Anti-OJ (Anti-isoleucyl-tRNA Synthetase) Autoantibody- Positive Anti-synthetase Syndrome: a Case Report

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Case report

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Abstract

Background: Anti-OJ (anti-isoleucyl-tRNA synthetase) autoantibody-positive anti-synthetase syndrome(ASS) is a rare systemic autoimmune diseases that manifest as an inflammatory myopathy and interstitial lung diseas.

Case presentation: We present a case of anti-OJ antibody-positive ASS with recurrent joint pain, fever, significantly elevated inflammatory markers, occult myositis but no interstitial pneumonia in a 75-year-old male patient. The patient was misdiagnosed for more than one year. Recurrent hepatocellular carcinoma (HCC) was confirmed after 1 year of the diagnosis of ASS, and the clinical symptoms were relieved after surgical resection.

Conclusion: We report this rare case of anti-OJ antibody-positive ASS with atypical manifestations to raise awareness of the disease for clinicians.

Background

Anti-aminoacyl transfer RNA synthetase (ARS) is one of the most common types of specific autoantibodies in patients with polymyositis/dermatomyositis (PM/DM) [1]. These patients often present with fever, arthritis, Raynaud's phenomenon, myopathy, mechanic's hand and interstitial lung disease (ILD), called synthetase antibody resistance syndrome. Based on the different types of anti-synthetase antibodies, there are different anti-synthetase syndrome (ASS) subtypes, and 10 anti-synthetase antibodies have been found [2, 3], among which anti-jo-1 antibody is the most common anti-synthetase antibody (approximately 20–30% of PM/DM patients) [4]. Anti-OJ antibodies are found in less than 5% of PM/DM patients [5]. Patients with different clinical subtypes of ASS have different anti-synthetase antibodies and different clinical manifestations, chest imaging findings, and prognoses, among other characteristics [6]. Currently, there are still few clinical reports on anti-OJ antibody-positive ASS. Here, we present a case of anti-OJ antibody-positive ASS with clinical manifestations that differ from those previously reported.

Case Presentation

A 75-year-old male, a retired worker,was admitted to our hospital with recurrent joint pain for more than 1 year, fever for 6 months and recurrence for one week. Both large and small joints were involved, such as the left ankle, the third metacarpophalangeal joint of the right hand, the right shoulder, and the left wrist. The joint pain affected the patient's activity. One year prior, he repeatedly visited the orthopaedic clinic and intermittently took etoricoxib. Six months prior to this presentation, the patient was admitted to our hospital with fever. A complete blood count showed an increased white blood cell (WBC) count of 30,500/μl (neutrophil: 90.1%) with mild anaemia (haemoglobin: 11.9 g/dl) and a platelet count of 194×10^9/l. The laboratory data further showed inflammation markers [C-reactive protein (CRP): 140.79 mg/dl, erythrocyte sedimentation rate (ESR): 34 mm/hr, procalcitonin (PCT): 0.48 ng/ml and ferritin: 460.8 ng/ml]. Tests for

rheumatoid factors and cyclic citrullinated peptide (CCP) IgG antibodies and the antinuclear antibody titre were negative. Computed tomography (CT) of the chest and abdomen revealed postoperative changes indicating liver cancer. Colour ultrasound of the heart was normal. During the hospital stay, the patient had repeated episodes of fever and joint pain; a bone marrow puncture and biopsy were performed, and the results were normal. Dual-energy CT for gout indicated a few urate crystals deposited in the bilateral radiocarpal joints, while the blood uric acid levels were normal. Infectious fever and gout were considered, and the patient was successively treated with piperacillin/tazobactam sodium (4.5 g q8h intravenously for 11 days), imipenem (1.0 g q8h intravenously for 6 days), linezolid (0.6 g q12h orally for 10 days) and loxoprofen (60 mg q12h orally for 3 days). The patient improved and was discharged on the 24th day of hospitalization.

Two months prior to this presentation, the patient was admitted to our hospital again with similar symptoms. The laboratory data were as follows: WBC count: 16,600/μl (neutrophil: 92.1%), CRP: 97.3 mg/l,ESR: 79 mm/h, and PCT: 0.09 ng/ml. Human leucocyte antigen-B27 (HLA-B27), tuberculin test and T-SPOT-TB were negative. Abdominal CT indicated multiple new low-density foci in the liver, and enhanced magnetic resonance imaging (MRI) of the upper abdomen showed multiple scattered enhanced nodules in the liver, indicating that metastasis should be considered (Fig. 1A, B). However, positron emission tomography-computed tomography (PET-CT) showed that inflammatory lesions should be considered first. The patient was treated with levofloxacin (0.5 g qd intravenously for 5 days) and etoricoxib (60 mg q12h orally for 7 days). The patient was discharged on the 7th day of hospitalization.

The patient had a nonspecific ailment, chronic viral hepatitis B and long-term use of lamivudine. He had a history of HCC surgery 11 years ago and received three cycles of postoperative chemotherapy. No tumour recurrence was found in regular re-examinations, and the last follow-up was 2 years ago. He also had a history of "hypertension, type 2 diabetes" of more than 10 years, both of which were well controlled with drugs.

At this presentation, the physical examination showed that the skin on the right third metacarpophalangeal joint was red and swollen with obvious tenderness, and there was tenderness in the right shoulder, lumbosacral region, lower back, left wrist joint and left ankle joint; in addition, there were also several areas of muscle tenderness, such as the lateral muscle of the left thigh. The blood routine was as follows: WBC: 36,800/μl (neutrophil: 95.6%), CRP: 261.86 mg/l, PCT: 0.11 ng/ml. The enhanced MRI of the upper abdomen was repeated and revealed that many of the nodules in the liver disappeared, except for the nodule in segment VI (Fig. 1C, D). Because of the muscle tenderness, we conducted a further physical examination and found that the patient had decreased proximal muscle strength and muscle weakness for several months. Although multiple creatinine kinase (CK)/creatine kinase-MB (CK-MB) tests were normal, a myositis antibody test was completed and was positive for anti-OJ antibodies. Enhanced MRI of the left thigh and lower leg showed abnormal T2 signals in the medial thigh muscle group (Fig. 2). Muscle biopsy suggested myositis (Fig. 3). The patient did not have the

clinical manifestations of ILD by chest high-resolution computed tomography (HRCT) or mechanic’s hand.

The patient was eventually diagnosed with ASS and treated with prednisone 30mg/day for 10 days (treatment stopped by the patient), after which the condition was in remission. The patient intermittently took antipyretic analgesics and had occasional joint pain and fever. After 1 year of follow-up, enhanced MRI of the upper abdomen showed a mass occupying the right hepatic lobe (segment VI) that had become enlarged, and recurrence was considered (Fig. 1E). Postoperative pathology showed HCC. After the operation, the patient's joint pain, fever and muscle weakness improved. At present, the patient has been followed up for nearly 3 years and has not been treated with drugs for ASS; his general condition is good, with no interstitial pneumonia(Fig. 4).

Discussion And Conclusions

ASS is a heterogenous, rare group of systemic autoimmune diseases that manifest as an inflammatory myopathy. In 2010, Connors et al. [7] formally proposed the diagnostic criteria for ASS, namely, positive for serum anti-synthetase antibody and at least one of the following clinical manifestations: Raynaud's phenomenon, arthritis, ILD, fever, or mechanic’s hand.

In this case, the patient had no imaging manifestations of interstitial pneumonia and was mainly characterized by multiple episodes of arthritis and fever. Clinically, the joint pain was severe, while the myositis was insidious.This is different from previous reports. Marie et al. [8]proposed that the incidence of ILD is higher among patients with ASS without anti-JO-1 antibodies than in those with ASS with anti-JO-1 antibodies. Hamaguchi et al.[9] found that the clinical manifestations of the anti-OJ antibody-positive ASS subtype were not obvious, and usually only ILD was present. So the diagnosis of this case is extremely difficult, finally, the patient was transferred to the departments of orthopaedics, infectious medicine, and rheumatology, among others, resulting in a misdiagnosis for more than one year. In addition, we found that ASS could cause the increase of inflammatory markers, which has not been reported before.

The association between PM/DM and malignant diseases has been reported and confirmed [10]. Studies have found that ASS and interstitial pneumonia have a negative correlation with cancer-associated myositis [11–13], but there are also cases of various ASS-related diseases combined with malignant tumours [14–15]. In this case, myositis, arthritis and fever were manifestations of paraneoplastic syndrome. It is possible that the patient's specific immune system was immature before HCC resection, so there was no autoimmune response against the joints or muscles, even in the presence of anti-OJ antibodies against HCC cell antigens. However, memory B cells retain the ability to generate an immune response to these liver cancer antigens. As the cancer recurs, B-cell production of OJ antibodies is triggered; the subsequent number of antibodies may be high enough to cause autoimmune inflammation of the joints and muscle tissues expressing OJ-like antigens[16].

ASS usually has a poor prognosis, depending on the involvement of interstitial pneumonia [17]. Some patients positive for anti-OJ antibodies have a good prognosis [18–20]. In this case, the patient was not treated with drugs after tumour resection, and the disease stayed in remission.

We reported the first case of anti-OJ antibody-positive ASS associated with HCC recurrence in which the patient presented with recurrent arthritis, fever, significantly elevated inflammatory markers and occult myositis. We need to raise awareness of this rare disease and pay special attention to exclude the presence of tumours.

Abbreviations

Anti-OJ: anti-isoleucyl-tRNA synthetas; ASS: anti-synthetase syndrome; HCC: hepatocellular carcinoma; PM/DM: polymyositis/dermatomyositis; ILD: interstitial lung disease; WBC: white blood cell; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; PCT: procalcitonin; CCP: cyclic citrullinated peptide; CT: computed tomography; HLA-B27: leucocyte antigen-B27; MRI: Magnetic resonance imaging; PET-CT: positron emission; CK/CK-MB: tomography-computed; creatinine kinase/creatine kinase-MB; HRCT: chest high-resolution computed tomography.

Declarations

Acknowledgments

Not applicable.

Authors' contributions

Ji-na Gu wrote the paper. Wang Yan and Qiao-ling Gao provided technical or material support. Lin Chen has designed the paper. All authors contributed to the article and approved the submitted version.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by Ethics Committee of Hwa Mei Hospital, University of Chinese Academy of Sciences.

Consent for publication

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Competing interests

The authors declare that they have no competing interests.

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Figures

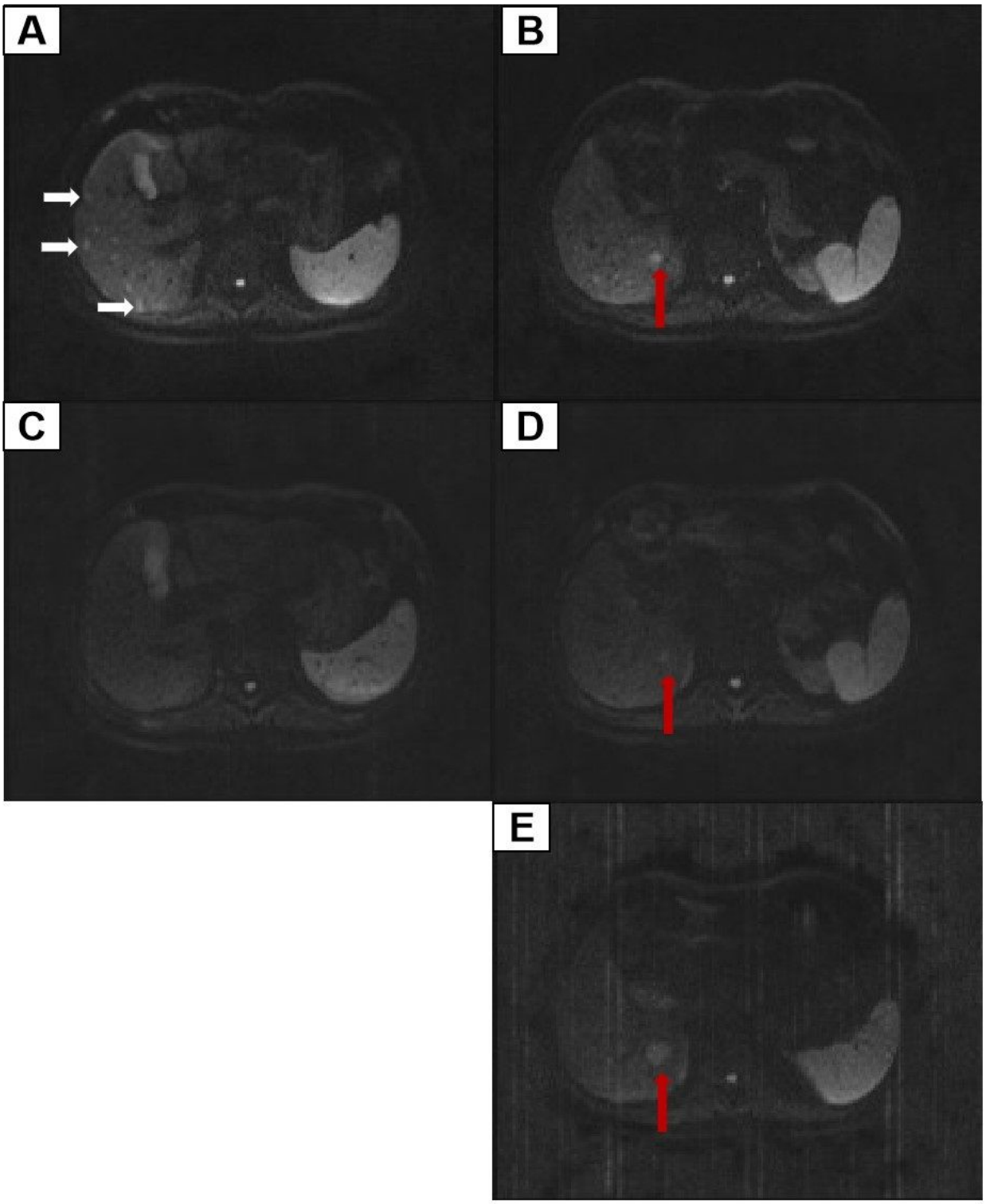

Figure 1

MRI scans of the upper abdomen. Two months prior (A, B): diffusion-weighted imaging showing multiple small nodules in the liver with high signal (white arrows). Figures C and D: diffusion-weighted imaging showing a reduction in the size of the nodule in segment VI (red arrows) and disappearance of the other nodules (arrows). After 1 year of follow-up (E): the nodule in segment VI with high signal was enlarged.

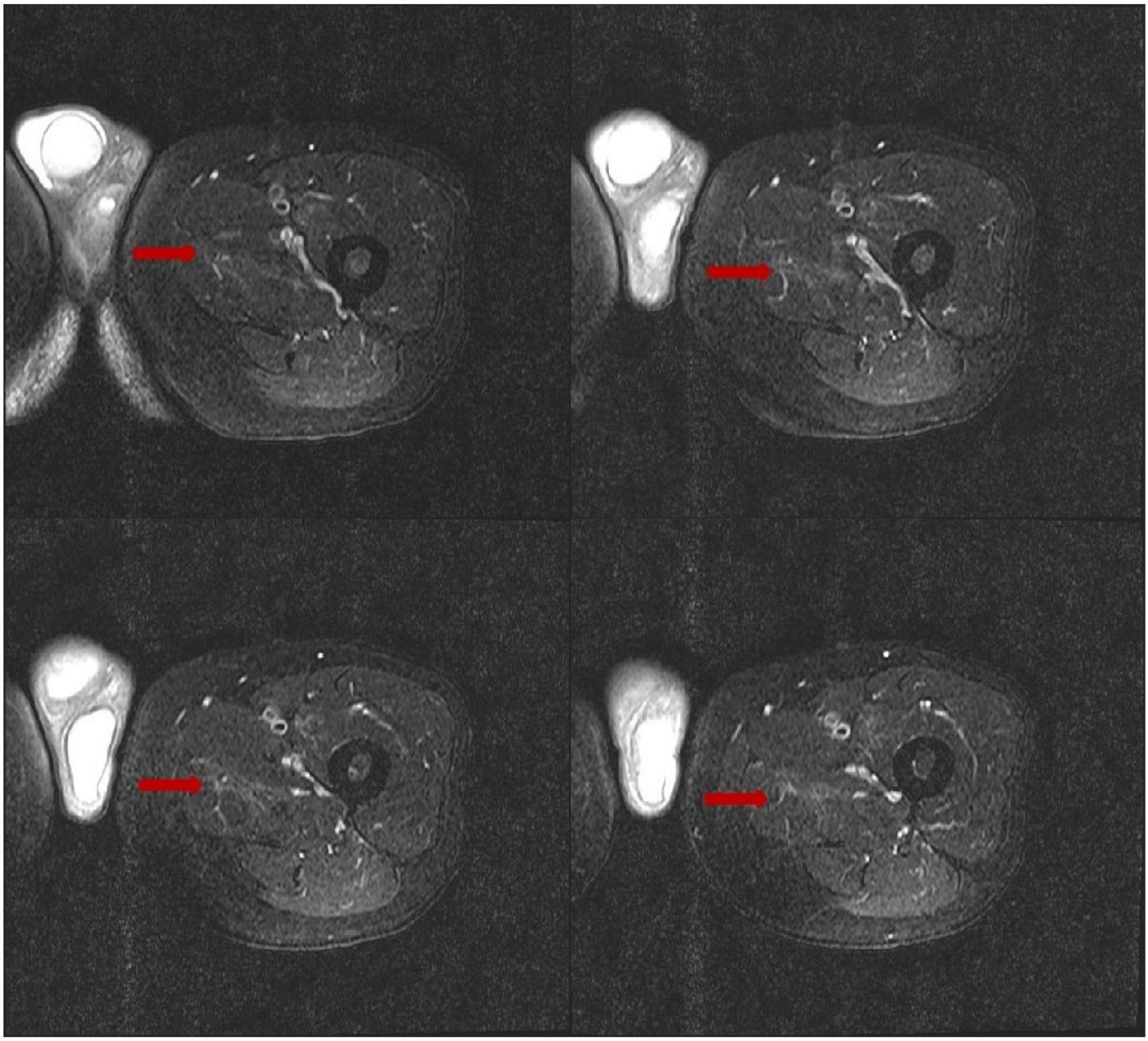

Figure 2

MRI of the left lower limb muscles. Turbo spin-echo fat-suppressed T2-weighted imaging showing abnormally high signals (red arrows) in the medial thigh muscle group.

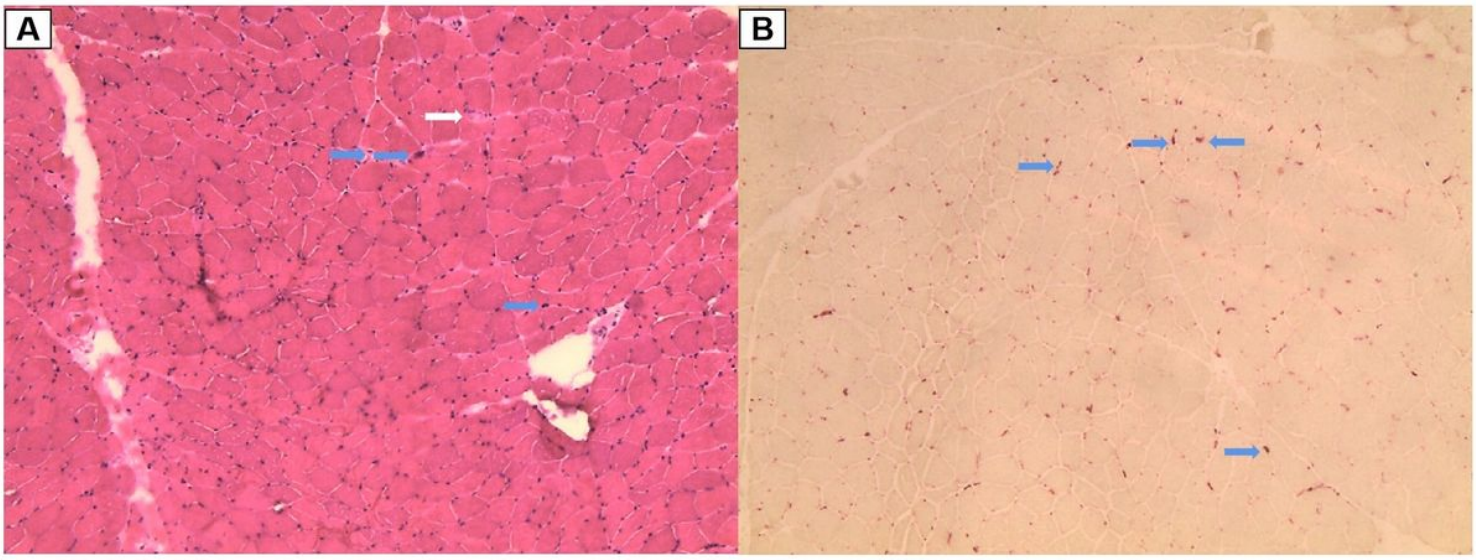

Figure 3

Muscle biopsy of the left lower limb(10×10). Nuclear aggregation (blue arrows) and degeneration of muscle fibre (white arrow) are seen after staining with haematoxylin and eosin (H&E) (A). Inflammatory cells (blue arrows) surround fibres stained with acid phosphatase.

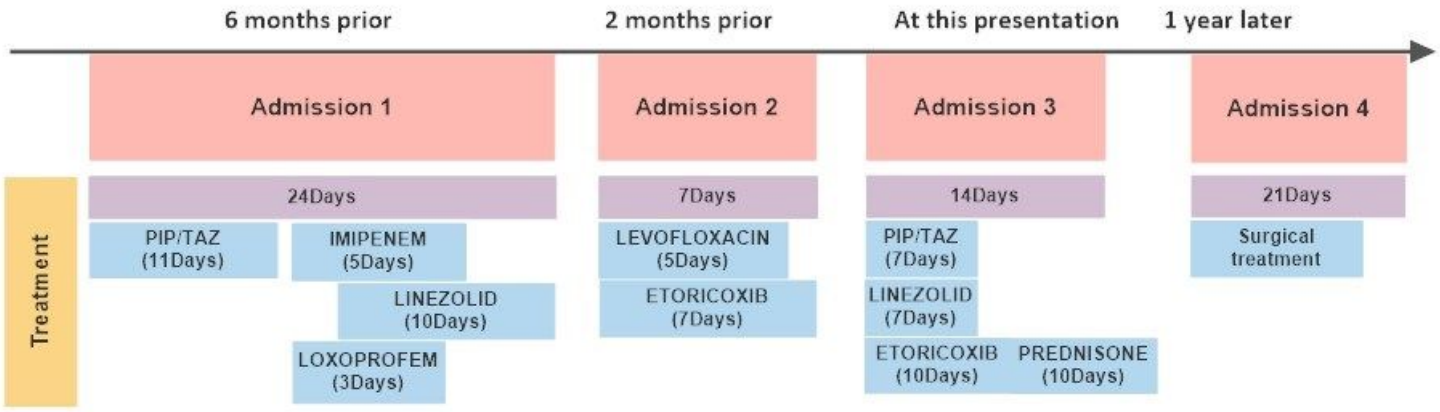

Figure 4

Timeline of main hospitalizations and interventions. Abbreviation: PIP/TAZ (piperacillin-tazobactam).

Supplementary Files

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