

## Cytomegalovirus esophagitis presents as chest pain in a renal transplant recipient

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### *To the Editor,*

Cytomegalovirus (CMV) infection occurs in a large proportion of transplant patients and is the most common viral cause of clinical disorders in these patients. In particular, CMV esophagitis is the second most common gastrointestinal (GI) manifestation, next to colitis. No patient is asymptomatic, and the clinical manifestations include difficult or painful swallowing (59%), nausea or vomiting (42%), abdominal pain (19%), weight loss (25%), fever (20%), and diarrhea (20%) [1]. Our case is unique because it is the first reported case of CMV esophagitis that presented with radiating right chest wall pain without other symptoms. Our patient was treated successfully by intravenous (IV) ganciclovir.

A 48-year-old male was hospitalized with a 2-day history of chest wall pain. In 1988, the patient developed an end stage renal failure secondary to hypertension. After 2 months of hemodialysis, he received a renal allograft from his father, which failed after 12 years due to chronic rejection. In May 2008, he received a second cadaveric renal allograft, and was treated thereafter with an immunosuppressive regimen of tacrolimus, mycophenolate mofetil and prednisone. He was discharged after 3 weeks, but returned to the emergency room 2

days later presenting with pain in his right chest wall.

Continuous and severe pain was localized in the right nipple area, and breathing or changing posture did not appreciably influence the severity of the pain. No dyspnea, heartburn, or dysphagia was present, and there was no tenderness on palpation. His temperature was 36.0°C, and his vital signs were stable. The results of the physical examination and laboratory data were normal. The electrocardiogram (ECG) was normal and no mediastinal widening or pulmonary congestion was noted on chest radiograph. Soon after admission, the patient underwent empiric treatment with acetaminophen and tramadol for his chest pain, without a clinical response. Follow-up markers of myocardial injury and ECG showed no interval change. Skin examination showed no evidence of herpes zoster infection. A bone scan was negative, and a computed tomographic (CT) scan of the chest was normal. A nerve block was conducted by an anesthesiologist to address the patient's continuous and increased right chest wall pain, but no clinical response was noted.

On the 8th hospital day, endoscopic examination revealed a deep ulcerative lesion and whitish plaque (Fig. 1). The distance from the incisor was 28 cm. An endoscopic biopsy revealed an

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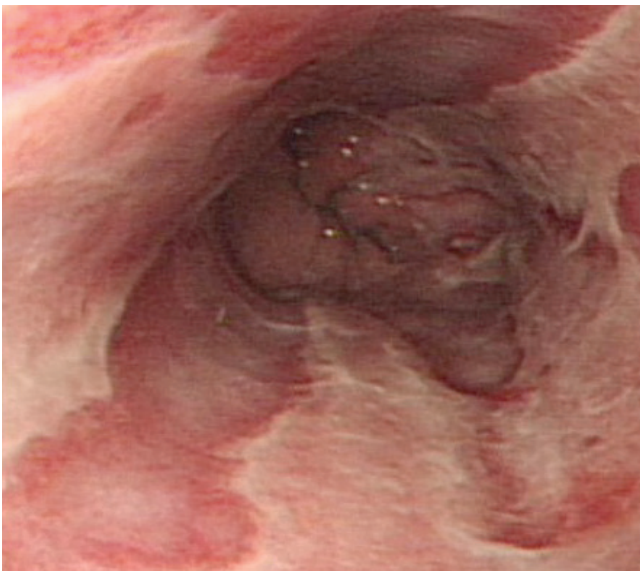
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ulceration with viral inclusion-like structures in the epithelium, suggestive of virus-induced esophagitis. CMV esophagitis was confirmed by CMV immunohistochemical stain using a biopsy sample (Fig. 2), although the results of CMV polymerase chain reaction and antigen were normal at that time. The patient was treated with ganciclovir (5 mg/kg intravenously every 12 hours) for CMV esophagitis. By day 2, his symptoms had improved rapidly. He received IV ganciclovir treatment for 14 days, which was then changed to oral valganciclovir. The patient had no more localized chest wall pain.

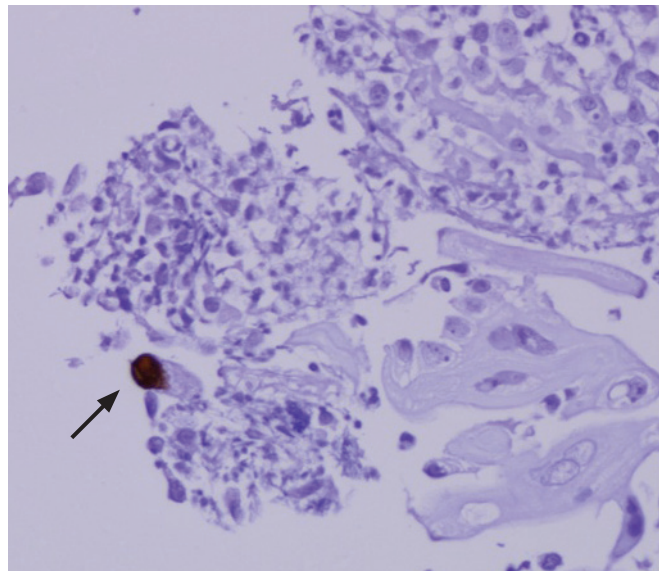
In summary, this case is interesting because it is a rare example of CMV esophagitis that presented only as radiating right chest wall pain, without dysphagia or epigastric pain, after renal transplantation. Upon first examination in the emergency room, we believed the pain was derived from costochondritis; however, the local tenderness lasted only a few hours and the pain severity increased. Next, we considered herpes zoster infection, but skin vesicles never appeared. Soft tissue infection and mass were ruled out by chest CT. The patient had liver cirrhosis, so we performed an endoscopic examination to confirm esophageal varices. We did not expect to find the cause of his pain. Duodenoscopic examination revealed CMV esophagitis, not esophageal varices.



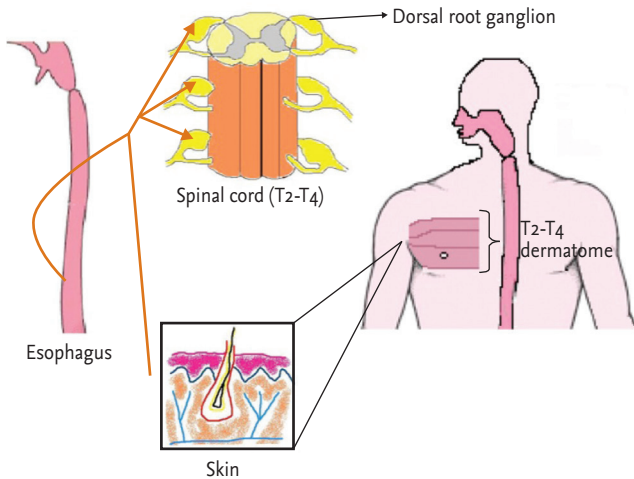
**Figure 1.** Endoscopic finding shows deep ulceration and whitish plaque in the mid- to distal esophagus.

We have noticed that patients with CMV esophagitis could present with right chest wall pain, especially at the T2 to T4 level. This phenomenon can be explained by viserosomatic reflex. This symptom arose from an esophageal problem radiating to the vagus nerve. Sensory information from the esophagus reaches the central nervous system (spinal neuron) via vagal and spinal visceral afferent fibers; furthermore, these neurons receive convergent somatic input from the thoracic wall. This convergence of visceral and somatic input provides a neural basis that explains the esophageal pain referral to the chest area [2]. Localized visceral stimuli produce patterns of reflex responses in segmentally related somatic structures (Fig. 3). For example, the oropharynx radiates to T1 to T2, the esophagus to T2 to T4 (right) and the duodenum to T6 to T8 (right). Our patient complained of T2 to T4 right somatic pain, and treatment of the somatic findings improved visceral symptoms.

To date, few cases of CMV disease with atypical presentation in renal transplant patients have been reported. In one case of CMV esophagitis, the patient presented with epigastric pain that decreased in the supine position, increased while sitting and further increased when standing or walking [1]. A similar case report of CMV gastritis was reported with postural epigastric pain. In another case, a patient presented



**Figure 2.** Pathologic finding of esophageal biopsy. Note brown stained cytomegalovirus inclusion (arrow) (immunohistochemical stain,  $\times 400$ ).



**Figure 3.** Viscerosomatic reflex of the esophagus.

with fever, leukopenia, and thrombocytopenia 1 week after undergoing an external hemorrhoidectomy [3]. Biopsy of the hemorrhoidal tissue showed CMV, which was confirmed via a positive PP65 antigenemia. The patient improved after ganciclovir treatment. In our case, the patient presented only with radiating right chest wall pain. This pain differed from chest pain such as angina pectoris, which is usually described as a squeezing or burning substernal sensation that radiates to the back, neck, jaw, or arms. It was also distinguished from typical esophagitis pain that presents with moderate to severe focal substernal pain with swallowing. In severe cases of CMV esophagitis, patients tend to drool or spit to avoid swallowing. Such misery is not uncommon with CMV since the majority of cases are characterized by one or more deep ulcerations, usually in the distal third of the esophagus. Our patient presented only with right nipple area somatic pain, which was neither retrosternal chest pain nor GI despite a deep ulceration in the distal third portion. This type of pain has not been described as a specific symptom in any other clinical entity.

The importance of this type of atypical presentation is that clinicians must be aware of the hazards of CMV infection in immunocompromised patients, even with an unusual presentation [3,4]. We conclude that the possibility of CMV disease should be explored in all kidney transplant patients within the first 6 months posttransplantation because massive immunosup-

pressive therapy for the prevention of graft rejection increases the risk for CMV infection. In particular, the risk factors are: 1) treatment induction with thyroglobulin, 2) transplantation recipients with donor seropositive/recipient seronegative (D+/R-) status, 3) African-American recipients, 4) patients older than 50 years, and 5) cadaveric donor recipients [5]. In our case, the donor kidney was cadaveric, which might increase the possibility of CMV infection. Despite infection, early diagnosis and treatment helped resolve the problem with a good prognosis in this case. It is critical to assess the recipient's potential for CMV infection, and to initiate prophylactic or preemptive treatment with ganciclovir before serious complications develop.

**Keywords:** Chest wall pain; Cytomegalovirus esophagitis; Viscerosomatic reflex

### Conflict of interest

No potential conflict of interest relevant to this article is reported.

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