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CASE SERIES
Heart failure

Solid organ transplantation in heart transplant patients: description of two highly complex cases: a case series

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Background Heart transplantation has become a developed and routine technique, constituting the treatment of choice in advanced heart failure when other therapies have failed. The number of transplanted patients who require transplantation of another organ in their evolution or simultaneous transplantation is increasing. Experience in this scenario is still limited.

Case summary We present two unusual cases of patients who, after receiving a cardio-bipulmonary transplant and isolated cardiac transplant, respectively, require sequential transplantation of another organ in their evolution. In the first case, as a consequence of immunosuppressive drugs, there is a progressive deterioration of renal function that requires renal transplantation after years of peritoneal dialysis. In the second case, shortly after cardiac transplantation, severe emphysematous chronic obstructive pulmonary disease of quick evolution was diagnosed, requiring one-lung transplantation after needing ambulatory oxygen therapy. The evolutionary complications of both cases are presented.

Discussion Patients with multiple organ transplantation represent a challenge as this situation is less frequent, due to the added difficulties in the adjustment of immunosuppression and the specific complications of each organ. However, multidisciplinary follow-up of these patients has led to improved survival.

Keywords Multiple organ transplantation • Solid organ transplant • Immunosuppression • Multidisciplinary team • Myocardiopathies • Case series

ESC curriculum 2.1 Imaging modalities • 6.1 Symptoms and signs of heart failure • 6.5 Cardiomyopathy • 7.3 Critically ill cardiac patient • 7.5 Cardiac surgery

Learning points

- The number of combined solid organ transplant patients is increasing; a prior transplant modifies surgical risk and immunosuppressive management.
- Immunosuppression management is complex; changes and inconsistencies increase the risk of opportunistic infections and organ damage.
- Multidisciplinary management by expert teams can achieve survival rates comparable to single-organ transplants.

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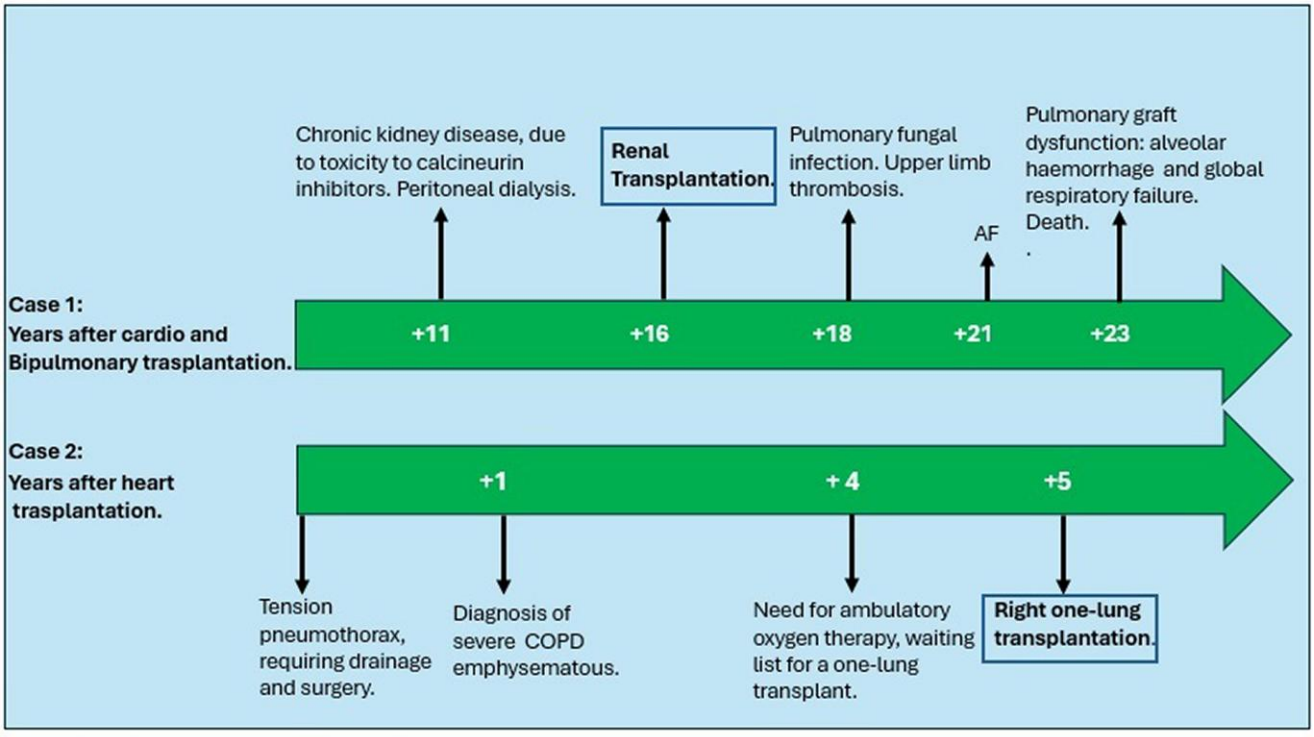
Introduction

Heart transplantation (HT) is a well-established procedure. In Spain, it was first performed in May 1984. Since that date, around 300–350 heart transplants have been performed each year, recently exceeding 10 000 procedures. Most of these transplants have been isolated heart transplants, with about 1%–2% being performed in combination with kidney, liver or lung transplants.[1]

The number of heart transplanted patients who need another organ in their clinical course and are transplanted is not known exactly because this variable is not recorded in the Spanish Cardiac Transplant Registry. However, it is well established that renal transplantation is the most common due to chronic and progressive renal dysfunction caused, among other causes, by calcineurin inhibitors.[2] It is probably followed by haematopoietic progenitor transplantation, particularly as a treatment for light-chain amyloidosis (AL) associated with cardiac dysfunction.[3]

We describe two very rare and highly complex transplant cases performed during the course of HT. A renal transplant performed 16 years after a simultaneous cardio-bipulmonary transplant, and a single-lung transplant conducted 4 years after a heart transplant.

Summary figure



Timeline of the case report (in years).
COPD: chronic obstructive pulmonary disease.

Patient 1

The first case involves a 59-year-old male with hypertension and dyslipidaemia who had undergone cardio-bipulmonary transplantation in 2001 via clam-shell thoracotomy due to idiopathic dilated cardiomyopathy and giant bilateral pulmonary emphysema. Immunosuppressive treatment included tacrolimus and mycophenolate (*Figure 1*).

Over time, the patient developed advanced chronic kidney disease due to calcineurin inhibitor toxicity, requiring renal replacement therapy with peritoneal dialysis for over 11 years after transplantation. The patient was considered a candidate for renal transplantation and was placed on the waiting list. In 2017, +16 years after his initial transplantation, he underwent a deceased donor renal transplant, with the graft implanted in the right iliac fossa. Initial immunosuppressive therapy included basiliximab and corticosteroids. Basiliximab was later discontinued, tacrolimus was introduced, and mycophenolate mofetil was replaced with everolimus following the centre's protocol.

The patient evolved without incident, starting diuresis 12 h after renal transplantation and presenting good progression, without cardiac or pulmonary dysfunction.

During the following years, the patient continued his follow-up with the cardiac, pulmonary and renal transplant units jointly, presenting echocardiographies with preserved function of both ventricles and mild valvulopathies, respiratory functional tests in the normal range and adequate renal function.

As evolutionary complications, the patient presented a pulmonary fungal infection by Aspergillus that required admission and treatment with intravenous isavuconazole in 2019 (+18 years post cardiopulmonary transplantation). During that admission he suffered an upper limb thrombosis requiring full-dose anticoagulation (*Figure 2*).

In 2022 (+5 years post-renal transplantation) the patient experienced an episode of subacute renal failure with baseline creatinine rising

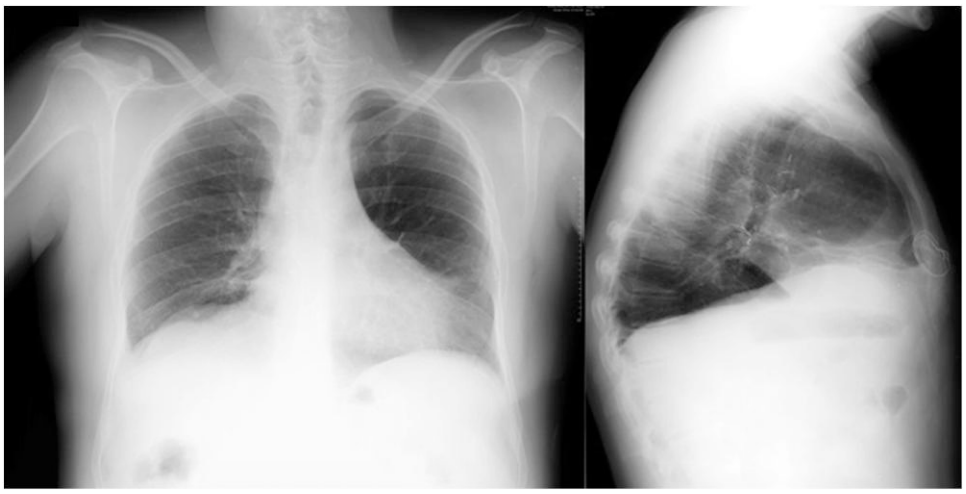


Figure 1 Postero-anterior and lateral chest X-ray after cardiac and bipulmonary transplantation.

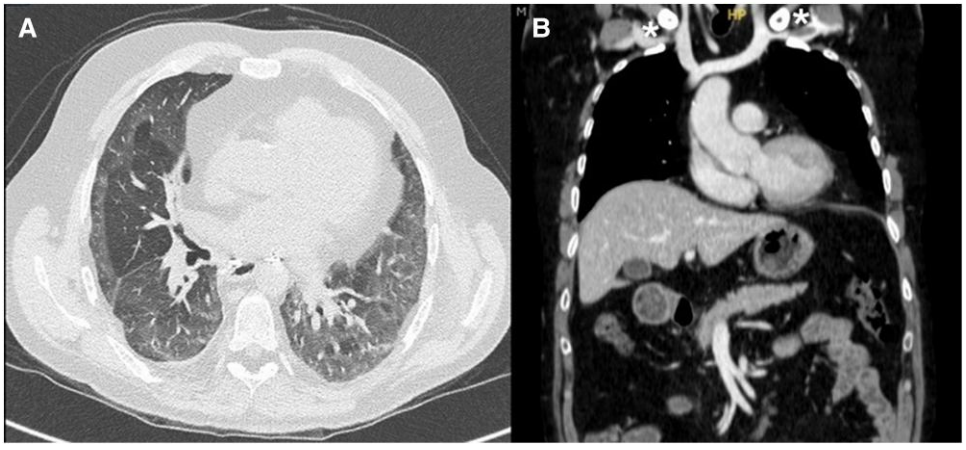


Figure 2 *(A)* Chest computer tomography with bilateral bronchiectasis, diffuse bronchial wall thickening, small areas of consolidation and pleuropulmonary fibrosis tracts. Moderate pericardial effusion. *(B)* Thoracic-abdominal-pelvic computer tomography with contrast, proximal deep vein thrombosis in both upper limbs, greater in the left upper limb (left subclavian vein). *marking thrombosis. Computer tomography (CT).

from 1.1 to 2.11 mg/dL and glomerular filtration rate dropping from 78 to 34 mL/min. Renal ultrasound ruled out vascular alterations and local complications. Proteinogram, light chains and complement were normal, tumour markers, serology and autoimmunity were negative. Viral load for Epstein–Barr virus, cytomegalovirus and BK polyomavirus was negative. Proteinuria was found to be 0.17 g/day. Antihypertensive drugs were suspended due to hypotension tendency. With all this, improvement was achieved up to creatinine 1.5 mg/dL. In 2023 he presented an episode of paroxysmal atrial fibrillation, prompting the initiation of permanent anticoagulation.

In 2024 (+23 years after cardiopulmonary transplantation, +7 years after renal transplantation), the patient was admitted with dyspnoea, fever and desaturation. Pulmonary thromboembolism was ruled out and he was diagnosed with pulmonary graft dysfunction. During admission he developed hypovolemic shock due to an abdominal haematoma in the anterior rectum. An active abdominopelvic haemorrhage was detected with a focus from the left epigastric artery that required embolization by interventional radiology, together with haemoptotic sputum due to alveolar haemorrhage (*Figure 3*). Despite receiving intensive treatment, including prophylactic intravenous antibiotic until infection was ruled out, red blood cell, platelets, and fibrinogen transfusions, anticoagulation reversal, exclusion of fungal infection reactivation, embolization of the bleeding focus, and careful immunosuppressant level management, the patient remained in global respiratory failure with progressive clinical deterioration. Finally, with no signs of improvement, palliative measures were prioritized and the patient died during this admission at +23 and +7 years after cardiopulmonary and renal transplantation, respectively, with the diagnosis of lung transplant rejection.

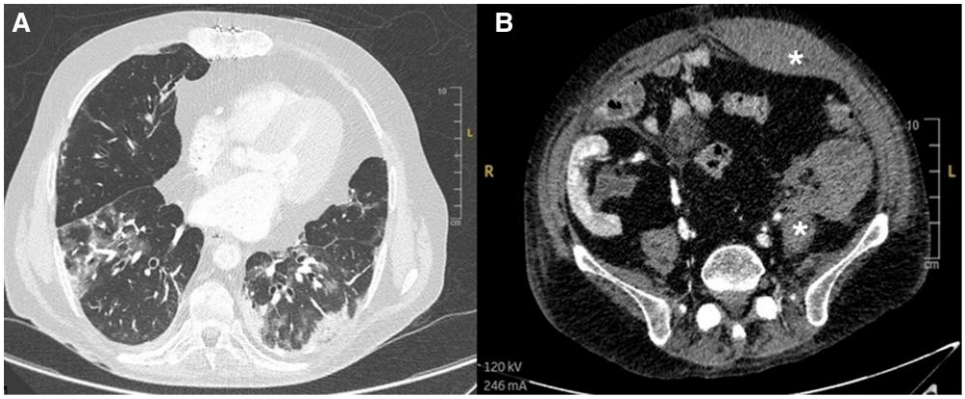


Figure 3 *(A)* Chest computer tomography, patchy parenchymal opacities in all lobes with ground glass pattern suggestive of alveolar haemorrhage. Moderate pericardial effusion. *(B)* Left retroperitoneal haematoma, abdominal wall haematoma in the anterior rectus abdominis, contrast leakage due to active bleeding from the left epigastric artery. *marking haematoma. Computer tomography (CT).

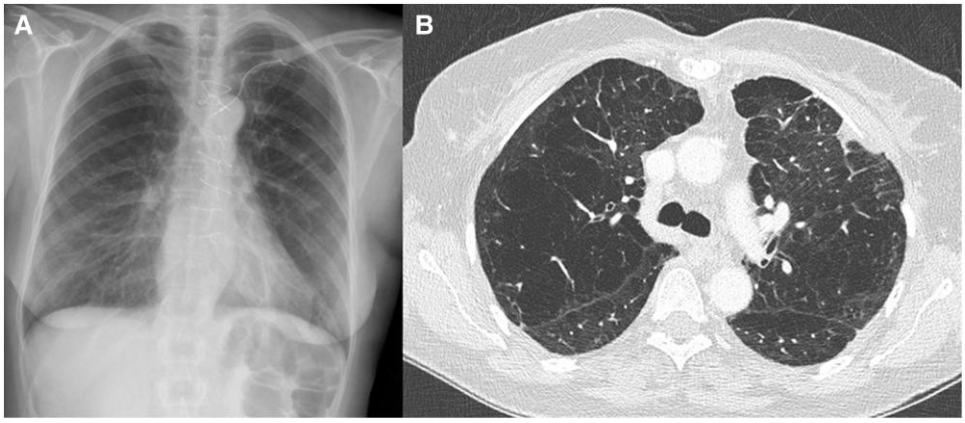


Figure 4 *(A)* Postero-anterior chest X-ray with hyperclarity in upper lobes due to emphysema (signs of chronic obstructive pulmonary disease). *(B)* Chest computer tomography with severe confluent type centroacinar emphysema, predominantly in upper lobes, simultaneous presence of paraseptal emphysema. Computer tomography (CT).

Patient 2

The second case involves a 57-year-old woman, a former smoker, with HT by bicava technique in 2019 for obstructive hypertrophic cardiomyopathy with a very severe gradient and severe mitral regurgitation due to systolic anterior motion. Genetic testing confirmed an R891fs mutation in the MYBPC3 gene.

During follow-up, the patient experienced a complication within the first month post-transplant: a tension pneumothorax requiring drainage and subsequent surgery (bullectomy by left minithoracotomy). During the procedure, lung biopsy samples were obtained, revealing altered pulmonary parenchyma with diffuse and sub-pleural emphysema, sub-pleural bulla formation, patchy interstitial fibrosis, patchy chronic pleuritis with foci of reactive mesothelial hyperplasia, respiratory bronchiolitis and anthracosis. No evidence of malignancy was found. Following this episode, a pulmonary evaluation and ongoing follow-up were initiated and the patient was diagnosed with severe emphysema with a body max index, airflow obstruction, dyspnoea, and exercise score of 4 points. Imaging studies revealed bullae in both lungs and reduced radiopharmaceutical uptake in the upper fields, particularly in the antero-apical segment of the right upper lobe on perfusion scanning (*Figures 4* and *5*). The patient had previously experienced dyspnoea and was a former smoker; however, this was initially attributed to her heart disease and pulmonary function tests prior to transplantation showed only mild obstruction.

Four years after HT, the patient was cardiologically stable with appropriate immunosuppressive levels of mycophenolate and tacrolimus. However, she experienced progressive respiratory decline, eventually requiring ambulatory oxygen therapy. After verifying normal cardiac function, ruling out pulmonary hypertension by right heart catheterization, and excluding coronary involvement, she was placed on the waiting list for a single-lung transplant at the end of 2023.

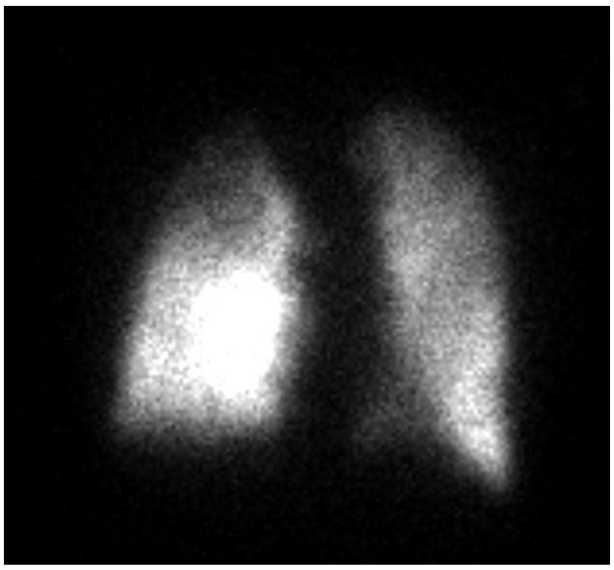


Figure 5 Perfusion scan, antero-posterior projection with radiopharmaceutical hypocapture in superior fields mainly in the antero-apical segment of the right upper lobe.

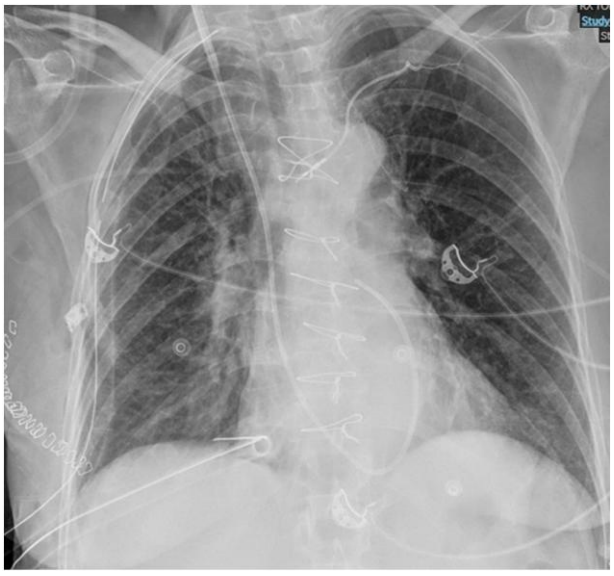


Figure 6 Postero-anterior chest X-ray after right lung transplantation.

In February 2024 (+5 years HT) a right single-lung transplant was performed (*Figure 6*). As a post-surgical complication she developed a sub-pleural intra-parenchymal haematoma in the right lower lobe, related to the surgical suture. This was managed conservatively and showed favourable evolution (*Figure 7*). Acute rejection was ruled out based on the absence of neutrophils in bronchoalveolar lavage and biopsy showing no signs of acute cellular rejection. Her recovery progressed well, and at discharge, she remained on immunosuppressive therapy with tacrolimus, mycophenolate mofetil and prednisone.

Currently, the patient continues joint follow-up with cardiology and the lung transplant unit. She maintains preserved cardiac function, no significant valvular disease and no signs of pulmonary hypertension on echocardiography, with stable oxygen saturation.

Discussion

Although combined and sequential HT with other organs is not uncommon, certain combinations are unusual, such as the two cases presented (sequential combined cardio-bipulmonary and renal transplantation and sequential single-lung transplantation).

Patients with more than one transplanted organ represent a challenge both surgically and during postoperative management due to a higher risk of complications. On one hand, it has been described that these transplants may have a lower risk of rejection due to a higher antigenic load.[4] However, in clinical practice, the risk of immunological rejection remains elevated due to less established protocols. This underscores the need for rigorous long-term monitoring of these patients.

Irregularities or modifications in immunosuppressive therapy increase the risk of opportunistic infections. Cytomegalovirus and Epstein–Barr virus are common in all three organ types involved in the cases (lung, heart, and kidney) with pulmonary function being most severely affected. Opportunistic bacterial infections such as Nocardia are prevalent in highly immunosuppressed patients, particularly lung transplant recipients. Additionally, parasites like Toxoplasma gondii pose a greater risk to heart transplant recipients, who are particularly susceptible. Fungal infections are common in patients with high levels of immunosuppression regardless of the organ transplanted. Aspergillus infections primarily affect lung and heart transplant recipients and can lead to invasive aspergillosis, a potentially fatal condition due to its ability to spread to other organs, as observed in the clinical case presented.[5]

Despite the additional challenges associated with multi-organ transplantation, short-term survival outcomes (1–5 years) are comparable to those of single-organ transplants in published series. This highlights the importance of careful patient selection to maximize benefits, as well-selected candidates can achieve survival rates similar to those of single-organ transplantation. However, a significant selection bias exists, as many patients die while on the waiting list or are removed due to emerging contraindications before transplantation.[6] Regarding long-term survival, data remain limited due to the rarity of these cases and the small sample sizes in available studies. Generally, when the lung is involved (as in cardiopulmonary transplantation), long-term survival is comparable to that of isolated lung transplantation but somewhat worse with respect to cardiac transplantation, and when rejection or infections occur, they tend to affect the lung predominantly and not the heart.[7] In cases of amyloidosis requiring combined heart-liver transplantation, some studies report better survival outcomes with combined transplantation compared with isolated HT.[8]

Ensuring optimal management and favourable outcomes of these complex patients requires a multidisciplinary approach involving experts from various transplant specialities. Therefore, it is important that this type of patients and multiple organ transplants are performed in high-level transplant centres with the presence of all the specialities involved in combined transplantation.

Despite the inherent challenges, advancements in surgical techniques, medical management and intensive care have significantly improved both outcomes and life expectancy for these patients.

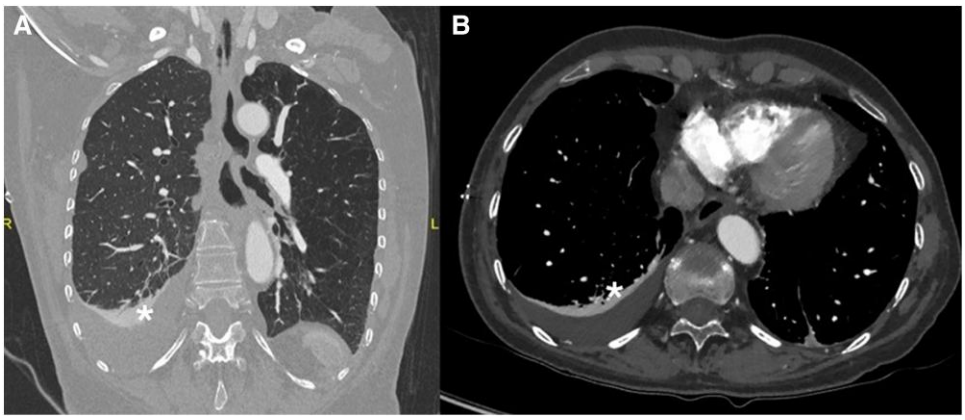


Figure 7 Thoracic-abdominopelvic computer tomography. *(A)* coronal section, *(B)* axial section; showing sub-pleural intra-parenchymal haematoma in the right lower lobe in relation to the surgical suture. *marking haematoma. Computer tomography (CT).

Lead author biography

Borja Guerrero Cervera, Degree in Medicine from the University of Valencia. Cardiologist at the Hospital Universitari i Politècnic La Fe, Valencia (2020–2024). His areas of research and publications are mainly heart failure and cardiomyopathies.

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Consent: In accordance with the COPE guidelines, the authors confirm that the patients have provided written consent for the submission and publication of this case series.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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