

List of Responses

Dear Editors and Reviewers:

We sincerely thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Malignant Acanthosis Nigricans with Leser-Trélat sign and Tripe Palms: A Case Report" (NO.: 56859). These comments, as well as the important guiding significance to our research, are all valuable and vital for the improvement of our paper. We have studied your comments carefully and revised our manuscript accordingly in hopes of meeting with your approval. Revised portions are marked in the revised version. The main corrections in the paper and the responses to the reviewer's comments are as follows:

Responds to the reviewer's comments:

1. Response to comment: (The location and appearance of the lesion in this case are different from those reported in previous similar cases.)

Response: In this case, acanthosis nigricans mainly appeared on the face and neck and as papillary wart-like hyperkeratosis with dark brown pigmentation on the areola. These manifestations are different from the extensive rash of most patients in previous reports^[1, 2]. Furthermore, the lesions of Leser-Trélat sign were mainly distributed on the face, neck, chest, back, and head, reaching more than 40 lesions, thereby not completely consistent with the typical Leser-Trélat sign^[1, 2]. Meanwhile, tripe palms mainly occurred on both palms; small, smooth, papillary projections in the shape of tripe palm were observed, consistent with the typical tripe palm^[3].

- 1 **Zhang N**, Qian Y, Feng AP. Acanthosis nigricans, tripe palms, and sign of Leser-Trélat in a patient with gastric adenocarcinoma: case report and literature review in China. *Int J Dermatol* 2015; **54**: 338-342 [PMID: 23675743 DOI: 10.1111/ijd.12034]
- 2 **Pentenero M**, Carrozzo M, Pagano M, Gandolfo S. Oral acanthosis nigricans, tripe palms, and sign of Leser-Trélat in a patient with gastric adenocarcinoma. *Int J Dermatol* 2004; **43**: 530-532 [PMID: 15230897 DOI: 10.1111/j.1365-4632.2004.02159.x]
- 3 **Chen WT**, Chu CH. Tripe palm: a paraneoplastic manifestation of gastric cancer. *Cmaj* 2019; **191**: E366 [PMID: 30936168 DOI:10.1503/cmaj.181104]

2. Response to comment: (We should describe the patient's symptoms related to cancer before diagnosis, and we should also describe the positive or negative symptoms of autoimmune disease and laboratory data for differential diagnosis, as we have described in this paper.)

Response: His face and torso had hyperpigmentation a year before he presented with such symptoms, and he had been experiencing upper abdominal pain for more than 1 month. Nonetheless, he did not have abdominal distention, hematemesis, black stool, anorexia, anemia, and other related positive symptoms and signs. Furthermore, blood routine, urine routine, stool routine, ENA spectrum, biochemistry, fasting blood glucose, erythrocyte sedimentation rate, immunoglobulin, complement, and thyroid function (triiodothyronine, thyroxine,

thyroid-stimulating hormone) test results were normal.

3. Response to comment: (We should explain why chemotherapy is available and also define the diagnostic staging of gastric cancer, which we have already described in this article.)

Response: The preoperative clinical stage of the patient was CT3N3bMx. Considering the late stage of the patient and the high risk of direct surgery, we administered three cycles of neoadjuvant chemotherapy preoperatively to shrink the tumor lesion and reduce the clinical stage^[4]; then, we further evaluated the need for surgical treatment.

4 **Das M.** Neoadjuvant chemotherapy: survival benefit in gastric cancer. *Lancet Oncol* 2017; **18**: e307 [PMID: 28483410 DOI: 10.1016/S1470-2045(17)30321-2]

4. Response to comment: (Acanthosis nigricans, Leser–Trélat sign, and tripe palms are frequently associated with advanced cancers. We would like to remind clinicians that some relevant examinations can be performed according to these special manifestations to diagnose malignant tumors as soon as possible. Our explanation was vague in the original manuscript; thus, we have made several modifications in the revised version.)

Response: The three special manifestations, namely, acanthosis nigricans, Leser–Trélat sign, and tripe palms, must be considered before or during the occurrence of tumor or skin lesions. If a patient has skin lesions, especially multiple lesions, and the symptoms worsen, or if progressive emaciation, which highly suggests malignancy in the internal organs, the healthcare team should undertake a comprehensive medical examination, determine the potential of visceral tumor, and provide the necessary treatment as soon as possible to achieve the best curative effect. Our case suggests that clinicians should pay more attention to these special manifestations, search for rare diseases, and monitor closely these patients in order to make timely diagnosis and treatment and improve the prognosis.

5. Response to comment: (I have modified the picture according to the suggestions.)

Response: Thank you for your comments.

6. Response to comment: (I have modified the picture according to the suggestions.)

Response: Thank you for your comments.

We tried our best to improve the manuscript by revising it according to your comments and suggestions. Such revisions will not influence the content and framework of the paper.

We sincerely hope that the revised manuscript is now suitable for publication in your journal.

Once again, thank you very much for your comments and suggestions.