

Dear Editor,

I am pleased to resubmit for publication in your journal the revised version of Manuscript

NO: 78967, entitled FIBROUS HAMARTOMA OF INFANCY WITH BONE DESTRUCTION OF THE TIBIA:A CASE REPORT.

I really appreciated the suggestions from you and the reviewers, which I have tried to address.

Following your suggestions throughout the manuscript and the reviewers' comments, I made the some changes and additions.

To follow, answers to each of the two reviewers:

Reviewer's code: 05916273

Thank you for your appreciated and accurate observations. In particular, in answer to each of them

1、 How long after the surgery?

Response: Thank you for your valuable question. We followed-up the patient for 36 months and she did not show any signs of recurrence.

2、 Just a case report not enough evidence to reach such a sweeping conclusion

Response: Thank you for your valuable question. In our first operation, the lesion was removed with a margin of 1 cm, and the lesion recurred 4 months after the operation. In the second operation, the lesional tissue was removed with a margin of 1.5 cm. After 36 months of follow-up, no recurrence was found in the patient. We evaluated the postoperative outcomes after the two operations. We found that fibrous hamartoma with bone destruction may show a better response with resection margins of 1.5 mm than those of 1 mm. To the best of our knowledge, no report on the resection margins of fibrous hamartoma has been documented.

3、 Do you mean low compared to the surrounding tissue or normal?

Response: Thank you for your pertinent question. We apologize for the ambiguous description. We meant 'normal tissue'.

4、 Something is missing!

Response: Change the sentence to wound closure was completed in layers.

5、 How long after the surgery?

Response: Thank you for your valuable question. We followed-up the patient for 36 months and she did not show any signs of recurrence.

6、 Do you think this is sufficient to rule out a recurrence?

Response: Thank you for your insightful question. The child was followed up over telephone calls every 3 months within 1 year of the operation, and every 6 months thereafter (the child is located in a remote area in northwest China, and transportation is extremely inconvenient. Since the outbreak of the COVID-19, our province is one of the hardest-hit areas by the epidemic, outbreaks occur every half a year, and each time, the closure period is long. It is extremely difficult to follow-up children in our hospital, so a follow-up over the telephone is adopted). During the follow-up period, the patient's family informed that the skin color of the child at the surgical site was normal, skin temperature was normal, there was no obvious swelling and pain, her activities were

normal, and no obvious claudication was found. Therefore, we believe that the child's surgical results were satisfactory and there was no sign of recurrence.

7、 Will infiltrative not be a better word?

Response: Thank you for your pertinent suggestion. We agree that 'infiltrative' will be a better word. We have made the change in the manuscript.

8、 Please state the duration of follow up

Response: Thank you for your valuable comment. No obvious abnormality was found during the follow-up period of 36 months after the second surgery.

9、 May not

Response: Thank you for your insightful suggestion. We agree that 'may not' would be more suitable. We have made the change in the manuscript.

10、 Correct the indiscriminate use of capital letters in referencing (i.e the journal topic). See references 2 and 5

Response: Thank you for your significant suggestion. References have been revised as per your suggestion, including references 2 and 5.

Reviewer's code: 02482011

Thank you for your appreciated and accurate observations. In particular, in answer to each of them

1、 SMA

Response: Thank you for your insightful question. SMA is short for Smooth Muscle Actin

2、 Ki-67

Response: Thank you for your valuable question. Ki-67 protein has been widely used as a proliferation marker for human tumor cells for decades. In recent studies, multiple molecular functions of this large protein have become better understood. Ki-67 has roles in both interphase and mitotic cells, and its cellular distribution dramatically changes during cell cycle progression. These localizations correlate with distinct functions. For example, during interphase Ki-67 is required for normal cellular distribution of heterochromatin antigens and for the nucleolar association of heterochromatin. During mitosis, Ki-67 is essential for formation of the perichromosomal layer (PCL), a ribonucleoprotein sheath coating the condensed chromosomes. In this structure, Ki-67 acts to prevent aggregation of mitotic chromosomes. Here, we present an overview of functional roles of Ki-67 across the cell cycle and also describe recent experiments that clarify its role in regulating cell cycle progression in human cells. Ki-67 was first identified as an antigen in Hodgkin lymphoma cell nuclei (Gerdes et al. 1983) that is highly expressed in cycling cells but strongly down-regulated in resting G0 cells (Gerdes et al. 1984). This characteristic has made Ki-67 a clinically important proliferation marker for grading multiple types of cancers (Gerdes et al., 1987; Dowsett et al., 2011), with well-established prognostic value in large studies (Luo et al., 2015; Pyo et al., 2015; Pezzilli et al., 2016; Richards-Taylor et al., 2015).

Sincerely
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