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Right Arm Weakness and Vaginal Spotting: A Curious Case of Paraneoplastic Necrotizing Myopathy Associated with Endometrioid Adenocarcinoma

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Right Arm Weakness and Vaginal Spotting: A Curious Case of Paraneoplastic Necrotizing Myopathy Associated with Endometrioid Adenocarcinoma

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Case Description

A 71-year-old female with no known medical or statin-use history initially presented with right arm weakness, notably in the forearm and biceps, and vaginal spotting. Subsequently her bilateral arms and shoulders became weak. She was found to have rhabdomyolysis with creatine kinase of 150,000s, but quickly improved and amphiphysin antibody was negative. Her weakness progressed to the lower extremities along with intermittent dysphagia and quickly became bed-bound within a 2-week period while inpatient. A D&C and CT chest, abdomen, and pelvis revealed poorly differentiated endometrioid adenocarcinoma, grade 3. Left deltoid biopsy revealed areas of scattered necrotic muscle fibers, scattered regenerating muscle fibers, and very mild perivascular lymphocytic inflammation, positive staining for major histocompatibility complex-1 and complement C5, and extensive endomysial alkaline phosphatase positivity. Left quadriceps biopsy revealed mild neurogenic changes and type 2 predominant atrophy. Anti-nuclear antibody was 1:640, but subsequent autoimmune and paraneoplastic panels were negative. A steroid course was completed with minimal improvement. One day prior to the planned hysterectomy, patient decompensated with respiratory failure and deceased shortly after family elected hospice care.

Discussion

Risk factors for Necrotizing Autoimmune Myopathy (NAM) include statin-use, cancer, connective tissue disease, but mostly classified as idiopathic. In recent years, immune-mediated necrotizing myopathy (IMNM) has been proposed as an alternative term given the uncertainty of whether NAM has a true autoimmune componentry. However, it is now recognized as a heterogenous disorder with many overlapping features but a distinct process from polymyositis, dermatomyositis, and inclusion body myositis. Paraneoplastic Necrotizing Myopathy is a rare form of Necrotizing Autoimmune Myopathy that is more often associated with gastrointestinal tumors, small cell lung cancers, and breast cancers. Treatment is often guided by the presence of autoantibodies and underlying neoplastic processes. Creatine kinase in NAM is often elevated on initial presentation. Our patient had concurrent rhabdomyolysis that quickly improved to the 3000s U/L. The diagnosis of NAM is most supported by biopsy showing necrosis of the muscle fibers with scattered regeneration. Importantly, NAM is characterized by staining with only mild to no inflammation, which is observed in our patient's deltoid biopsy. However, this is with the caveat that the patient has already received steroids prior to the biopsy, which could theoretically reduce the inflammation seen. However, with the clinical history, pathological support, and lack of antibody (anti-SRP, Jo-1, HMGCR), a diagnosis of polymyositis/dermatomyositis is much less likely. Interestingly, there are complement C5b9 (marker for complement C5 cleavage) positivity with reduced oxidative staining, which has been described as associated with cases of paraneoplastic necrotizing myopathy.

Lab Results

Initial CK	154,161 U/L
ESR	Normal
CRP	217 mg/L (Normal range: <10.0 mg/L)
ANA	1:640
Jo-1	Neg
SRP	Neg
HMGCR	Neg

***Abbreviations:** CK, creatine kinase; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; ANA, antinuclear antibody; SRP, signal recognition particle; HMGCR, 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase.*

Conclusions

The clinical history of vaginal spotting and upper extremity weakness with no known medical history presents a diagnostic challenge for clinicians. Paraneoplastic syndromes must be suspected in the differentials and timely workup is needed given the highly variable and often morbid disease course. Our patient presents with a rare form with upper greater than lower extremity weakness, positive ANA, and positive muscle biopsy for necrotic muscle fibers with positive staining for major histocompatibility complex-1 and complement C5.

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