ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2020 March 6; 8(5): 854-1001

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

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World Journal of Clinical Cases

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Proofing Production Department Director: *Yun-Xiaojian Wu*

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Semimonthly

EDITORS-IN-CHIEF
Dennis A Bloomfield, Bao-Gan Peng, Sandro Vento

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2307-8960/editorialboard.htm

EDITORIAL OFFICE
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PUBLICATION DATE
March 6, 2020

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World J Clin Cases 2020 March 6; 8(5): 963-970

DOI: 10.12998/wjcc.v8.i5.963

ISSN 2307-8960 (online)

CASE REPORT

Muscular involvement of extranodal natural killer/T cell lymphoma misdiagnosed as polymyositis: A case report and review of literature

Li-Hui Liu, Qing Huang, Yun-Hai Liu, Jie Yang, Han Fu, Lin Jin

ORCID number: Li-Hui Liu (0000-0002-1813-2488); Qing Huang (0000-0001-8928-6030); Yun-Hai Liu (0000-0001-7514-3581); Jie Yang (0000-0001-6604-7811); Han Fu (0000-0002-3190-2838); Lin Jin (0000-0002-5578-1663).

Author contributions: Huang Q dominated and guided the completion of this article; Liu LH started and finished in writing and basic ideas; Liu YH provided a lot of guidance and corrections; Yang J and Fu H provided lots of help in the process of improving the article.

Supported by the National Natural Science Foundation of China, No. 81400978.

Informed consent statement: Consent was obtained from the patient for publication of this report and the accompanying images.

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

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).

Li-Hui Liu, Qing Huang, Yun-Hai Liu, Jie Yang, Lin Jin, Department of Neurology, Xiangya Hospital of Central South University, Changsha 410008, Hunan Province, China

Li-Hui Liu, Qing Huang, Yun-Hai Liu, Jie Yang, Lin Jin, Department of Geriatrics Stroke Center, Cerebrovascular disease clinical research center of Hunan province, Changsha 410008, Hunan Province, China

Han Fu, Department of Dermatology, Xiangya Hospital of Central South University, Changsha 410008, Hunan Province, China

Corresponding author: Qing Huang, MD, PhD, Professor, Department of Neurology, Xiangya Hospital of Central South University, 87 Xiangya road, Changsha 410008, Hunan Province, China. qinghuang_stroke@126.com

Abstract

BACKGROUND

Natural killer (NK)/T cell lymphoma is a rare and highly aggressive malignant tumor, and is a special form of non-Hodgkin's lymphoma. Although extranodal involvement is frequently found in tissues such as the skin, testicular and gastrointestinal tract *etc*, its presence in skeletal muscle has scarcely been reported in the literature.

CASE SUMMARY

We report a case of extranodal NK/T cell lymphoma with muscle swelling as the first clinical manifestation. A 42-year-old man, who initially presented with localized swelling in the double lower extremities, demonstrated gradual facial and eyelid swelling, and his imaging results showed multiple sites of muscle damage throughout the body. The final pathological results suggested NK/T cell lymphoma, and immunohistochemistry showed CD20 (-), CD3 (+), CD30 (+), CD56 (-), EBER (+), Ki67 (60%), TIA-1 (+) and CD68 (±) staining. The muscle swelling significantly improved after treatment with chemotherapy regimens.

CONCLUSION

This disease is difficult to diagnose and highly invasive, and should be included in the differential diagnosis of unexplained muscle swelling.

Key words: Lymphoma; Extranodal natural killer/T cell lymphoma; Muscular; Polymyositis; Muscle swelling; Case report

Manuscript source: Unsolicited manuscript

Received: September 26, 2019
Peer-review started: September 26, 2019
First decision: November 21, 2019
Revised: November 23, 2019
Accepted: December 13, 2019
Article in press: December 13, 2019
Published online: March 6, 2020

P-Reviewer: Han JH, Sugimura H
S-Editor: Tang JZ
L-Editor: Filipodia
E-Editor: Liu MY

Core tip: Extranodal natural killer/T cell lymphoma (NK/T cell lymphoma) is a distinct clinicopathologic entity in non-Hodgkin's lymphoma, having various extranodal manifestations, and a high incidence in Asian and South American populations. In this article, we describe a 42-year-old Asian man who presented with muscle swelling as the first clinical manifestation, and was initially diagnosed with polymyositis. Upon further examination, he was definitively diagnosed with extranodal NK/T cell lymphoma. Therefore, we provide a review of the literature to further understand extranodal NK/T cell lymphoma in muscles.

Citation: Liu LH, Huang Q, Liu YH, Yang J, Fu H, Jin L. Muscular involvement of extranodal natural killer/T cell lymphoma misdiagnosed as polymyositis: A case report and review of literature. *World J Clin Cases* 2020; 8(5): 963-970
URL: https://www.wjgnet.com/2307-8960/full/v8/i5/963.htm
DOI: https://dx.doi.org/10.12998/wjcc.v8.i5.963

INTRODUCTION

Natural killer (NK)/T cell lymphoma is a rare disease in non-Hodgkin's lymphoma (NHL), accounting for about 5%-18% of NHL[1]. It most commonly presents as destructive lesions in the nasal cavity and other midline facial structures. About 1/3 of these occur in nonnasal areas[2], also known as extranodal types and including the skin, testicles, liver, and spleen; however, it is rarely found in skeletal muscle[3-5]. Herein, we report a case with calf muscle swelling as the unique initial manifestation, showing progressive development with a final diagnosis *via* muscle biopsy as NK/T cell lymphoma. We also discuss the cause of the initial misdiagnosis of polymyositis and review the relevant literature about extranodal NK/T cell lymphoma-affected muscles.

CASE PRESENTATION

Chief complaints

A 42-year-old man presented with bilateral calf swelling for 5 mo, as well as left facial swelling for 4 mo.

History of present illness

At 1 mo prior, the patient had presented to a local hospital with bilateral calf and left facial swelling. During the hospital visit, the patient had intermittent low fever. The laboratory examination showed that the erythrocyte sedimentation rate was 31 mm/h. Electromyography indicated that there were more positive phases and fibrillation potential in the left gastrocnemius muscle, thus hinting at the possibility of myogenic damage. Magnetic resonance imaging of calf muscles indicated abnormal signals in the bilateral gastrocnemius and soleus muscle. Therefore, the first muscle biopsy was considered, and the pathological result of the left gastrocnemius muscle revealed a large amount of spindle cell infiltration, accompanied by necrosis and regeneration of individual muscle fibers (unfortunately, the results of immunohistochemistry were missing). The patient was considered for "polymyositis" and treated with methylprednisolone for 10 d, and the swelling of both the calf and face was slightly improved. However, 1 mo later, the patient developed drooping of the right eyelid.

History of past illness

The patient had a good health record.

Personal and family history

The patient had no relevant personal or family history.

Physical examination upon admission

A physical examination showed both calves were swollen, the left facial region had slightly intumescentia compared to the contralateral side, and there was right eyelid swelling and drooping.

Laboratory examination

Serum lactate dehydrogenase was elevated (379-901 U/L, reference: 120–250 U/L), Epstein-Barr virus (EBV) and DNA was significantly increased (3.13-5.19 × 10^5 IU/mL, reference: < 400 IU/mL). Serum creatine kinase was normal (105-220 U/L, reference: 50-310 U/L).

Imaging examinations

Cranial magnetic resonance imaging scan enhancement was reported for the subcutaneous soft tissue masses in the left cheek and forehead, as well as thickening of the right levator palpebrae superioris. Whole-body positron emission tomography/computed tomography (PET/CT) showed multiple areas of muscle swelling, with decreased muscle density and increased metabolic dispersion (Figure 1). The left portion of the posterior wall and the left wall of the oropharynx showed soft tissue masses, with abnormally increased metabolism. Finally, puncture biopsies of the left calf muscle and left pharyngeal side wall were completed. Examination of the left leg revealed a small amount of tissue that was mainly necrotic, but the tumor could not be excluded. The pathological diagnosis of the left side pharyngeal wall showed NK/T cell lymphoma, and immunohistochemistry showed CD20 (-), CD3 (+), CD30(+), CD56 (-), EBER (+), Ki67 (60%), TIA-1 (+) and CD68 (±) staining (Figure 2).

FINAL DIAGNOSIS

The patient was diagnosed with extranodal NK/T cell lymphoma.

TREATMENT

The patient received a chemotherapy regimen of methotrexate, dexamethasone, etoposide, and pegaspargase.

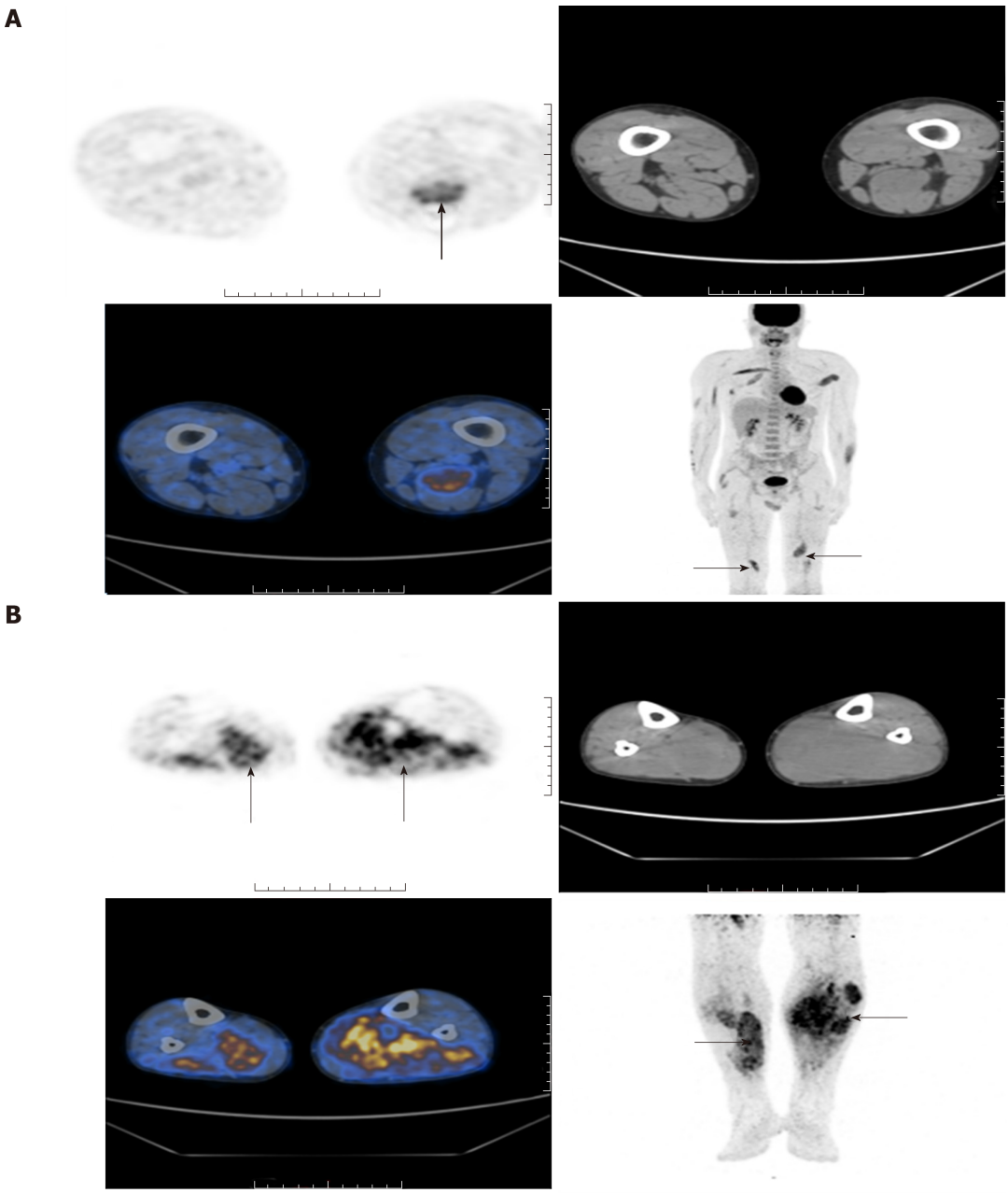
OUTCOME AND FOLLOW-UP

The swelling of both the calf and face of the patient was rapidly and significantly improved (Figure 3). Additionally, the swelling of the right eyelid improved and could be slightly raised. Over the following 8 mo, the patient received chemotherapy five more times, and still had intermittent fever, but the muscle swelling did not worsen.

DISCUSSION

Extranodal NK/T cell lymphoma is a malignant tumor, strongly associated with EBV and a poor prognosis. The typical pathological features include diffuse lymphocytic infiltration, showing angiodestruction as well as angiocentric growth, and is often accompanied by fibrinoid changes in blood vessels and coagulative tissue necrosis[6]. The typical immunohistochemical characteristics are as follows; CD2(+), cytoplasmic CD3(+), CD56(+), EBV(+) and cytotoxic granule-associated protein(+) staining, which include granzyme B, TIA-1 and perforin[7].

This patient initially presented with swelling in the bilateral gastrocnemius and soleus. In a recent review of the literature, only about seven cases of extranodal NK/T cell lymphoma had been reported with an initial manifestation of myopathic symptoms[4,8-13], and these were primarily diagnosed initially as myositis (Table 1). Two cases was considered to be granulomatous myositis[8,11], two cases were diagnosed as polymyositis[4,12] and one as phlegmonous myositis[10]. In only one of these cases, the presence in gastrocnemius and soleus muscle was initially diagnosed as peripheral eosinophilia[13]. Our patient was diagnosed as polymyositis by his first attending physician in the local hospital, and the reasons for this could be as follows: Multiple muscle swelling, low fever, lactate dehydrogenase, and erythrocyte sedimentation rate elevation. Furthermore, electromyography indicated myogenic damage was possible, and muscle biopsy showed necrosis and regeneration of the individual muscle fibers. Thus, the patient received methylprednisolone treatment, but the muscle swelling continued to progress. Subsequently, he came to our hospital, and the diagnosis of "polymositis" was called into question by our attending physician. Firstly, the muscle swelling did not improve, but instead increased after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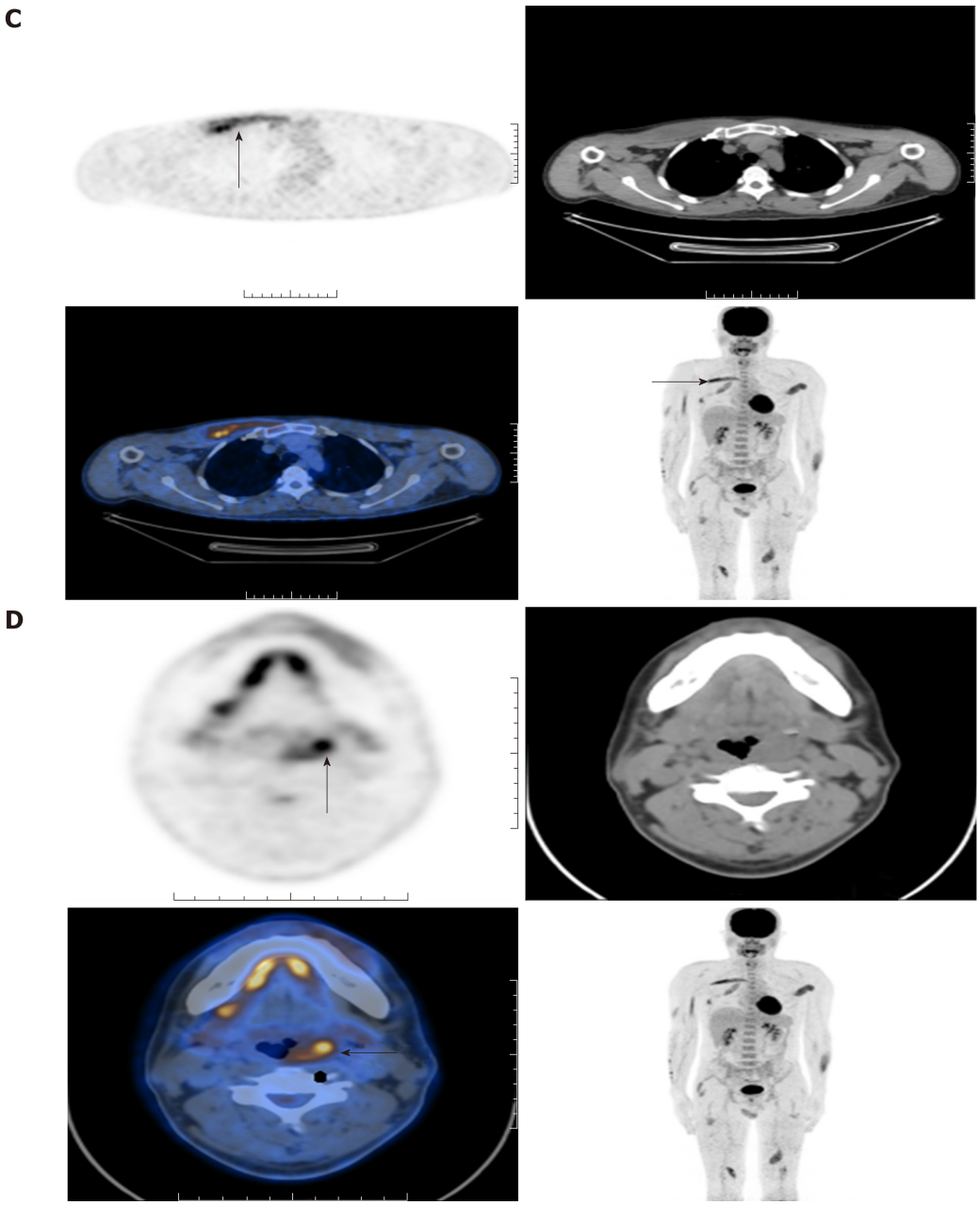

Figure 1 Positron emission tomography/computed tomography scans. A positron emission tomography/computed tomography scan showing multiple intensely fluorodeoxyglucose -avid muscle lesions scattered throughout the body (SUVmax of 8.9). A: The bilateral thigh (arrows); B: Both calves (arrows); C: The right pectoralis major (arrows); D: Fluorodeoxyglucose-avid lesions in the oropharynx (arrows, SUVmax of 6.3).

methylprednisolone therapy. Secondly, the muscle swelling in this patient was mainly localized in the distal *vs* proximal limb. Lastly, the laboratory examination revealed that the EBV DNA quantitation was significantly elevated, and there was a lack of testing for myositis-related antibodies. Therefore, we planned to arrange for this patient to complete myositis antibody and whole-body PET/CT examination, however he only chose the whole-body PET/CT. The results showed multiple sites of muscle damage throughout the body. Thus, the relevant tissue biopsies were tested, and the diagnosis of NK/T cell lymphoma was confirmed by lateral pharyngeal biopsy.

The lateral pharyngeal biopsy showed diffuse heterotropic lymphocytic infiltration, consistent with NK/T cell lymphoma. Immunohistochemistry showed that the lymphoid cells were CD20 (-), CD3 (+), CD30 (+), CD56 (-), EBER (+), Ki67 (60%), TIA-1 (+) and CD68 (±). In contrast with typical extranodal NK/T cell lymphoma immunohistochemical characteristics, the CD56 in this patient was negative and CD30 was positive. It is known that while CD30 is closely related to anaplastic large cell lymphoma, its expression in extranodal NK/T cell lymphoma is infrequent[14]. There have been literature reports that EBV is believed to be a key component in the

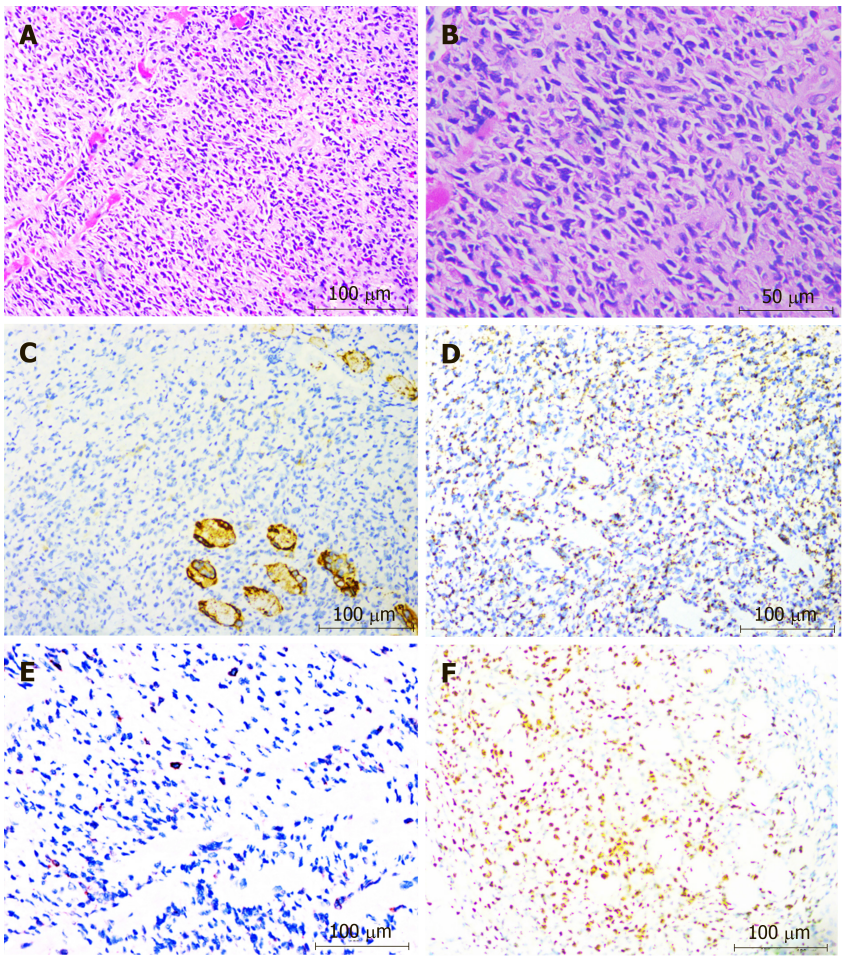

Figure 2 Immunohistochemical staining. A and B: Histological findings of the pharyngeal wall (hematoxylin-eosin: panel A, × 200; panel B, × 400), showing diffuse infiltration with atypical lymphoid cells; C: Immunohistochemical staining for CD56 was negative (× 200); D-F: Immunohistochemical staining was positive for TIA-1 (panel D, ×200), CD30 (panel E, × 200) and EBER (panel F, × 200).

etiology of extranodal NK/T cell lymphoma, and can induce CD30 expression by the infection and transformation of lymphocytes[15]. We thus think that the CD30 positivity in this patient was associated with the high expression of EBV. The literature suggests that $CD3^+$ $CD56^+$ EBV^+ is an important clue to diagnose NK/T cell lymphoma[16], but there have been studies that demonstrate that CD56 is not a specific biomarker for NK cells, and can be expressed on other blood cells, such as T cells[17]. Finally, the patient received a chemotherapy regimen of methotrexate, dexamethasone, etoposide and pegaspargase. The muscle swelling improved, and conditions were stable over the next five additional rounds of chemotherapy.

CONCLUSION

It is extremely rare for extranodal NK/T cell lymphoma to be involved in skeletal muscle. This disease is difficult to diagnose and highly invasive, usually leading to delays in treatment. This should be included in the differential diagnosis of progressive and unexplained muscle swelling. A definitive diagnosis always requires adequate viable tissues for pathological and immunocytochemical characterizations. Finally, selecting the appropriate chemotherapy regimen can significantly improve symptoms or delay the development of disease.

Table 1 Comparisons with previous cases of extranodal natural killer/T cell lymphoma with manifested myopathic symptoms

Ref.	Age/sex	Initial diagnosis	Muscle involvement	Other involved organs	EBV	Outcome	Survival from initial onset
Kawaguchi *et al*[8]	54/M	GM	Generalized muscle, face, jaw, pharynx	Skin, liver, spleen	+	Death	19 mo
Yap *et al*[9]	73/M	PE	Left pectoralis major	-	+	Recovery	-
Yang *et al*[10]	23/M	PhM	Left lower limb	Nasopharynx, spleen	+	Death	2 mo
Min *et al*[11]	53/M	GM	Right lower extremity	Nasal, skin	+	Death	8 mo
Chan *et al*[12]	68/F	PM	Right forearm, face	Lung, oropharynx	+	Death	1.5 mo
Chim *et al*[4]	34/F	PM	Right forearm	Liver, bone marrow	+	Death	Unknown
Paik *et al*[13]	52/F	PE	Both lower limbs	Lung	+	Death	26 mo
Our case	42/M	PM	Both lower limbs, face	Pharynx, eyelid, optic nerve	+	Improved	-

GM: Granulomatous myositis; PE: Peripheral eosinophilia; PhM: Phlegmonous myositis; PM: Polymyositis; M: Male; F: Female; +: Positive; -: Negetive; EBV: Epstein-Barr virus.

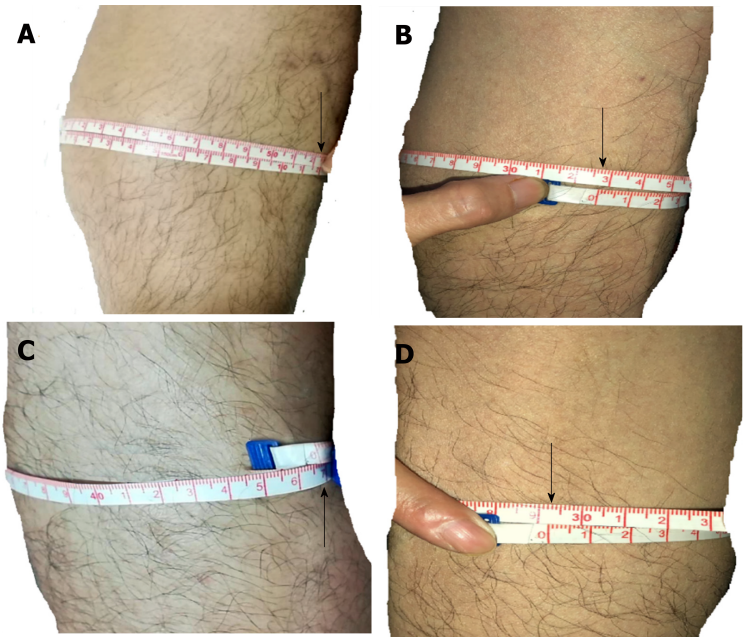

Figure 3 Calf circumference before and after chemotherapy treatment. A and B: The left calf circumference was 52.5 cm and 32.7 cm, respectively, before and after chemotherapy treatment; C and D: The right calf circumference was 46.8 cm and 29.2 cm, respectively, before and after chemotherapy treatment.

ACKNOWLEDGEMENTS

We thank professor Zheng-Hao De of the pathology department and professor Wei-Hua Liao of radiology for technical assistance.

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