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AN OVERVIEW ON TYPES, DIAGNOSIS AND TREATMENT OF MYOSITIS

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ABSTRACT
Muscle inflammation is a hallmark of the autoimmune illness myositis. Muscle inflammation is a common secondary symptom of lupus, scleroderma, and vasculitis patients, although the condition can manifest in many different ways. It includes the following types like polymyositis, dermatomyositis, juvenile myositis, ocular myositis, necrotizing myopathy, sporadic inclusion myositis and toxic myositis. Accurate diagnosis of myositis requires a detailed medical history and physical examination. A laboratory examination typically shows elevated CK, but it is also possible to find myositis-specific autoantibodies and other enzymes including LDH, AST, or ALT. Magnetic resonance imaging (MRI) can identify changes in signal intensity inside the muscle.Since a biopsy is the only method available to differentiate between the various myositis subtypes, it is both the most crucial and invasive step in making the right diagnosis. The pharmacological treatment incudes glucocorticoids, adrenocorticotrophic gel, methothrexate, azathioprine, cyclophosphamide, hydroxy chloroquine, calcineurin inhibitors, mycophenolate mofetil, intravenous Immunoglobulins, biological and non biological products. The non pharmacological treatment includes interchange of plasma and leukapheresis, exercises e.t.c.,

KEYWORDS: Muscle inflammation, Myositis, Autoimmune, MRI, Immunoglobulins and leukapheresis.

DEFNITION
Muscle inflammation is a hallmark of the autoimmune illness myositis. Muscle inflammation is a common secondary symptom of lupus, scleroderma, and vasculitis patients, although the condition can manifest in many different ways. Not just muscles, but the entire body can be impacted by myositis.[1] This normally deteriorates over time. Myositis is caused by immune system malfunction, which causes it to target healthy tissue by mistake.[2]

TYPES OF MYOSITIS
It includes the following

A. Polymyositis (PM)
Polymyositis usually occurs in people over the age of 20, affecting more women than men. The biggest symptom is muscle weakness that begins in the trunk (neck, hips, back and shoulders) and worsens over time. Autoantibodies for myositis can help with accurate diagnosis and, in certain situations, may help with prognosticating the course of the disease and possible therapy results. PM may be accompanied by lung illness and, to a lesser extent, malignancy. Currently, it is believed that individuals frequently fit into one of the other types of myositis, and PM is overdiagnose.

B. Dermatomyositis (DM)
it is a type of myositis that is simple to diagnose since it causes a purple rash that resembles a heliotrope flower. The rash usually develops across the joints, including the knuckles, elbows, knees, and toes, as well as the eyelids, face, chest, neck, and back. It's one of those ailments that affects the skin and the muscles. Due to the disease's rapid progression, problems must be avoided by seeking medical attention right once. Additionally, there is a higher chance of several malignancies in patients with dermatomyositis.

C. Juvenile myositis (JM)
Juvenile myositis (JM), which affects children under the age of 18, is typified by muscle weakness in the neck, shoulders, back, and torso. Another symptom of juvenile dermatomyositis is a red, spotty skin rash.Juvenile myositis (JM), which affects children under the age of 18, is typified by muscle weakness in the neck, shoulders, back, and torso. Another symptom of juvenile dermatomyositis is a red, spotty skin rash.

D. Occular myositis (OM)
The extraocular muscles of the eye, which govern eye movement, are impacted by orbital or ocular myositis (OM), an incredibly uncommon inflammatory disease. Diplopia, or double vision, and orbital discomfort are

common symptoms of orbital myositis. OM typically affects adult women who are young to middle-aged. The majority of the time, treatment is effective, but there is no known cure, and finding a physician who understands OM can be challenging.

E. Necrotizing myopathy (NM)
also known as immune-mediated necrotizing myopathy (IMNM) or necrotizing autoimmune myopathy (NAM), is characterized by muscle weakening and signs of muscle cell death. It is now recognized as a distinct type of myositis, although it was once classified under the polymyositis diagnosis.

F. Sporadic inclusion body myositis
The most prevalent myopathy in adults over 50 is sporadic inclusion body myositis (sIBM), a rare autoimmune degenerative muscle-wasting illness. It is typified by asymmetric, gradually progressing muscular atrophy and weakening in the distal rather than the proximal regions.

G. Toxic myositis
Medical professionals think that some prescription drugs and illegal narcotics are the cause of toxic myositis. Statins are a class of medication that lowers cholesterol and is one of many drugs that may be the cause of the illness,[2.3,4,5]

DIAGNOSIS
Accurate diagnosis of myositis requires a detailed medical history and physical examination. Rather than a proximal weakness, which is similar in DM, PM, and NM, the paresis distribution can show a pattern typical for IBM. A laboratory examination typically shows elevated CK, but it is also possible to find myositis-specific autoantibodies and other enzymes including LDH, AST, or ALT.

Acute injury may be observed, and the needle EMG of the afflicted muscles typically shows a myopathic pattern. None of the patients with the diagnoses of DM, PM, or IBM had a normal needle EMG, according to a retrospective Dutch investigation involving 98 myositis patients. Magnetic resonance imaging (MRI) can identify changes in signal intensity inside the muscle.

Since a biopsy is the only method available to differentiate between the various myositis subtypes, it is both the most crucial and invasive step in making the right diagnosis. Making sure that muscular dystrophy and other inherited myopathies are ruled out is very important. To achieve this, it is important to choose a representative muscle for the biopsy: usually, this muscle should demonstrate moderate paresis. MRI can help to identify end-stage changes of tissue destruction.

To identify an ILD, a chest X-ray ought to be taken. In individuals with anti-synthetase autoantibodies and anti-CADM, high-resolution CT scans may be undertaken. This method enables the identification of pulmonary alterations before the onset of clinical symptoms. Regular cardiological exams should be performed on patients who have a high risk of cardiac involvement. When taking prednisone at a dose greater than 5 mg per day, evaluation of bone density should be taken into account.

A high incidence of self-reported dysphagia in patients with myositis suggests that questions about this topic should be asked during every examination. When dysphagia is reported, further diagnostics such as videofluoroscopy or flexible endoscopic evaluation of swallowing may be performed. Although dysphagia is reported to be highly frequent in IBM, patients with DM and PM also frequently display signs of swallowing difficulties.[6,7]

TREATMENT
a) Pharmacological treatment
1. Glucocorticoids
Despite the absence of clear data derived from randomized controlled trials, treatment with GCs remains the first therapeutic approach in clinical practice for patients with IIMs. The treatment is able to reduce muscular inflammation, and more than 60% of the patients show improvement of muscle symptoms when treated with GCs. This occurs in particular in the first 6 months after the start of the treatment. High GC doses have also been used successfully for lung involvement.
Prednisone or an equivalent dosage of 1 mg/kg/day was administered to GCs as part of the conventional therapy approach. When there are contraindications, such as diabetes mellitus, hypertension, or glaucoma, a lower dosage should be considered. In certain situations, a greater dosage of up to 2 mg/kg/day may be recommended, but it should not exceed 80–100 mg/day. When a patient has a severe illness, an induction therapy with intravenous methylprednisolone pulses (500–1000 mg/day for three days straight) is sometimes advised. Examples of such patients are those with significant muscle weakness, dysphagia, quickly developing interstitial lung disease (ILD), or skin ulcers.

Although several strategies for GC tapering have been put out, the higher dose should typically be kept for 2-4 weeks before being progressively lowered by 20–25% per month until a level of 5–10 mg/day of prednisone, or an equivalent, is obtained. Strict clinical and laboratory monitoring, including measurement of muscle strength using proven techniques (e.g., manual muscle test 8 (MMT8)) and serum muscular enzymes, should be carried out during the reduction of GCs.

Patients treated with GCs frequently experience side effects (SEs), which can include weight gain, cushingoid appearance, diabetes mellitus, dyslipidemia, systemic artery hypertension, osteoporosis, thinning skin, gastric intolerance, infections, hirsutism, cataracts, and glaucoma.

2. Adrenocorticotropic gel
For a duration of 12 weeks, ACTH gel was injected subcutaneously once or twice a week. Further research is required to assess the safety and effectiveness of ACTH gel in patients with IIM, even though the medication was well tolerated and did not cause any serious side effects.

3. Hydroxychloroquine
hydroxychloroquine Treatment of skin involvement in DM using antimalarials (hydroxychloroquine 400mg/day (HCQ) or quinacrine) in combination with GCs with or without immunosuppressors has been shown to be successful, according to observational studies. headache, disorientation, skin eruption, and gastrointestinal toxicity (nausea, vomiting, diarrhea) and Antimalarial retinopathy is the most serious adverse event that can occur.

4. Methotrexate
Take Methotrexate (MTX) and azathioprine are regarded as the immunotherapeutic medicines of choice when treating muscle involvement. Up to 20–25 mg of MTX per week can be given orally, subcutaneously, or intramuscularly. To minimize negative effects and patient withdrawal from MTX, appropriate folic/folinic acid therapy should occur after MTX treatment. Because of its teratogenic properties, women should not use MTX during pregnancy. Infections, hepatotoxicity (excess liver enzyme) and cirrhosis are the most frequent adverse events (AE) associated with MTX.

5. Azathioprine
Typically, oral administration of AZA begins at 50 mg/day and increases incrementally by 25–50 mg every two weeks to a maximum of 2 mg/kg/day. Patients taking AZA should have routine testing for renal function, liver enzymes, and total blood cell count. Typical side effects include nausea, liver damage, and bone marrow suppression. The combination of these two medications can be tried for patients who did not react to MTX or AZA alone; in these individuals increases muscle strength.

6. Calcineurin Inhibitors
The primary actions of calcineurin inhibitors (CNIs), such as tacrolimus (TAC) and cyclosporine-A (CYA), are to reduce the activity of genes that code for cytokines such as IL-2 and to decrease T cell activation. Oral administration of CYA typically involves two daily doses of 2 to 4 mg/kg/day.[47] TAC can be taken twice daily at a starting dose of 1 mg, titrated to 1-2 mg/day until the desired blood levels of 5–20 ng/ml are attained. Nephrotoxicity, hepatotoxicity, hypertension, hypertrichosis, gingival hyperplasia, headaches, and hypertrichosis are among the side effects of CNI treatment that carry a risk of toxicity. This risk rises as drug dosages do.

7. Mycophenolate Mofetil
A prodrug called mycophenolate mofetil (MMF) lowers the synthesis of guanosine nucleotides by preventing T and B cell growth. MMF is taken orally in doses of 500 mg twice daily up to a daily dose of 2-3 g refracted in two doses each day. Although gastrointestinal problems (diarrhea, vomiting, and nausea) and blood cell count abnormalities (severe neutropenia, among others) are rare, MMF is usually well tolerated. It is not advised to receive MMF medication while pregnant.

8. Cyclophosphamide
Cyclophosphamide (CYC) has been utilized to treat patients with progressing ILD in particular who have severe rheumatic disease symptom. For DM patients with quickly progressing ILD, combination therapy combining CYC and CYA may be a potential treatment option. However, some patients may not be satisfied with the outcome. Additionally, it has been noted that patients with anti-MDA5 autoantibodies and severe ILD may benefit from combined therapy with rituximab. Although CYC is typically only used to treat lung involvement, it has also been shown to be beneficial for treating muscular symptoms, as well, as it can enhance muscle strength and lower serum levels of muscle enzymes.

Oral dosing can also be given, however IV pulses (0.3–1 g/m2 or 10–30 mg/kg) delivered at weekly to monthly intervals for 6–12 months was the most commonly utilized therapeutic method. Recently, a lower dosage strategy has been suggested, similar to that for lupus nephritis (500 mg every other week for up to 12 administrations), with high efficacy and no serious side effects.

Potentially serious side effects, including myelosuppression (neutropenia), hepatotoxicity, renal toxicity, hemorrhagic cystitis, infections, permanent ovarian failure leading to infertility, and secondary cancer, restrict the use of CYC therapy. It is not recommended to use CYC when pregnant.

9. Intravenous Immunoglobuins
Intravenous immunoglobulins (IVIG) are preparations made from combined IgG preparations from thousands of donors. They include antibodies that are directed against several foreign and self-antigens in addition to a wide variety of infections. IVIG treatment for dysphagia has been shown to be effective in treating otherwise treatment-resistant IBM patients.

The therapeutic dose of IVIG was experimentally established to 2 g/kg/months in three to five refracted administrations, as previously suggested by Imbach et al. Depending on the severity of the ailment and how well the patient responds to the treatment, the number of therapeutic cycles may vary. Immunosuppressive medications and IVIG might also be taken together. In myositis, subcutaneous immunoglobulin (SCIG), which is self-administered once a week using a programmable

pump, has recently been found to be a useful substitute for IVIG. Compared to hospital-based IVIG, this treatment seems to be a safe, effective option that lowers the patients' quality of life less.

IVIG is regarded as a reasonably safe treatment. Fifteen to twenty percent of the infusions have been associated with adverse effects, most of which are moderate and temporary, involving headaches, fevers, chills, and myalgias. Anecdotally, the use of high-dose IVIG in patients with IIM has been linked to hemolytic anemia, hyperviscosity syndrome, congestive heart failure, and acute lung damage from transfusion. Patients with IgA deficiency have been documented to experience anaphylaxis. IVIG may pose a danger for the blood-borne spread of diseases that are not detected [83••]. In patients with infections [10] and neoplasia [90], when an immunosuppressive strategy may be harmful, IVIG is thought to be safe. Despite the paucity of current information, IVIG can be used when pregnant.

10. Biological products

a.Rituximab

A chimeric monoclonal antibody called rituximab (RTX) targets the CD20 protein, which is mainly expressed on the surface of B cells. The most often prescribed biologic for the treatment of IIM has been found to be RTX. In IIM, refractory muscle, lung], skin, or joint involvement are the primary indications for RTX treatment. Individuals with anti-ARS], anti-SRP, and Mi-2 antibodies seem to respond better to treatment than patients without myositis-specific autoantibodies (MSA). Following B cell depletion, anti-Jo1 and anti-Mi2 autoantibody levels dropped and were associated with a decline in disease activity.

RTX is typically administered as two 1-g infusions spaced two weeks apart; after six months, it may be repeated. Additional treatment plans that were suggested included 375 mg/m2 per week for four weeks in a row.

While rituximab is usually well tolerated, adverse events do occur occasionally. The most frequent adverse event associated with RTX treatment is infusion responses, which can also be severe. These reactions mostly happen during the initial infusion and are less common in individuals who were premedicated with intravenous GCs, antipyretics, and antihistamine medications. For individuals with a history of ischemic heart disease, cardiac monitoring is advised both during and after RTX infusions due to a potential cardiotoxic impact. Pneumococcal and influenza vaccinations are advised prior to treatments, as infections during treatment are rather prevalent and can be both bacterial and viral.

11. Other biologicical-products

Some case reports have shown success with the use of abatacept, a fusion protein that inhibits T cell immunological function.A recent small randomized open trial raised the possibility that intravenous abatacept infusions could have an impact on muscle weakness in PM or DM patients who are not responding to therapy.

a. Tumor necrosis factor (TNF) may contribute to the pathophysiology of IIM; nonetheless, there has been disagreement over the efficacy of anti-TNFα treatment for IIM patients. Even though some authors suggested that etanercept may have a role in DM as a steroid sparing drug, other studies did not support this finding, and some patients' conditions worsened. Although infliximab (IFX) was found to be effective in certain patients in a recent randomized controlled trial (RCT), most clinical results were disappointing. Furthermore, several writers noted that individuals with psoriatic, rheumatoid, and psoriasis may develop myositis as a result of anti-TNF alpha medication. In conclusion, TNF blockers should only be used in cases when other therapy have failed for adult patients with IIM. They are generally not advised in this regard.

b. Tocilizumab has been evaluated with encouraging results in two case reports, as interleukin (IL)-6 has been observed to correlate with myositis disease activity. Clinical trials are currently being conducted to determine whether tocilizumab is effective for IIM patients.

c. An IL-1 receptor antagonist called anakinra was tried in limited case series and case reports, showing promise in certain patients.

Although they are being studied for the treatment of IIM, other medications such tofacitinib, basiliximab, sifalimumab, and alemtuzumab are not advised for use in ordinary clinical practice.

Non Pharmacological Treatment

A. Interchange of plasma and leukapheresis

In a clinical experiment conducted in 1992, 39 patients underwent plasma exchange and leukapheresis, despite some reports indicating hopeful results. However, the patients' muscle strength did not significantly increase when compared to the placebo group. Adverse events, including the implantation of a central venous catheter, significant vasovagal episodes, infusion responses, and a decrease in hemoglobin, have been linked to apheresis treatments. Therefore, guidelines put forward by the American Society of Apheresis prohibit the use of therapeutic apheresis in DM and PM, citing its perceived ineffectiveness or danger. However, it might be useful in patients with acute, nonresponsive, life-threatening diseases.

In patients with severe ILD undergoing clinically amyopathic DM with anti-MDA5 positivity, a recent therapeutic protocol that included hemoperfusion with polymyxin B in addition to the usual immunosuppressive treatment has shown promising results. However, controlled trials are required to confirm this effect.

B. Exercise and physical treatment

Exercise and physical treatment In recent years, it has been determined that exercise is a crucial supplementary component of treatment for those diagnosed with IIM. For people with IIM, exercise may enhance muscular metabolism, physical ability, autonomy, and quality of life. The suggested workouts include cycling, resistance training, and treadmill walking.

C. Diet and Life-style Modifications

Adults received an induction therapy of 20 g/day for eight days, followed by maintenance therapy of 3 g/day. Although there was no correlation seen between creatine supplementation and adverse outcomes, patients with renal impairment should be treated with caution.[7,8,9,10 and 11]

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