

Dear Editor,

I greatly appreciate valuable insights and comments from you and two anonymous reviewers for improving our manuscript (MS). I am also pleased to resubmit our revised MS for your consideration, which I believe has been improved significantly and sufficiently to satisfy the standard of *World Journal of Clinical Cases*.

Enclosed please find our revision notes, in which our point-by-point response.

I look forward to receiving your favorable decision on my MS, and thank you very much for your attention and help in advance!

Sincerely Yours,

Yinglei Miao

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Comment of the Academic Editor to the authors:

1、 Please provide the author contributions. The format of this section should be like this:

Author contributions: Wang CL and Liang L contributed equally to this work; Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed research; Wang CL, Zou CC, Hong F and Wu XM performed research; Xue Jz and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed data; and Wang CL, Liang L and Fu JF wrote the paper.

Response: Added, thanks.

ORCID number: Juan Luo (0000-0001-8400-2246); Yinghan Jiang (0000-0001-8327-2671); Zi Lei (0000-0001-5664-0291); Yinglei Miao (0000-0003-2512-757X).

Author contributions: Juan Luo, Yinghan Jiang, Zi Lei, and Yinglei Miao contributed equally to this work; Juan Luo and Yinglei Miao designed research; Yinghan Jiang and Zi Lei performed research; Juan Luo and Yinglei Miao wrote the paper.

2、 Please add those statements.

Response: Added, thanks.

Informed consent statement: Informed consent to publish was obtained from the patient..

Conflict-of-interest statement: The authors declare that they have no competing interests.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

3、 Please provide and upload the approved grant application form(s).

Response: Uploaded, thanks.

4、 Please provide the telephone and fax number of the author.

Response: Added, thanks.

Telephone: 0086-13708498467

Fax: 0871-65324888

5、 Abstract: The structured abstract should be at least 250 words. The abstract subsections will include background, case summary, and conclusion, written as:

BACKGROUND (no more than 80 words)

What does this case report add to the medical literature? Why did you write it up?

CASE SUMMARY (no more than 150 words)

What were the chief complaints, diagnoses, interventions, and outcomes?

CONCLUSION (no more than 20 words)

What is the main "take-away" lesson from this case?

Response: Revised, thanks.

BACKGROUND:

Anaplastic large cell lymphoma (ALCL) is a CD30-positive T cell lymphoma, a rare type of non-Hodgkin lymphoma. The current WHO classification system divides ALCLs into anaplastic lymphoma kinase (ALK)-positive and ALK-negative groups. ALCL rarely presents in the gastrointestinal tract.

CASE SUMMARY:

A 54-year-old male was admitted to the department of gastroenterology for abdominal pain. He presented with lower abdominal pain, diarrhea and recurrent oral and penile ulcers. He was misdiagnosed with Behcet's disease and treated with prednisone. But after one month, he was hospitalized in another hospital for reexamination. This time, the lesion on the penis was biopsied for histological examination. The final pathological diagnosis was ALCL, ALK-negative (ALCL, ALK-). The patient was treated with CHOP chemotherapy. However, he died within one month.

CONCLUSION:

Gastrointestinal ALCL needs to be considered in the differential diagnosis to avoid delaying treatment. Repeated biopsy is the most important for early diagnosis and treatment.

Reviewer's Responses to Questions

Comments to the Author

Reviewer #1:

Major comments.

1. Authors should describe whether the diagnostic criteria of Behcet's disease was fulfilled or not. Only endoscopic finding are compatible with Behcet, mention it.

Response: Revised as follow (in the second paragraph of the discussion part) , thanks.

best of our knowledge, only one case reported pC-ALCL presenting as paraphimosis^[18]. Our case is the second reported case of ALCL in the penis and the first one of systemic ALK-negative ALCL. The incidence of primary intestinal lymphomas is very rare. Gastrointestinal lymphomas account for 20% of them, and most of them are mucosa-associated lymphoid tissue lymphomas^[19, 20]. We present a case of primary ALCL arising in the oral cavity, penis, and colon, which was initially diagnosed as Behcet's disease. In 2013, the International Study Group (ISG) criteria for Behcet's disease presents a new criteria that ocular lesions, oral aphthosis and genital aphthosis are each assigned 2 points, while skin lesions, central nervous system involvement and vascular manifestations 1 point each. A patient scoring ≥ 4 points is classified as having Behcet's disease. So this patient just fit the criteria. But finally, the morphologic and phenotypic features were found to be consistent with systemic ALCL, ALK-. This may be because the presence of inflammation with neutrophil infiltration affects the mucosa in systemic ALCL^[21]. Therefore, in our case,

2. Staging should be mentioned in diagnosis. Additionally, the results of bone marrow and CNS invasion should be mentioned, if evaluated.

Response: The patient had no bone biopsy and CNS examination. We added the staging at the diagnosis. Thanks for suggestions.

3. It is important what is the cause of death in this case. If relapse is casue, upfront aggressive treatments should be considered. In this case, 54-year-old is mid age, so we

can select new salvage therapy, such as Breutuximab Vedoin, and Istodax etc, and autologous and/or allogeneic SCT might be also effective treatment.

Response: Thanks for suggestions. Unfortunately we did not have the new drugs, and the patient was poor. So we did not select new salvage therapy. And the patient died soon because of colon perforation and septic shock .

Minor comments

1. Systemic ulcer lesions were temporarily improved after chemotherapy?

Response: Sorry, because of the short disease course and suddenly death, the patient did not check the colonoscopy again.

2. Clinical characteristics and outcome of 9 cases should be shown in Table for intelligibleness.

Response: Added a table, thanks.

Table1 Primary ALK negative ALCL of the gastrointestinal tract in our current study and in the literature

Author, year, ref	Gender; Age	Presenting symptom; impression	Primary site	Biopsy or surgery	Perforation	Marrow involvement	Treatment	Follow-up
Sakakibara Y et al., 2015 ¹⁰	M 65	A painful hard mass in the left buttock.	Ascending colon	Colon biopsy	(-)	(-)	Six cycles of CHOP	Achieved complete remission
Tian C et al., 2016 ¹¹	M 39	Epigastric pain with low-grade fever	Stomach	Stomach biopsy	(-)	(-)	Four cycles of CHOP, then two cycles of Hyper-CVAD/MA	Died 3 months later
Zhang W et al., 2017 ¹²	M 82	Weakness	Stomach	Stomach biopsy	(-)	(-)	Brentuximab	Clinically improved

Lee YY et al., 2017 ¹³	F 64	Not mentioned	Oesophagus	Segmental resection of distal oesophagus and proximal partial gastrectomy	(-)	(-)	Various regimens and transplantation after relapse	Died 63 months later
	M 59	Not mentioned	Stomach	Partial gastrectomy	(-)	(-)	CHOP	No evidence of disease after 81 months
	F 70	Epigastric pain with poor appetite	Stomach	Total gastrectomy and liver biopsy	(-)		CHOP and ESHAP	Died 21 months later
	M 65	Fever	Jejunum	Segmental resection	(+)	(+) (focal)	Nil	Died 0.7 month later
	M 88	Not mentioned	Terminal ileum	Segmental resection	(-)	(-)	CHOP	Alive with disease after 4 months
	M 37	Not mentioned	Terminal ileum	Right hemicolectomy	(-)	Not done	Nil	Died 0.7 month later
Current study	M 54	Lower abdominal pain and diarrhea	Colon	Penis biopsy	(+)	Not done	One cycle of CHOP	Died 1 month later

Reviewer #2:

The manuscript titled "Anaplastic lymphoma kinase-negative anaplastic large cell lymphoma masquerading as Behcet's disease: A Case Report and Review of Literature" adds nothing to the existing scientific literature in the field. It can only be published for educational purposes if the authors handle to revise the manuscript adding a table consisting of clinical features and treatment modalities with outcome of previously reported 9 cases.

Response: Added a table, thanks.

Table1 Primary ALK negative ALCL of the gastrointestinal tract in our current study and in the literature

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