

Responses to Reviewers

Responses to Reviewer #1

This is a case report of Wilms Tumor and dilated cardiomyopathy, which is rare but suggestive of presence of the tumor. Please clarify the followings:

1. Did the patient have acute myocarditis, in addition to cardiomyopathy? If so, please clarify how cardiac inflammation was identified. Was the CPK level elevated? Were MRI and viral infection panel performed?

We thank the reviewer for this comment. This patient has acute myocarditis, in addition to dilated cardiomyopathy because cardiac enzymes were elevated. Serum CKMB was 6.1 ng/mL (normal: < 4.8 ng/mL) and troponin T was elevated (50 pg/mL, normal: < 14 pg/mL). MRI was not performed in this patient. Viral panel study was negative such as enterovirus, CMV, EBV, etc.

Additionally, we added laboratory value of serum CKMB (highlighted in yellow color) in laboratory testing section in our revised manuscript (page 7, last paragraph 1, line 4).

2. In order to clarify the origin of the elevated chromogranin A, renin, and aldosterone, were contents of these substances compared with those of adjacent tissues? How about performing immunohistochemical analysis?

We thank the reviewer for this comment. Immunohistochemical analysis was not performed in this patients. However, plasma renin and aldosterone were markedly elevated in this case. Plasma renin activity was 34.75 ng/mL/hr (normal: 0.06-4.69 ng/mL/hr). Plasma aldosterone was 961 pg/mL (normal: 20-180 pg/mL). After three courses of chemotherapy, the tumor mass decreased in size and plasma renin activity was 19.06 ng/mL/hr (normal: 0.06-4.69 ng/mL/hr). Additionally, his plasma renin decreased to a normal level (2.83 ng/mL/hr) after tumor removal.

3. What caused cardiomyopathy?

We thank the reviewer for this comment. Several studies postulated renin and vasoactive mediators causing the congestive heart failure and cardiomyopathy (ref#3-6). Two hypotheses have been proposed for the etiology of hyperreninemia, including a mechanical compression of the renal artery leading to renal ischemia and a production of renin by the Wilms tumor. In our case, the tumor mass displaced the left renal vessels, with a gross invasion causing a filling defect of thrombus in the left renal vein that was likely the cause of the elevated serum renin. The hyperreninemia resulted in increased angiotensin II, aldosterone and vasoconstriction, as

well as fluid retention, all leading to hypertension and dilated cardiomyopathy. In addition, several studies have demonstrated that angiotensin II plays an important role in cardiac remodeling and dysfunction, regardless of the hemodynamic abnormality.

Responses to Reviewer #2

The manuscript is well-written, with descriptive figures and an informative table. It deserves publication especially for educational purpose.

We thank the reviewer for this comment.
