showing peribronchial fibrotic process (black arrow).
Sensitivity of CT for diagnosis of chronic rejection is however still limited [5].

1.5. Infections

The incidence of infections after LT is 34–59% [9], more frequent than in other organ transplant patients. Bacterial and fungal infections are the most frequent in the first month after LT. Viral infections are more common in the second and third postoperative months. Unfortunately, no specific radiographic or CT findings can allow an accurate distinction between bacterial, viral, and fungal etiologic agents [9]. Patients with pulmonary infections after LT may have normal findings at CXR. CT can show ground-glass opacities, tree-in-bud pattern, consolidation, nodules, septal thickening, pleural effusions, and bronchiectasis [9,10] (Fig. 5).

Bacterial infection, especially due to gram-negative bacteria, can show consolidation (94%), ground-glass opacity (81%), nodules (44%), tree-in-bud appearance, and pleural effusions (75%) [9]. Mycobacterium abscessus is the most frequent atypical bacteria, while reactivation of pulmonary tuberculosis has been reported in 2% [10]. Nocardiosis can present a nodular or consolidative pattern.

Fungal infections, most often due to Aspergillus and Candida albicans [6,9], are associated with a high mortality rate and occur 2 to 9 weeks after transplantation [9]. CMV infection is the most common viral pathogen following LT and is also the second most frequent cause of pneumonia, after bacterial infection. It occurs 1–6 months post-LT. Pneumocystis jirovecii is uncommon nowadays, thanks to the universal prophylaxis.

1.6. Posttransplant lymphoproliferative disease (PTLD)

PTLD refers to a spectrum of diseases in transplanted patients ranging from abnormal lymphoid hyperplasia to true neoplasia, with a prevalence of 2 to 10% within 1 year of LT [11]. Mortality remains high, ranging from 40 to 90% [11]. Deep immunosuppression, a greater quantity of lymphoid tissue in the pulmonary allograft [11], and a history of viral infection (especially Epstein–Barr) are risk factors for PTLD. At imaging, single or multiple nodules or masses, predominantly basal and peripheral [6], are the most frequent manifestation
1.7. Pleural complications

Pleural complications after LT can be divided into pleural effusion, empyema, and pneumothorax. They are often bilateral owing to the fact that the pleural space frequently becomes a unique interconnected space in bilateral LT [4] (Fig. 7).

Pleural effusion occurs in the early postoperative period [4,12] and usually resolves within 2 weeks. It tends to be hemorrhagic, becoming less hemorrhagic and more serous after 7 days [13]. Long-term pleural changes (59%) include pleural thickening (48%), calcifications (4%), and effusion (3%). The frequency of empyema varies between 3% and 8% in various series [13]. It occurs usually 6 weeks after LT and is more common after bilateral LT [13]. Fungal pathogens, particularly C. albicans, are the most frequent pathogens. Empyema is associated with poor survival requiring an aggressive therapeutic approach [13]. Pneumothorax is a common complication and usually resolves with drain placement. A transient air leak is seen in 10% of patients and resolves within 1–2 weeks. A persisting pneumothorax beyond 1 week can suggest bronchial dehiscence or ruptured bulla.

1.8. Airway anastomotic complications

Airway anastomotic complications include bronchial dehiscence, bronchial stenosis, bronchomalacia, as well as bronchovascular, bronchopleural, and bronchomediastinal fistula. Globally, the incidence of airway complications is 15% [14]. The principal risk factors are donor bronchi ischemia [14], postoperative infection, acute rejection, prolonged mechanical ventilation, and mismatch in the sizes of donor and recipient bronchi.

Bronchial anastomotic dehiscence typically occurs 2–4 weeks after LT. With CT, bronchial anastomotic dehiscence can be directly demonstrated as a site of bronchial wall discontinuity [15], with extraluminal mediastinal air adjacent to the bronchus [15]. Persistent air pneumothorax, pneumomediastinum, or posterior air collection are indirect CT signs of bronchial anastomotic dehiscence [6,15] (Fig. 8).

Bronchial stenosis and bronchomalacia are long-term complications typically occurring 2 to 9 months after LT [6]. Bronchial stenosis is the most frequent complication of large airways and occurs at the site of the anastomosis, or distally.

1.9. Vascular complications

Vascular anastomotic complications are uncommon [4] and include pulmonary artery and vein stenosis. Pulmonary embolism and pulmonary infarction have been reported to be as high as 27% and 40%, respectively. The risk of infarction could be related to the insufficient bronchial arterial supply in the early postoperative period and thus to fewer available collaterals.

1.10. Complications of the native lung

In patients receiving a single LT, complications are 14–15% more frequent and are attributable to infection, malignancy (related to the patients’ underlying risk factors, as well as immunosuppressive therapy), pneumothorax, bronchopleural fistulas, and pulmonary embolism [16] (Fig. 9).

1.11. Recurrence of primary disease

Recurrence of primary disease has an incidence of approximately 1% and has been described to occur months to years following LT [16]. Sarcoidosis is the most common condition to recur; other frequent recurring conditions are Langerhans cell histiocytosis (Fig. 10) and lymphangioleiomyomatosis (LAM) [16].

2. Conclusion

Postoperative imaging and its interpretation in patients with LT is a challenging task. Complications following LT are diverse and can be serious. The radiologist’s contribution to the multidisciplinary team approach involves an understanding and early recognition of these complications, as well as of their temporal evolution, for the most appropriate postoperative management of these vulnerable patients.
References

Fig. 9. Complications of native lung. Noncontrast chest CT, showing a hyperinflated emphysematous left native lung, with compression of the right transplanted lung, as well as an adenocarcinoma in the left native lung (white arrow).

Fig. 10. Recurrence of primary disease. (A) Pulmonary Langerhans cell histiocytosis (PLCH) before LT; (B) PLCH recurrence 3 years after bilateral LT.