**Name of Journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 61156

**Manuscript Type:** CASE REPORT

**Chest pain in a heart transplant recipient: A case report**

Chen YJ *et al*. Heart transplant recipient with chest pain

Yu-Jen Chen, Chien-Sung Tsai, Tsai-Wang Huang

**Yu-Jen Chen,** Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei 11490, Taiwan

**Chien-Sung Tsai,** Division of Cardiovascular Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei 11490, Taiwan

**Tsai-Wang Huang,** Division of Thoracic Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei 11490, Taiwan

**Author contributions:** Chen YJ and Huang TW performed the surgery, reviewed the literature, and contributed to the drafting of the manuscript; Tsai CS was responsible for the revision of the manuscript for important intellectual content; all authors issued final approval for the version to be submitted.

**Corresponding author: Tsai-Wang Huang, PhD, Associate Professor, Chief Doctor,** Division of Thoracic Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, No. 325 Sec.2, Chenggong Road, Neihu District, Taipei 11490, Taiwan. chi-wang@yahoo.com.tw

**Received:** November 26, 2020

**Revised:** January 26, 2021

**Accepted:** April 12, 2021

**Published online:**

**Abstract**

BACKGROUND

Heart transplantation is recommended for the treatment of patients with refractory heart failure. Chest pain after heart transplantation is usually considered noncardiac owing to the denervated heart. However, data from case reports on tacrolimus-induced achalasia after heart transplantation are limited. We aimed to present a case of tacrolimus-induced achalasia that developed after heart transplantation, which was successfully relieved by laparoscopic Heller myotomy.

CASE SUMMARY

A 67-year-old man with a history of Type 2 diabetes mellitus, hyperlipidemia, and dilated cardiomyopathy had congestive heart failure following orthotopic heart transplantation with tacrolimus treatment 12 years ago. At the 10-year follow-up after the heart transplantation, the patient presented with persistent cough, dysphagia, heartburn, and retrosternal chest pain lasting for 2 wk. Upper endoscopy revealed no specific findings. Two years later, the patient experienced the same symptoms, including chest pain lasting for 4 wk. Esophagogram and manometry confirmed the presence of achalasia. Previous reports showed that discontinuing calcineurin inhibitor (CNI) treatment and endoscopic botulinum toxin injection could treat CNI-induced achalasia. Owing to the risk of rejection of the transplanted heart and considering the temporary benefits of botulinum toxin injection in achalasia, the patient underwent laparoscopic Heller myotomy. Dysphagia was relieved without complications. Eight months later, he had no signs of recurrence of the achalasia.

CONCLUSION

In transplant patients with chest pain and gastrointestinal symptoms, CNI-induced achalasia may be one of the differential diagnoses. Esophagogram/manometry is useful for diagnosis.

**Key Words:**Heart transplantation; Refractory heart failure; Chest pain; Achalasia; Esophagogram; Case report

Chen YJ, Tsai CS, Huang TW. Chest pain in a heart transplant recipient: A case report. *World J Clin Cases* 2021; In press

**Core Tip:** Chest pain after heart transplantation usually present with noncardiac symptoms due to the denervated heart. Its differential diagnosis includes acute allograft dysfunction caused by acute myocardial infarction, myocarditis, hypertensive crisis, or infections. However, data from case reports on tacrolimus-induced achalasia after heart transplantation are limited. In this case involving a rare complication of tacrolimus-induced achalasia after heart transplantation, we successfully treated the patient with laparoscopic Heller myotomy. This case highlights that calcineurin inhibitor -induced achalasia should be considered in transplant patients with atypical chest pain. Esophagogram or manometry may be helpful for its diagnosis.

**INTRODUCTION**

Heart transplantation is the definitive treatment for patients with refractory end-stage heart failure. Although coronary artery disease develops within 3 years of heart transplantation, chest pain after heart transplantation is usually considered noncardiac because the transplanted heart is assumed to be denervated[1]. Nevertheless, atypical symptoms of chest pain in transplant patients should be evaluated further. We experienced a unique case of a heart transplant recipient who complained of chest pains and was subsequently diagnosed with achalasia after a series of investigations.

Achalasia is an uncommon esophageal motility disorder of an unknown etiology characterized by failure of the relaxation of the lower esophageal sphincter (LES) and loss of esophageal peristalsis. It may be caused by trauma or medications. Previous case reports describe patients diagnosed with calcineurin inhibitor (CNI)-induced achalasia[2]. The possible mechanism for CNI-induced achalasia is the inhibition of nitric oxide synthase, resulting in esophageal motility[3,4]. However, data from case reports on tacrolimus-induced achalasia after heart transplantation are limited. We present a case of tacrolimus-induced achalasia that developed after heart transplantation, which was successfully relieved by laparoscopic Heller myotomy.

**CASE PRESENTATION**

***Chief complaints***

A 67-year-old man presented to our institution with complaints of persistent cough, difficulty in swallowing liquid and solid food, heartburn, and retrosternal chest pain lasting for 4 wk.

***History of present illness***

Twelve years ago, the patient underwent orthotopic heart transplantation on February 13, 2008, with tacrolimus treatment without any postoperative complications. During follow-up at 10 years after the heart transplantation, the patient complained of persistent cough, dysphagia, heartburn, and retrosternal chest pain lasting for 2 wk. Upper endoscopy showed spasm of the lower esophagus, and achalasia was suspected. However, the symptoms were relieved spontaneously.

***History of past illness***

He had a history of type 2 diabetes mellitus, hyperlipidemia, and dilated cardiomyopathy with congestive heart failure status post orthotopic heart transplantation (donor: 26-year-old male).

***Personal and family history***

The patient did not consume alcohol or have the habit of smoking. There were no specific family health histories, such as mediastinal and pulmonary diseases or cancer.

***Physical examination***

He was hemodynamically stable and had normal heart sounds, fine right basal inspiratory lung rales, and normoactive bowel sounds. His blood pressure was 119/79 mmHg, heart rate was 86 beats/min, respiration rate was 18 breaths/min, and body temperature was 36.2 °C. He had no jugular vein distention, no pitting edema, symmetrical and free lung expansion and normal breathing sounds, and no palpable mass or muscle guarding over the abdominal region.

***Laboratory examinations***

Laboratory findings were as follows: white blood cell count, 7.36 × 103/μL; neutrophil count, 78.1%; and lymphocyte count, 13.9%. The endomyocardial biopsy revealed no evidence of rejection. Electrocardiogram revealed a sinus rhythm without ST-segment elevations.

***Imaging examinations***

Esophagogram (Figure 1) showed failure of relaxation of the LES with a diverticulum and a dilated esophagus with the bird's beak sign. Manometry (Figure 2) revealed abnormal peristalsis of the esophagus with a high residual pressure of LES.

**FINAL DIAGNOSIS**

Based on the history and findings of the imaging examinations, the patient was diagnosed with CNI-induced achalasia.

**TREATMENT**

The patient underwent laparoscopic Heller myotomy.

**OUTCOME AND FOLLOW-UP**

After the procedure, the symptoms of dysphagia were relieved without complications. The patient recovered well and was discharged from the hospital. At 8 mo after hospital discharge, he had no symptoms of dysphagia or recurrence of achalasia.

**DISCUSSION**

Owing to cardiac denervation, most transplant patients complain of atypical chest pain due to acute allograft dysfunction caused by acute myocardial infarction, myocarditis, hypertensive crisis, or infections[5]. Additionally, transplant patients suffer from not only atypical chest pain but also gastrointestinal symptoms. CNI-induced achalasia should be one of the differential diagnoses. Esophagogram or manometry is recommended for its diagnosis.

To the best of our knowledge, there had been no case report of tacrolimus-induced achalasia forming after heart transplantation and successfully relieved by laparoscopic Heller myotomy. Based on the onset time of achalasia in our case, operative trauma of the vagal nerve was less likely. A previous report showed that changing different CNIs and endoscopic botulinum toxin injection could treat CNI-induced achalasia[2]. In our case, switching from tacrolimus to cyclosporine was not considered owing to the risk of rejection of the transplanted heart. Moreover, the onset time of CNI-induced achalasia in our case was different from that of the previous report[2] owing to the development of dysphagia immediately after the initiation of CNI. Botulinum toxin injection was not considered owing to its temporary benefits in achalasia. Subsequently, laparoscopic Heller myotomy was considered in our case.

**CONCLUSION**

We recommend screening for calcineurin inhibitor-induced achalasia if transplant patients complain of atypical chest pain with gastrointestinal symptoms. The condition can be diagnosed using an esophagogram or manometry.

**ACKNOWLEDGEMENTS**

We thank Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan.

**REFERENCES**

1 **Stark RP**, McGinn AL, Wilson RF. Chest pain in cardiac-transplant recipients. Evidence of sensory reinnervation after cardiac transplantation. *N Engl J Med* 1991; **324**: 1791-1794 [PMID: 2038368 DOI: 10.1056/nejm199106203242507]

2 **Campos M**, Matlock R. Endoscopic Botulinum Toxin Injection for Tacrolimus-Induced Achalasia in a Renal Transplant Recipient. *Gastroenterology Res* 2019; **12**: 171-173 [PMID: 31236159 DOI: 10.14740/gr1168]

3 **Cook LG**, Chiasson VL, Long C, Wu GY, Mitchell BM. Tacrolimus reduces nitric oxide synthase function by binding to FKBP rather than by its calcineurin effect. *Kidney Int* 2009; **75**: 719-726 [PMID: 19177155 DOI: 10.1038/ki.2008.697]

4 **Hämäläinen M**, Lahti A, Moilanen E. Calcineurin inhibitors, cyclosporin A and tacrolimus inhibit expression of inducible nitric oxide synthase in colon epithelial and macrophage cell lines. *Eur J Pharmacol* 2002; **448**: 239-244 [PMID: 12144947 DOI: 10.1016/s0014-2999(02)01947-7]

5 **DeFilippis EM**, Nayor M, Lewis EF. Chest Pain and Shortness of Breath After a Heart Transplant. *JAMA Cardiol* 2017; **2**: 1271-1272 [PMID: 28975203 DOI: 10.1001/jamacardio.2017.2337]

**Footnotes**

**Informed consent statement:** Informed written consent was obtained from the patient to publish this report and any accompanying images.

**Conflict-of-interest statement:** The authors declare that they have no conflict of interest.

**CARE Checklist (2016) statement:** The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/Licenses/by-nc/4.0/

**Manuscript source:** Unsolicited manuscript

**Peer-review started:** November 26, 2020

**First decision:** January 23, 2021

**Article in press:**

**Specialty type:** Gastroenterology and hepatology

**Country/Territory of origin:** Taiwan

**Peer-review report’s scientific quality classification**

Grade A (Excellent): A

Grade B (Very good): 0

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Zhang DM **S-Editor:** Zhang L **L-Editor: P-Editor:**

**Figure Legends**



**Figure 1 Esophagogram.** A dilated esophagus with the bird's beak sign, esophageal dysmotility, and failure of relaxation of the lower esophageal sphincter; Status after median sternotomy with surgical wire fixation for heart transplant.



**Figure 2 Manometry.** Abnormal peristalsis of the esophagus with high residual pressure of the lower esophageal sphincter.