Reviewer's report

Title: A patient presenting breast cancer with an unusual paraneoplastic syndrome: a case report

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Reviewer: Eroboghene Ubogu

I am familiar with the literature and believe that this case meets one of the 9 criteria for evaluation in the journal: Other

If other, please specify:

Rare association of a progressive disease process.

Has the case been reported coherently?: No

Is the case report authentic?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: No

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

General Comments:

The paper by Silvestre J et al describes a presumed paraneoplastic necrotizing myopathy temporally associated with locally advanced ductal invasive carcinoma of the breast in a 53 year old woman with no initial evidence for distant metastases. The paper attempts to demonstrate that the neuromuscular deterioration that occurred in the patient was not directly related to chemotherapy or other more common causes of proximal muscle weakness. The authors do a good job introducing and discussing paraneoplastic necrotizing myopathy based on their literature review, and the reported clinical management and outcomes described are satisfactory.

The main limitations of the paper include incoherence (due to poor grammatical
structure) and the use of non-standard medical terminology in describing the neuromuscular disease. The paper requires extensive revision of the text to correct these deficiencies. The key diagnostic tool to justify their conclusions (the muscle biopsy) was not adequately described by the authors to demonstrate the key pathologic features, and additional enzyme/immunohistochemical staining (as suggested by Levin et al: reference number 5) that aids to confirm the diagnosis was not performed. I would like to provide a detailed critique of each aspect of the manuscript.

Specific Comments:

Title and Abstract: The title should be revised to correct grammatical errors and clearly emphasize the paraneoplastic necrotizing myopathy. Grammatical errors should be corrected in the abstract as well. Is it necessary to include the race and national origin of the patient in this case report? Do any of the above contribute to understanding the disease? "Inferior members" is not a commonly used medical term. "Lower extremities" is more conventional. If the Medical Research Council (MRC) scale is being used to grade strength, this should be mentioned. What did the electromyogram show that suggested evidence for necrotizing myopathy? What were the characteristic lesions found on muscle biopsy?

Introduction: This is generally satisfactory. Once again, grammatical errors (e.g "constituted only" on line 2 of paragraph 2) need to be addressed.

Case Presentation: Once again, grammatical errors need to be addressed.

As previously stated, is the race and national origin of the patient relevant to the case presentation? What is the rationale for mentioning the gynecological history in such detail? History of toxin exposures (recent and remote) that could cause a toxic necrotizing myopathy should be mentioned. "Lumbalgia" is a vague term not commonly used. "Lower back pain" is a simple and well understood term. The authors should change "irradiation" to "radiation" to refer to the spread of pain. The neurological examination does not mention if the weakness (which I presume is based on the 5-point MRC scale) involves one or both lower extremities. "Crural" is not a commonly used term. Quadriceps femoris is the accepted medical term of the quadriceps muscles of the thigh. What was the rationale for a presumptive diagnosis of "secondary neuropathy due to docetaxel" in light of the isolated proximal involvement and lack of sensory deficits?

The results of the electromyogram (and I presume included nerve conduction studies) are vague. What were the findings that suggested a necrotizing muscular lesion? Which muscles demonstrated these findings? Where there any subclinical changes on the electromyogram that suggested a more widespread proximal myopathy (e.g involvement of upper extremities or paraspinal muscles)? Were both lower extremities studied? On which side was the muscle biopsy performed? How soon after the electromyogram was the muscle biopsy performed?
The description of the muscle biopsy (Figures 1 and 2) is inadequate both in the text and figure legends. The Figure legends need revision to include the key findings demonstrated. Scale bars (or magnifications) should be provided. The authors should clearly highlight which features on the photomicrographs support the diagnosis of necrotizing myopathy. Fibrofatty replacement of muscle tissue is not the most dominant feature of the figures. The authors need to point out features such as variability in muscle fiber size, atrophic fibers, pyknotic nuclear clumps, necrotic and regenerating fibers, and should demonstrate lack of "inflammatory infiltrate" via negative immunohistochemical staining for T-cells, B-cells or plasma cells and macrophages, as well as membrane attack complex (C5-9) on frozen sections. If this is not possible, the authors should state why these were not done and exercise caution in making a definitive diagnosis.

Which viral serologies were tested for? At a minimum, HIV and HTLV need to be excluded.

In terms of high-dose steroid use, was any gastrointestinal or osteoporotic prophylaxis co-administered? What was the time frame after initiation of steroid therapy and the initial neurological deterioration? For how long was the higher dose steroid regimen (3 mg/kg/day) administered for? Were any steroid-sparing agents used (in addition to the chemotherapy regimen), and were the medications well-tolerated by the patient with minimal side effects (considering that the authors mentioned that she was obese in the initial history. It is probably better to state how much she weighed rather than make a statement on obesity based on physical features). How soon after very high dose steroid therapy did the patient regain some ability to walk and demonstrate improvement in muscle enzyme levels? What has been the duration of follow-up and has the patient experienced any relapses?

Discussion: The authors do not adequately point out the deficits on the muscle biopsy that confirm the diagnosis, or show lack of inflammatory infiltrates using standard immunohistochemical techniques. I believe that the clinical presentation did not warrant a hypothesis of chemotherapy-induced polyneuropathy, and importantly, I presume that the authors did not find any evidence for a sensory or sensorimotor polyneuropathy on nerve conduction studies.

The authors should explain what they mean by "the patient's response to anti-tumoral therapy was always deficient". The authors should provide the references that support their assertion that neurological deterioration associated with paraneoplastic syndromes is associated with tumor aggressiveness and inadequate response to therapy (in light of the fact that on many occasions, neurological signs and symptoms are the presenting features of an occult neoplasm).

Conclusions: The authors should also provide evidence that necrotizing myopathy confers a worse prognosis on the underlying neoplastic disease relative to patients without this complication. Do the patient die due to neuromuscular weakness or the underlying cancer being more aggressive?
Quality of written English: Not suitable for publication unless extensively edited

Declaration of competing interests:

I declare that I have no competing interests.