

Necrotizing myopathy as paraneoplastic disorder in tonsillar squamous cell carcinoma

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ABSTRACT

Introduction: Myositis including polymyositis and dermatomyositis has been reported in different types of cancer mainly lung, breast and ovarian cancer. **Case Report:** We report a case of necrotizing myopathy presenting in a 59-year-old patient after a recent diagnoses of squamous cell carcinoma of the tonsil. Three weeks later, the patient was admitted for worsening generalized weakness, dysphagia and constipation. Patient was bed bound requiring full assistance. Physical examination was significant for symmetrical weakness in his proximal muscle groups of upper and lower extremity. Creatinine kinase (CK) was 13,000 U/L with markedly elevated liver enzymes. EMG showed myotonia in all muscle groups with more prominence in axial and proximal muscles than distal. Following the biopsy of biceps muscle, IV steroid was initiated. IVIG was started later in addition to oral steroids due to suboptimal response. In the interim, biopsy showed severe necrotizing myopathy. Myositis Ab panel and paraneoplastic antibody panel including voltage gated potassium channel (VGPC) Ab, ANNA-1, ANNA-2 and PCA-1 Abs were negative. CK trended down to 1196 U/L after three

weeks of steroids with moderate improvement in the muscle weakness. **Conclusion:** Necrotizing myopathy can be associated with squamous cell carcinoma of tonsil. Serology may be negative and the presence of diffuse myotonia suggests myopathy. However, biopsy shows myofibers undergoing myophagocytosis with minimal inflammatory cells thus confirming necrotizing myopathy.

Keywords: Myotonia, Necrotizing myopathy, Paraneoplastic myopathy, Squamous cell carcinoma of tonsil

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INTRODUCTION

Paraneoplastic disorders affecting nerve and muscles are often a result of immune cross-reactivity between tumor and normal host cells [1, 2]. Myositis is an inflammatory disorder of skeletal muscles comprising of polymyositis, dermatomyositis and necrotizing myopathy. Often, patients with this disease experience progressive proximal muscle weakness. Casciola-Rosen et al. found regenerating cells in myositic muscles and several cancers known to be associated with myositis all express high levels of myositis specific autoantigens. [3]. The risk of cancer in patients with different myositis specific

antibodies (MSAs) has already been established in the literature [1, 3, 4]. Of the three forms, dermatomyositis has been most frequently described in relation to the cancer diagnoses. There are a few published reports on dermatomyositis associated with small cell carcinoma and adenocarcinoma of the lung, gastrointestinal, breast carcinoma, and ovarian and nasopharyngeal and squamous cell carcinoma of tonsil [5–11]. There are limited reports on paraneoplastic necrotizing myopathy [12–13], none in relation to squamous cell carcinoma of tonsil. We report an unusual case of necrotizing myopathy with negative myositis specific antibodies in a patient with recent diagnosis of squamous cell carcinoma of tonsil.

CASE REPORT

A 59-year-old male presented with dyspnea and fatigue. He was then diagnosed with HPV positive squamous cell carcinoma of his right tonsil after a biopsy that was performed six weeks prior to hospitalization. Patient was admitted for worsening generalized weakness, dysphagia and constipation. The weakness started about three weeks prior to admission and was progressively worsening. He reported an inability to move or transfer independently and was mainly bed bound requiring full assistance. In addition a worsening dysphagia to solid foods had led to decreased PO intake. Other past medical history was significant for 45 years of smoking and hypertension. On physical examination, patient was found to have symmetrical weakness in his proximal muscle groups of upper and lower extremity. He had an enlarged right tonsil and palpable cervical lymph nodes. Labs were remarkable for creatinine kinase (CK) 13579 U/L with elevated aldolase 109.4 U/L and markedly elevated AST 713 U/L and ALT 697 U/L. Rheumatological work up including HIV, myositis panel, anti-Jo Ab, Vitamin D 28U/L and CRP 1.2 mg/dl were negative.

Electromyography and a nerve conduction study showed myopathic changes in all muscle groups with more prominence in axial and proximal muscles than distal muscles. Moreover, it also depicted spontaneous activity of fibrillation potentials along with positive sharp waves and myotonic discharges indicating an inflammatory or necrotizing process. Therefore, treatment with steroids was deferred at that time until muscle biopsy was performed. The muscle biopsy (Figures 1–4) demonstrated widespread myopathic degeneration with most of the myofibers in various stages of necrosis and regeneration and minimal lymphocytic inflammatory infiltration in relation to the extensive amount of myofiber necrosis. Following the biopsy of biceps muscle, methylprednisolone was initiated. The CK started to trend down but clinically patient remained unchanged with no improvement in weakness. Therefore, intravenous immunoglobulin (IVIg) at a dose of 2g/kg

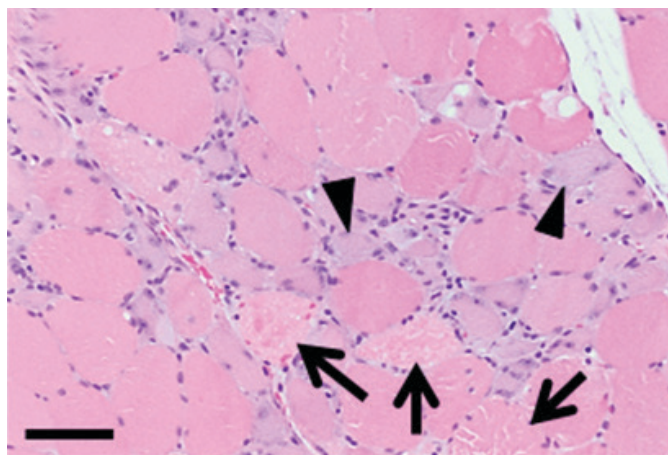


Figure 1: Muscle biopsy shows transversely sectioned muscle with widespread myopathic degeneration. Myofiber diameters and shapes are highly variable. Many myofibers are necrotic (arrows) and regenerating myofibers have basophilic (bluish) staining (arrowheads).

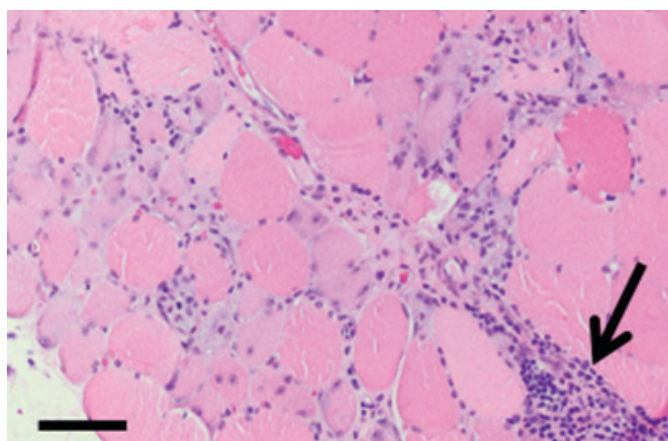


Figure 2: This is similar to Figure 1 because most of the myofibers are in various stages of necrosis and regeneration. The intensity of lymphocytic inflammatory infiltration (arrow) is mild relative to the extensive amount of myofiber necrosis.

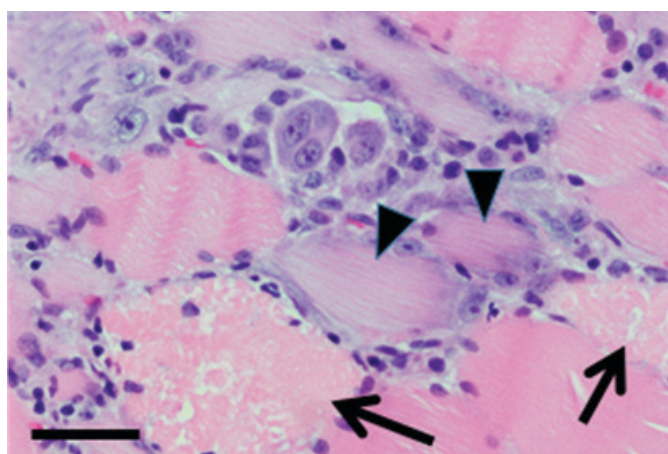


Figure 3: Necrotic (arrows) and basophilic myofibers (arrowheads). Darkly stained Type 1 myofibers highlights the widespread variation in myofiber sizes and shapes, due to extensive atrophy and necrosis.

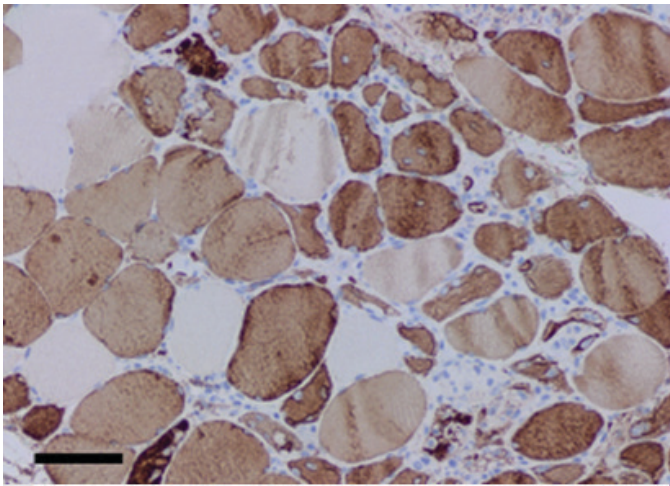


Figure 4: This is a paraffin section immunostained with fast myosin. Scale bars are 50 microns.

was started in addition to prednisone. In the interim, the pathology result of the biopsy specimen was reported to be consistent with severe necrotizing myopathy. The voltage gated potassium channel (VGPC) Ab, ANNA-1, ANNA-2 or PCA-1 Abs, Myositis Ab panel including SSA-52, (ENA) 60, SSB, Ribonucleic Protein, Jo-1 were negative. CK trended down to 1196 U/L after five doses of IVIG and prednisone 80 mg daily for four weeks. Clinically some improvement was noted in the upper extremity muscle groups. The patient was advised to follow up with oncology to initiate chemotherapy.

DISCUSSION

Paraneoplastic syndrome can precede or occur in concurrence with malignancy [1]. In our case, the symptoms started after a diagnosis of tonsillar squamous cell carcinoma. Other inflammatory myopathies such as dermatomyositis and polymyositis are well known to be associated with underlying malignancy [2–11]. Immune mediated necrotizing myopathy is characterized by necrotic muscle fibers with absent or minimal inflammation. They can be idiopathic, related to statins use, paraneoplastic or secondary to connective tissue disorder. In our case, patient was not on statins and was recently diagnosed with squamous cell carcinoma of tonsil. Necrotizing myopathy is relatively uncommon with only a handful of reports in the literature [12–13]. About 50% of patients with polymyositis or dermatomyositis have myositis specific antibodies [5–6]. Immune mediated necrotizing myopathy has three subsets based on serologic status: anti- SPR, anti-HMGCR and negative serology. Anti-HMGCR and seronegative IMNMs associated with a higher risk of cancer [14]. Our patient was not on statin and anti-HMGCR was not checked. However, presence of antibodies is also associated with other systemic involvement symptoms such as arthritis, heart failure, dermatitis, lung problems. Unlike the

inflammatory myopathies, there were no systemic signs in our patient, all the autoimmune work up including myositis extended panel was negative. The patient had no other signs and symptoms such as arthritis, skin rash, fever, interstitial lung disease. Cardiac involvement was ruled out by a normal echocardiogram.

Myotonia is easier to define on EMG than clinically. They are spontaneous painless discharges with a waxing and waning of both amplitude and frequency and signifies chronic depolarized muscle membrane [14–15]. The presence of myotonia on EMG supports myopathy, however the distinction between necrotizing and inflammatory myopathy can only be confirmed histologically. Biopsy results in our patient showed widespread necrosis of myofibers undergoing myophagocytosis with chronic inflammatory infiltrate which was more focal than that of a typical inflammatory myopathy. Muscle strength in our patient improved to some extent 3/5 with 5 doses of IVIGs and steroids. Therefore, it was recommended to continue prednisone 80 mg daily for a total of four weeks with monthly IVIG until further improvement along with the treatment of malignancy.

This is an unusual case of necrotizing myopathy associated with squamous cell carcinoma of tonsil. Patient's serology was negative and the presence of diffuse myotonia on EMG and muscle biopsy confirmed the diagnosis of necrotizing myopathy.

CONCLUSION

Necrotizing myopathy can be associated with squamous cell carcinoma of tonsil. Serology may be negative and the presence of diffuse myotonia suggested myopathy. However, biopsy showed myofibers undergoing myophagocytosis with minimal inflammatory cells thus confirming necrotizing myopathy. Treatment includes steroid, immunotherapy and treatment of underlying malignancy.

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Author Contributions

Bhanu Gogia – Conception of the work, Design of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Prashant Rai – Conception of the work, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Benjamin B. Gelman – Conception of the work, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Noushin Jazebi – Design of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Randal C. Reinertson – Conception of the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Kamakshi Patel – Conception of the work, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

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Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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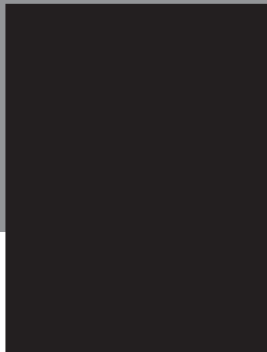
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