Tropical Myositis: A Not-So-Tropical Diagnosis in a Febrile Type 1 Diabetic Patient

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ABSTRACT

Introduction: Tropical myositis – also known as pyomyositis – is a subacute, primary infection of skeletal muscle. Long considered a diagnosis exclusive to tropical climates, recently it has been reported increasingly in historically nontropical climates. We present a case of tropical myositis in Madison, Wisconsin, occurring in a febrile type 1 diabetic patient without travel or known exposure.

Case Presentation: A 35-year-old male with a history of von Willebrand disease, type 1 diabetes, and financial insecurity resulting in insulin rationing presented with 2 weeks of generalized weakness. On exam, he had a multitude of large, erythematous "bumps" across his body, which had been increasing in size for more than 2 weeks. His blood glucose was 518, with leukocytosis and labs supportive of diabetic ketoacidosis. Computed tomography revealed extensive intramuscular and subcutaneous abscesses of the left chest, bilateral erector spinae, right gluteal muscles, bilateral thighs, left leg, and left upper and lower arm. Broad-spectrum antibiotics were initiated, as was treatment for diabetic ketoacidosis. Blood and urine cultures revealed oxacillin-susceptible *Staphylococcus aureus*. After clinical stabilization, he underwent initial incision and drainage of the abscesses. His condition would require 14 more operative incision and drainage procedures and wound closure attempts before he was discharged to a rehab facility after more than a month-long hospitalization.

Discussion: Severe tropical myositis is associated with high morbidity and high use of health care resources. The exponential rise in cases in the United States in recent years risks further stressing an already-burdened health care system. We explore potential causes of the increase in cases of tropical myositis in nontropical regions, including increasing rates of diabetes and poverty and climate change. Recent data suggest that the large majority of tropical myositis cases are caused by Panton-Valentine leukocidin toxin-producing *Staphylococcus aureus* strains. There is a theoretical mitigation of disease severity when patients receive early protein synthesis inhibitor antibiotic treatment, though these findings are limited to case reports and observational studies and lack controlled clinical trials. This case highlights the need for early identification, antibiotic administration, and surgical source control in suspected cases of tropical myositis.

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INTRODUCTION

Tropical myositis – or pyomyositis – is a subacute deep primary infection of skeletal muscle long considered to be a diagnosis exclusive to tropical climates. However, in the last 2 decades, tropical myositis increasingly has been reported worldwide.[1]

Tropical myositis was first described in detail in 1885 and first characterized within the United States in 1971.[2] Although more common in immunocompromised individuals, tropical myositis can be found in the immunocompetent – especially in tropical climates.[1] Tropical myositis has been reported to account for as much as 4% of all hospital admissions in tropical regions.[3] The rates of infection have been climbing in temperate climates, where tropical myositis was once extremely rare. In the United States, there was a three-fold increase in tropical myositis admissions from 2002 to 2014.[4] Australia saw an almost four-fold increase in pediatric tropical myositis cases during the same time period.[5]

Tropical myositis is associated with immunodeficient states, including HIV infection, diabetes, organ transplantation, chemotherapy, rheumatologic diseases, and malignancy, and it occurs more commonly in males, with a 6:1 male-to-female ratio.[3]

Tropical myositis commonly manifests with fevers, myalgias, and cramping in a specific muscle or multiple muscles.[3] The

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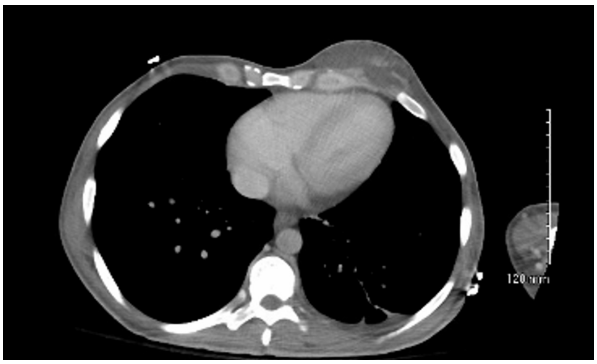
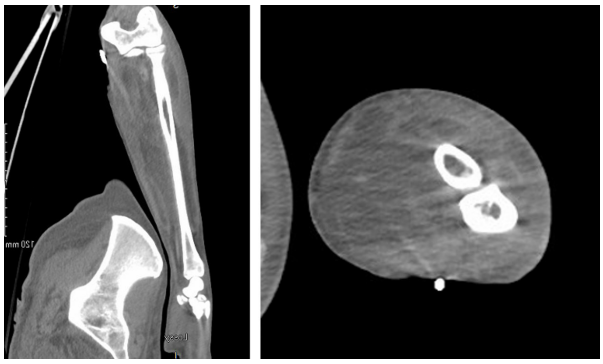
Figure 1. Computed Tomography of Patient's Chest



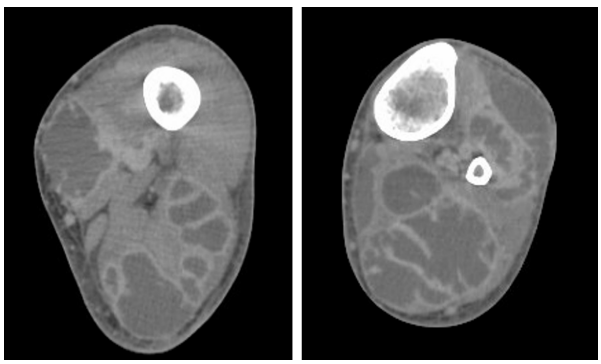
Left anterior lower chest wall abscess measuring 2.5 x 4.5 x 7.4 cm with surrounding soft tissue thickening and overlying phlegmonous soft tissue. Simple, small left pleural effusion.

Figure 2. Computed Tomography of Left Upper Extremity, Forearm, Coronal and Axial Views



Large complex, multiloculated, peripherally enhancing fluid collection within the brachioradialis and flexor musculature (7.7 x 5.7 x 18 cm). Intramuscular fluid collection with subcutaneous involvement along the posterior forearm (6.4 x 2.2 x 14.5 cm).

Figure 3. Computed Tomography of Left Lower Extremity, Thigh (Left) and Leg (Right)



Large multiloculated fluid collections within the distal hamstring musculature (7.6 x 4.5 x 11.5 cm); fluid and gas-filled collection within the medial thigh, predominantly within vastus medialis (4.3 x 6.4 x 17.7 cm). Loculated fluid collection within the medial head of the gastrocnemius (6.4 x 6.2 x 13.1 cm).

lower extremities and pelvic girdle muscles are the most common site of infection, but it can affect other muscles, including the pectoralis major, serratus anterior, iliopsoas, biceps, and spinal muscles.[3,6] Multiple muscle groups are involved in 12% to 40% of cases.[7] The most common causative organism is *Staphylococcus aureus* (*S aureus*).[6] The etiology is likely related to transient bacteremia with or without muscular trauma inducing seeding of the muscle leading to subsequent infection.[8]

Clinically, tropical myositis presents in 1 of 3 stages.[7] In the first stage of disease, patients present with generalized complaints—usually muscle aches or mild fever without clear formation of abscesses. Instead, affected muscles may feel "wooden" on palpation.[7] If untreated, it will progress to the second stage of disease, which is characterized by abscess formation.[7] Around 90% of diagnoses are made at this stage.[7] Patients present with worsened muscle pain, fever, and irregular muscle swelling, or fluctuance on exam. If missed in the second stage, patients may then progress to the third stage, which is characterized by severe systemic infection.[3]

It is imperative that tropical myositis be considered as part of the differential diagnosis for a patient presenting with generalized muscle complaints, fevers, and risk factors for tropical myositis (diabetes, muscular trauma, or immunocompromise). Our case describes a patient with tropical myositis who evaded early detection of disease and presented in the third stage of disease, resulting in a protracted hospital course. Our discussion focuses on the intersection of specific risk factors and their potential role in increasing rates of tropical myositis in nontropical areas. We discuss a theoretical framework by which a rise in temperate climate tropical myositis could be explained, highlighting the necessity of managing tropical myositis not only from a medical and surgical standpoint but also the social and environmental factors that put populations at risk for development of this debilitating disease process.

CASE PRESENTATION

A 35-year-old male who lost his balance in a public setting and was subsequently transported to the emergency department for severe weakness presented in the summer months with a past medical history of poorly controlled type 1 diabetes, von Willebrand disease, and financial insecurity resulting in insulin rationing. On arrival, he complained of excessive weakness lasting for 2 weeks. He endorsed dizziness, frequent urination, and severe thirst. Secondarily, he noted large "red bumps" on his left chest, left forearm, left thigh, and right calf. He described muscle aches for multiple weeks prior, though he was unsure of the exact time period. Aside from diabetes, he had no other history of immunocompromise or prior severe infections, nor did he have a history of illicit drug use.

On physical examination, the patient was alert and oriented, albeit in moderate distress with notable malaise. He had dry

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mucous membranes and was appreciably tachycardic. Muscle strength and sensation were grossly intact. Multiple large, erythematous masses were present on his left forearm, right hip, left chest wall, left thigh, and bilateral calves (the right draining purulent fluid). He had full passive range of motion in his extremities without pain out of proportion on exam. He was febrile, tachycardic, and normotensive. Initial laboratory analysis revealed significant leukocytosis, blood glucose of 518, metabolic acidosis, and elevated beta-hydroxybutyrate – concerning for diabetic ketoacidosis. Diabetic ketoacidosis protocol was begun in the emergency department.

Empiric antibiotic therapy of vancomycin, cefepime, and metronidazole also was initiated, with additional concern for severe infection given the patient's purulent abscesses on exam. Blood, body fluid, and urine cultures were drawn prior to initiation of antibiotics. Computed tomography of the chest, abdomen, pelvis, left forearm, and left knee was obtained, revealing diffuse intramuscular abscesses (Figures 1-3). Given the imaging findings, he was admitted to the general surgery inpatient floor for stabilization and plans for surgical management of his disease.

All cultures were gram-stained and revealed gram-positive cocci. Due to concern for bacteremia, the patient underwent transthoracic and transesophageal echocardiography on hospital days 1 and 2, respectively – both of which showed an absence of cardiac vegetations. Cultures speciated to oxacillin-susceptible *S aureus*, and antibiotics were narrowed to intravenous oxacillin. Additional infectious disease workup revealed normal oxidative burst via dihydrorhodamine test and negative HIV antibody/antigen testing.

On day 3 of hospitalization, the patient underwent extensive incision and drainage of the previously identified abscesses – producing copious amounts of purulent fluid from each. Achieving adequate source control of the infection proved difficult. He underwent extensive procedures, having 14 total operative debridements, fasciotomies, and attempted wound closures throughout his more than 30-day hospital stay. Given his diffuse muscular abscesses without clear nidus for infection, a diagnosis of primary pyomyositis – or tropical myositis – was made. By the end of his hospital stay, all wounds had been closed aside from the left forearm and left calf incisions, which were covered with wound vacuum with plans for surgical closure in the outpatient setting. Once medically stable and with confidence that source control had been achieved, the patient was discharged to a skilled nursing facility.

DISCUSSION

From 1971 to 1992, there were only 98 reported cases of tropical myositis within North America.[9] Since then, rates have increased significantly. From 2002 to 2014, there were more than 13 000 cases of tropical myositis in the United States.[4] During the same time period, rates of tropical myositis more than tripled, with an incidence of 0.0054% per hospital discharge in 2002 to 0.0209% in 2014.[4] A diagnosis of tropical myositis during that time period was significantly associated with a history of diabetes (type 1 and type 2),[4] of which our patient also had a history. He also faced financial insecurity, which resulted in insulin rationing that likely contributed in large part to his diabetic ketoacidosis. We believe this led to the immune compromise that produced the initial infection, as no obvious site of inoculation could be determined. Poverty and financial insecurity are well-known contributors to uncontrolled diabetes and increasing rates of diabetic ketoacidosis.[10] Incidence of both type 1 and type 2 diabetes increased each year during 2002-2012.[11] It is possible that the increased incidence of diabetes may have contributed to a rise in tropical myositis cases, though it may not explain the whole picture.

In temperate climates, the causal agent of tropical myositis is *S aureus* in more than 75% of all cases,[1] including our patient. *S aureus* strains containing the Panton-Valentine leucocidin (PVL) locus are associated with the development of soft tissue infections.[12] This locus codes for a specific pore-forming protein toxin secreted by the staphylococcal species. A recent genome-wide association study determined that *S aureus* containing the PVL locus alone increased odds of tropical myositis by more than 130-fold in Cambodian children, suggesting that *S aureus*-associated tropical myositis is critically dependent on the PVL locus.[13] For example, in sub-Saharan Africa – an area with high rates of tropical myositis – almost half of *S aureus* isolates contain PVL toxin.[14] Meanwhile, in Germany, where rates of tropical myositis are low, almost no *S aureus* isolates contain the PVL toxin.[14] This data may suggest a link between climate and the development of PVL-containing *S aureus* species.

We were unable to find any studies detailing the overall incidence of the PVL locus in *S aureus* species within the United States. However, new variations of *S aureus* species among cases of tropical myositis have been appreciated. Rates of oxacillin-resistant *S aureus* in cases of tropical myositis increased substantially from 1994 to 2006.[15] It is possible that variations in antibiotic usage over time have led to increased rates of PVL-containing *S aureus* species.

Recent evidence also suggests that climate change could offer a means by which once tropics-specific bacteria could colonize the skin microbiome of those living in historically temperate climates. Changes in average temperature and humidity associated with climate change could offer a potential mechanism for significant alterations in skin microbiome,[16] potentially favoring tropical myositis-associated pathogens like PVL-containing *S aureus* species. This warrants further investigation, though it may offer an explanation for the increasing incidence of tropical myositis in nontropical climates.

The suggestion that tropical myositis is critically dependent on toxin-secreting PVL-positive *S aureus* may offer insight into

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effective antibiotic management of tropical myositis. Empiric therapy with broad-spectrum antibiotics is the most beneficial initial management of presumed tropical myositis,[17] which fortunately was initiated promptly in our case. Because *S aureus*-associated tropical myositis may be critically dependent on toxin production,[13] early inhibition of bacterial toxin production with protein-synthesis inhibitors could theoretically prevent advancement of disease or lead to earlier resolution.[17] This also could prove helpful in preventing morbidity or mortality associated with severe disease. Multiple antibiotic classes have been shown to reduce production of PVL in vivo: macrolides, lincosamides (like clindamycin), rifampicin, and oxazolidinone.[18] To date, there is no current data on the favoring of one protein-synthesis inhibitor over another in the treatment of PVL-associated tropical myositis or their effects on limiting hospital course.

CONCLUSIONS

Tropical myositis, formally known as pyomyositis, is no longer a disease exclusive to the tropics. As such, it remains an important consideration as part of the differential diagnosis for immune-compromised patients presenting with diffuse myalgias and fever. There is a theoretical role for early adjunct initiation of protein-synthesis inhibitors given its association with PVL-containing *S aureus* species, though this remains an important area of investigation. The high systems cost associated with treatment of late-stage tropical myositis coupled with increasing rates of tropical myositis in temperate regions could further burden already highly stressed health care systems. Because of its association with diabetes, increasing rates of poverty, and possibly even climate change, the development of tropical myositis in historically temperate regions highlights the importance of appreciating and advocating for management of social determinants of health, such as poverty and climate change. Early recognition of tropical myositis and its risk factors is critical in preventing morbidity and mortality, as well as the high costs of treatment for patients and health care systems alike.

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