Responses for comments

Dear Editor and Reviewer:

We thank you very much for giving us an opportunity to revise our manuscript. Thanks a lot for the helpful comments and recommends and thank you for your time spent. According to the reviewers' comments, we have revised the manuscript. Revised portion are marked in red in the paper.

The main corrections in the paper and the responds to the comments are as follows:

Reviewer #1:

1.Authors have mentioned that no etiology exists, however, at another place they have mentioned PIK3CA mutation. Kindly modify the article accordingly. PIK3CA-related overgrowth spectrum (PROS) should be described in brief.

Answer: Thanks to your valuable suggestions and your careful review of my manuscript. As for the etiology of Klippel-Trenaunay syndrome(KTS), we did not accurately describe it. I have modified it accordingly. Please see the red font below:

Klippel–Trenaunay syndrome (KTS) is a congenital vascular malformation with a complicated etiology. It is sporadic and clinically rare in occurrence.

The etiology of KTS are complex and controversial. The somatic PIK3CA mutation is believed to cause abnormal hypertrophy of the blood vessels, bone, and soft tissues. Furthermore, chromosome translocation may be involved. A recent theory suggested that this disease is related to mesodermal dysplasia acting on angiogenesis.

In addition, I have described the PIK3CA-related overgrowth spectrum (PROS) briefly in the paper. Please see the red font below:

PROS is defined as a series of rare congenital disease syndromes due to mutations in *PIK3CA*.(See the answers to question 3 for more details)

2. The diagnosis of filariasis cannot be made given the clinical presentation. Authors make make necessary amendments in the title and the text.

Answer: Thanks to your valuable suggestions .Indeed, the diagnosis of filariasis cannot be made solely on the basis of clinical manifestations. Only through careful inquiry of the patient's medical history did we know that she had been diagnosed with filariasis in other hospitals and given anti-filariasis drugs, but we did not know the details. At the beginning, we almost thought that the swelling of the patient's left lower limb was filariasis as diagnosed in other hospitals. However, after careful physical examination of the patient and relevant examinations, we did not consider filariasis. But I have to say, at first sight of the patient's left lower limb, the first reaction was filariasis. Because before that, we didn't know about KTS.

I have modified it accordingly.Please check the red font below:

Herein, we have reported a case of KTS characterized by crossed-bilateral extremity involvement combined with lower gastrointestinal hemorrhage and hematuria. Based on our literature search, we could not find any other similar case. This patient was initially misdiagnosed in other hospitals to have filariasis and hemorrhoid bleeding.

3. Authors should discuss the findings, classification, and diseases following the ISSVA classification.

Answer: Thank you for your valuable suggestions . I have added the relevant information in this paper. Please see the red words below:

PROS is one of the subcategories in the latest (2018) ISSVA classification, which, in addition, to including KTS, it also includes fibroadipose hyperplasia or overgrowth (FAO); congenital lipomatous overgrowth, vascular malformations, epidermal nevi, scoliosis/skeletal and spinal (CLOVES) syndrome; fibroadipose infiltrating lipomatosis/facial infiltrative lipomatosis (FIL); hemihyperplasia multiple lipomatosis (HHML); macrodactyly; megalencephaly-capillary malformation (MCAP/M-CM); fibro-adipose vascular anomaly (FAVA); capillary, lymphatic, and venous malformations (CLVM) and lymphatic malformation (LM). These diseases are characterized by vascular malformations and tissue overgrowth. Because KTS has several overlapping clinical features with other syndromes such as CLOVES syndrome and Fibroadipose Vascular Anomaly (FAVA)[27], it needs to be distinguished from these diseases.

4. Visceral involvement is about 1%

Answer: Thanks to your valuable suggestions.I have added the relevant information to the article，Please see the red words below:

According to the literature, KTS marked by the involvement of both the gastrointestinal and urogenital systems is rare (about 1%) and only one case of KTS with crossed-bilateral extremity involvement has been reported.

5. Authors cannot be certain that it is the first case report. They should mention that according to their literature search, they could not find any other similar case.

Answer：Thank you so much. It is your valuable advice that makes me realize that our description of this point in the article is not accurate. We have made corresponding modifications, please see the red font below：

Herein, we have reported a case of KTS characterized by crossed-bilateral extremity involvement combined with lower gastrointestinal hemorrhage and hematuria. Based on our literature search, we could not find any other similar case.