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INTERPRETATION OF VIRAL MYOSITIS IN MUSCLE BIOPSY

Pathology

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ABSTRACT

Myositis is called as muscle inflammation. In myositis, inflammation damages the fibers of a muscle. Myositis is an inflammation of muscles. Affected individuals will have difficulty contracting their muscles because of the damage to the muscle fibers from the inflammation. The inflammation may be caused by the body attacking its own tissues (autoimmune), infection, drug side effects, or injury. After traumatic injury, myositis can occur in bruised areas. This causes muscles to be weak by interfering with the ability of the muscles to contract. Although myositis can cause muscle aches and muscle tenderness, weakness is usually the dominant symptom. Common symptoms include muscle soreness, weakness, difficulty swallowing, and trouble climbing stairs. Individuals affected by myositis may have a decrease in their muscle mass (atrophy) for long periods of time. Individuals affected by the flu or other viral infections often experience myositis during their recovery. This is frequently seen in young children and manifests as severe leg pain and inability to walk properly for a few days. Inclusion body myositis (IBM) is an inflammatory myopathy that is characterized by chronic, progressive muscle inflammation and muscle weakness. Symptoms usually begin after the age of 50, although the condition can occur earlier. The onset of muscle weakness usually occurs over months or years. This condition affects both the proximal (close to the trunk of the body) and distal (further away from the trunk) muscles.

Myositis is usually of short duration but In some cases, it persists for long duration. Chronic forms of myositis can lead to muscle atrophy and severe disability. In our case study we have collected 40 samples of muscle biospsy who were presented with flu like symptoms and also with repeated muscle aches.

KEYWORDS

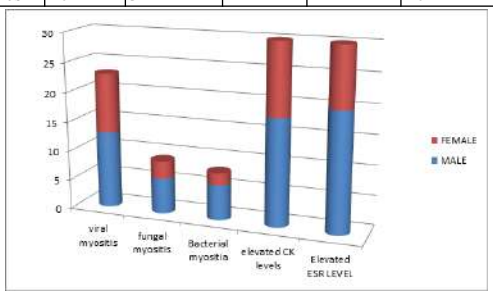
Viral Myositis, Muscle Biopsy, Influenza And Muscle Degeneration.

We have collected 40 cases of muscle biopsy sample in which males are 25 and females are 15cases during 2017 january to December 2018.

Most of the cases belong to young age group between 10 to 20 years.

Sex	10-20	20-30	30-40
males	15	5	5
females	8	5	2

sex	Viral myositis	Fungal myositis	Bacterial myositis	Elevated CK levels	Elevated ESR Levels
Males	13	6	6	18	20
females	10	3	2	12	10



INTRODUCTION :

Myositis is defined as inflammation of a muscle, especially a voluntary muscle, characterized by pain, tenderness, swelling, and/or weakness. The many different etiologies of myositis include infection, autoimmune conditions, genetic disorders, medication adverse events, electrolyte disturbances, and diseases of the endocrine system . Some idiopathic cases of polymyositis are suspected to be related to infectious agents, especially viruses such as the paramyxoviruses or enteroviruses Microorganisms may cause myositis via immune mechanisms without directly infecting the muscle In addition, they may cause infectious myositis, which is defined as infection of skeletal muscle. Bacterial myositis usually presents as a focal muscle infection, whereas viruses and parasites are often more diffuse in nature, leading to generalized myalgias or multifocal myositis. Pyomyositis is defined as an acute intramuscular infection that is secondary to hematogenous spread of the microorganism into the body of a skeletal muscle; Given the musculature's resistance to infection, bacterial myositis often occurs in the setting of muscular injury, surgery, ischemia, or the presence of a foreign body. Certain hosts, such as those with immunocompromising conditions, have a heightened risk of bacterial and fungal myositis.

Bacterial infections of the musculature are often categorized according to the inciting event, clinical presentation, including anatomic location, and the causative organisms into the categories of pyomyositis, psoas abscess, *S. aureus* myositis, group A streptococcal necrotizing myositis, group B streptococcal myositis, clostridial gas gangrene, and non clostridial myositis.

Fungal involvement of the musculature is uncommon but has been described in case reports. Most cases have involved Immuno compromised patients; occasionally fungal myositis has been reported in immunocompetent persons. Given the rising prevalence rates of immunocompromised hosts due to advanced therapies for cancer and rheumatologic conditions, as well as the aging of the population, the number of fungal myositis cases may increase. History of severe immunosuppression and evidence of other sites of fungal infection may point to a fungal etiology. Fungal myositis may be due to *Candida* spp. *Cryptococcusneoformans, Histoplasmacapsulatum, Coccidioides spp., Aspergillus spp., Pneumocystis jiroveci, and Fusarium spp.* Biopsy with culture is usually required to confirm the diagnosis of the fungal etiology; often the diagnosis of a fungal pathogen is not initially considered and is discovered by histopathologic examination or culture of the muscle tissue.

Parasitic myositis

A variety of parasitic infections may encyst in the musculature. The most commonly reported parasitic causes of myositis are *Trichinella* spp., *Taenia solium*, and *Toxoplasma gondii* (toxoplasmosis). However, a wide range of other parasites may cause myalgias or myositis. These include *Trypanosoma cruzi* (Chagas'disease) *Sarcocystis* spp. *Microsporidia* spp, *Toxocaracanis, Schistosoma spp., Echinococcus spp., EntamoebaHistolytica , Spirometramansonoides* (sparganosis) *Plasmodium falciparum* (malaria) , and *Onchocerca*

volvulus In addition, myositis caused by a new muspiceoid nematode was recently reported from Australia .

Viral myositis

A variety of viruses may cause myalgias, polymyositis,orvirus-associated rhabdomyolysis. Often the symptoms of myositis are diffuse in nature, and patients have other symptoms and signs attributable to the causative viral pathogen. The most commonly reported causes of viral myositis in the United States are influenza A and B viruses Several other viral pathogens, including enteroviruses HI, human T-cell leukemia-lymphoma virus (HTLV) type 1 , and hepatitis viruses (B and C) may cause myositis .

Myopathy-related disease or manifestation

Idiopathic inflammatory myopathies

Polymyolitis
Dermatomyositis
Inclusion body myositis
Myositis associated with collagen vascular diseases are Polyarteritis nodosum
Wegener's granulomatosis
Systemiclupuserythematosus
Rheumatoid arthritis
Scleroderma
Sjogren's syndrome
Leukocytoclastic vasculitis
Hypersensitivity vasculitis
Polymyalgia rheumatica
Mixed connective tissue disease
Adult Still's disease
Myositis associated with malignancies
Other forms of myopathies
Inflammatory myopathies
Myositis associated with eosinophilia
Myositis ossificans
Giant cell myositis
Myopathies due to drugs and toxins

DISCUSSION

viral infections that have been reported to cause rhabdomyolysis. Influenza is the most common viral etiology followed by HIV infection and enteroviral infection. The presenting symptoms in the patients are myalgias, weakness muscle tenderness, and edema. A review of viral causes of rhabdomyolysis with preponderance of influenza virus infections; influenza was repeatedly one of the most common infectious precipitants of rhabdomyolysis.

Muscle biopsies of patients with rhabdomyolysis shows lymphocytic infiltrate support the hypothesis of direct viral invasion. muscle biopsies of affected individuals have revealed viral inclusions, and, recently, DNA from varicella-zoster virus was identified by PCR analysis of muscle specimens from patients with rhabdomyolysis .

Influenza virus was subsequently demonstrated by hemagglutination and by direct EM of cultured specimens of the liver,CSF, and muscle from a patient with Reye's syndrome

Light microscopy revealed necrotic muscle fibers in large clusters surrounded by morphologically normal appearing muscle. Cytopathic changes consisting of granularity and vacuolization of the cytoplasm.retraction, and rounding of cell processes with swellingof the cell body occurred in the infected cell lines. Viral presence was confirmed by immunofluorescence and EM.

This evidence strongly suggests that direct viral invasion may have a causative role in precipitating rhabdomyolysis.

Biopsies of clinically affected musculature that are essentially unremarkable raise the possibility of a circulating "toxin" or cytokine causing rhabdomyolysis

The renal dysfunction associated with rhabdomyolysis arises from a variety of factors. Myoglobin obstructs tubules and is a direct renal toxin. Cortical ischemia and decreased glomerular infiltration are also injurious, and when these conditions are combined with hypovolemia, oliguric renal failure can result patients with influenza had renal failure.

Renal biopsies of these patients showed acute tubular necrosis and myoglobin casts obstructing Tubules.

Acute myositis is associated with multiple viruses, with influenza most commonly implicated. Viral studies show that influenza B is more likely than influenza A to cause myositis, likely due to the presence of NB protein in the membrane of influenza B, which is implicated in viral entry and may have myotrophic properties. Viral myositis is most commonly characterized as sudden onset of muscle weakness, pain and tenderness during the early recovery phase of the virus. Symptoms are often isolated to the calf muscles, but other muscle groups are involved in one third of cases. it is typically self-limiting, with recovery within one week of the onset of symptoms, but there are reports of rhabdomyolysis with renal failure and compartment syndrome.

Myositis occurs only in a small percent of those affected with influenza, and is most common in children (mean age eight years), possibly because of virus tropism for immature muscle cells, which has been documented in animal studies. It has, however, been reported in all age groups. Males are more commonly affected than females (2.4:1). It is associated with mildly to moderately elevated serum creatine kinase (CK) level. Muscle biopsy typically reveals muscle fiber degeneration and muscle necrosis with infiltration of leukocytes.

The novel 2009 influenza A (H1N1) virus was first identified in humans in April 2009 in Mexico with the first confirmed case in Utah on May third, 2001.The virus rapidly spread throughout the world, and the World Health Organization (WHO) declared it a pandemic on June 11, 2009.Epidemic levels of influenza like illness were reported in Utah from October 2009 to January 2010, and H1N1 was the only influenza in circulation in Utah during this time.The symptoms include fever, cough, sore throat, runny nose, body aches, headache, chills and fatigue.

Parvovirus B19 as a cause of myositis is rare and seldom reported. acute inflammatory myositis without arthritis in association with acute erythrovirus B19 infection reported recently. it is very rare one.

Clinical symptoms such as malaise and myalgias were present in these patients, similar topatients with primary viral infections with Epstein-Barr virus.and cytomegalovirus.

Myalgia is a common manifestation in DF and one of the criteria of a suspect case according to the WHO 1997 criteria. Though varying degrees of myalgias are commonly seen, muscle weakness is uncommon presenting manifestation. Myositis and/or elevated serum creatinine kinase (CK) were only reported infrequently with few cases with muscle paralysis or acute rhabdomyolysis . Patient presents with complaints like myalgia with or without reversible proximal muscle weakness, specially in lower limbs. Some may present as subclinical myositis with minimal symptoms and elevated serum CK levels and very rarely as rhabdomyolysis. Viral rhabdomyolysis, if diagnosed early, can easily be treated to reduce associated grave complications like acute renal failure.

A variety of skeletaleletal syndromes associated with HIV infection have been documented ranging from myopathy to polymyositis to rhabdomyolysis Muscle biopsies of patients with HIV-induced rhabdomyolysis revealed nonspecific inflammatory myopathy with focal necrotic areas and regenerating fibers.

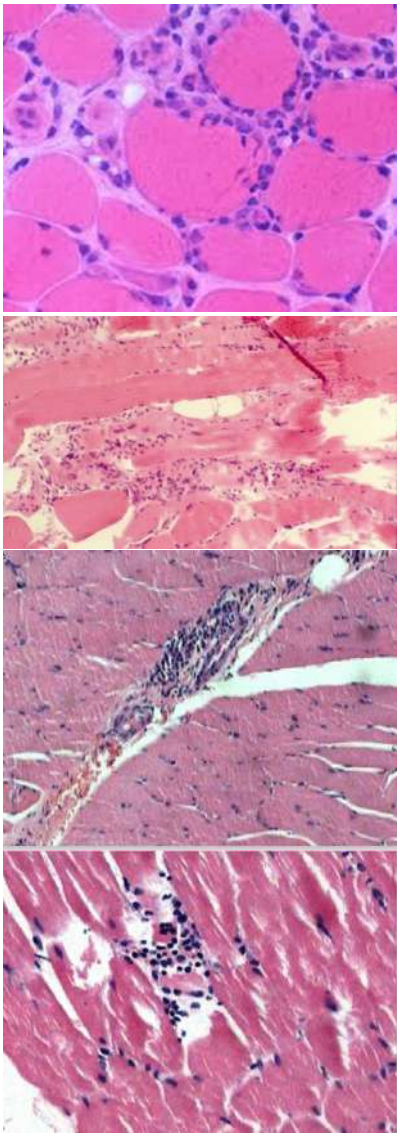
The first report of an HIV-associated inflammatory myopathy was published by Dalakas in 1986. Their patients developed AIDS-related complex soon after. HIV myositis may occur early in the disease, in the stage of full-blown AIDS, or be a manifestation of immune reconstitution after starting HAART. case usually presents as a subacute proximal weakness with or without myalgia.CPK may be raised to 10 to 15 times the normal value. EMG shows a myopathic pattern, often with features of muscle hyper-irritability. Overall, there may be little to distinguish the process from acquired polymyositis. Muscle biopsy reveals a perivascular, perimysial or endomysial mononuclear infiltrate, as well as necrotic and degenerating muscle fibers. Nemaline rods have been documented in some cases. HIV myopathy may present with rhabdomyolysis with myoglobinuria. In HIV wasting syndrome, there is a preferential atrophy of type II myocytes. Mycobacterial and other opportunistic infections may occur. In zidovudine-induced myopathy, mitochondrial dysfunction is the postulated etiology, and the histological hallmark is the demonstration of "ragged red fibers" on muscle biopsy. When HAART

is begun, immune reconstitution inflammatory syndrome (IRIS)-related myositis remains another concern.

Interesting insights have now been gained into the pathogenesis of HIV myositis. It was found that, HIV sequences or transcriptional products were not present within the muscle fibers or the cultured myotubes of patients with HIV myositis, thus indicating that viral replication does not take place within the muscle. HIV myositis is now considered to be caused by infection of the lymphoid cells, rather than direct infection of muscle fibers by the virus. A previous study of biopsy-proven HIV myositis has demonstrated no correlation of the severity of weakness or the stage of HIV infection with the CPK values at diagnosis. HIV myositis responded well in most cases to treatment with corticosteroids and immunosuppressive agents.

Due to the poor correlation between clinical findings and CPK values, as exemplified chiefly by cases 2 and 4, HIV polymyositis and the myopathy of HIV wasting syndrome could be reliably distinguished by muscle biopsy alone. This distinction is clinically significant as some cases of HIV polymyositis respond reasonably well to treatment. It would be ideal, therefore, that muscle biopsy be performed in all cases of HIV myopathy, especially when features of hyper-irritability are not evident on EMG.

We conclude that HIV myopathy may produce a wide variety of clinicopathological manifestations, necessitating proper characterization by all available means, including muscle biopsy. Moreover, HIV should be increasingly included in the differential diagnosis of patients presenting with features of inflammatory myositis.



- Skeletal muscle shows myopathic changes with evidence of myofiber degeneration and regeneration with lymphocytes invading non necrotic myofibers
- Predominant inflammatory cell is the CD8+ T lymphocyte
- Serum CK (creatine kinase) and aldolase are elevated in 90%
- Elevated sedimentation rate (ESR) of 50 - 100 in 40% and an ESR above 100 in 10% (Ann Rheum Dis 1993;52:857)

MRI T2 may show edema, which is useful in muscle biopsies

- Skeletal muscle shows myopathic features - occasional small rounded myofibers with mildly increased internal nuclei
- Individual myofibers show degeneration with possible macrophage infiltration to clear the necrotic myofiber
- May be myofiber regeneration with basophilic myofibers with large nuclei and prominent nucleoli
- Should be a prominent endo mysial inflammatory infiltrate (this can be attenuated if the biopsy is after steroids/therapy)
- Lymphocytes invading non necrotic myofibers are a diagnostic finding
- Occasional cases show only lymphocytes associated with necrotic myofibers and the possibility of polymyositis can be suggested if clinically applicable
- Biopsy can also show mild to moderate fibrosis

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