Answering reviewers

Dear professor:

I am very glad to hear from you. Thank you for reviewing the manuscript. I am grateful to you for the valuable suggestions provided. Here are responses to the reviewer comments:

Comment 1: Introduction section As Cutaneous epithelioid angiomatous nodule (CEAN) is a rare condition, please, add more general information. Do risk factors for CEAN exist? What are the possible complications of CEAN? What are CEAN therapeutic alternatives, if any?

The general information of CEAN has been added in Background. Only one case so far recently reported that patient's impaired immune status might be a risk factor for CEAN since it was first described in 2004. There are only about 32 articles in English related about CEAN and the complications of CEAN remains unclear. Surgical excision and cryotherapy are the treatments of choice for CEAN.

Comment 2: Case presentation section "A 19-year-old boy with NS intermittently had relapse of legs edema in the past 6 years, and found large black nodules". Does this edema obey to nephrotic syndrome or any other etiology? Is there any evidence of hypertension in the venous system or any lymphedema? The kidney disease seems to be an IgA related glomerulopathy, why so many immunosuppressive therapies? Did the patient´s treatment include renin-angiotensin system blockade? Was the patient always nephrotic? Was cyclosporine dose just 100 mg daily? Less than 2 mg/Kg/d? What happened to the kidney disease after cyclosporine withdrawal?

The edema obeyed to nephrotic syndrome (NS) because the results of doppler ultrasonography of the lower extremity and echocardiography were fine and there is no family history about hypertension. As for the many immunosuppressive therapies, the patient had relapse of NS for many times and it was difficult to have it under control only with methylprednisolone and the patient visited many other doctors before. In fact, the valsartan had been applied before this hospitalization and it was discontinued this time. The patient was hospitalized this time with the cyclosporine dose of 100 mg daily

and not always with the dose of 100mg daily. After cessation of cyclosporine and 16 months follow-up, the results of urine protein recently have been negative for several months with methylprednisolone and atorvastatin.

Comment 2: Discussion section As the authors mentioned the oncological potential of cyclosporine and, as CEAN seem to be an endothelial derived pathology, could it be added a comment about Kaposi´s sarcoma as it is also related to immunosuppression, tends to vanish with reduction of immunosuppressive therapy if any and is related to a chronic viral infection as CEAN could be as well? Conclusion section "The impaired immune status is one of risk factors for CEAN". Is it? Or is it just proposed?

It might be that *CEAN* was related to a chronic viral infection alike the Kaposi´s sarcoma. But no association with either infection or trauma has yet been described before. And one case published in 2018 reported that CEAN might be associated with immunosuppression and patient's impaired immune status. Impaired immune status is proposed to be one of risk factors for CEAN without strong enough evidences. And the odds of infection would increase with impaired immune status.

I would be happy to make any further changes that may be required.

We are looking forward to hearing from you.

Yours Sincerely,

Shuifu Tang

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