ISSN 2515-8260 Volume 10, Issue 01, 2023

A RARE INCIDENCE OF PARANEOPLASTIC MYOPATHY IN A CASE OF UROTHELIAL CARCINOMA- A CASE REPORT

Dr Bhumika Vaishnav
professor , Departmrnt of General Medicine , Dr Dy Patil medical college , hospital and research centre , Pune)

corresponding author
Dr AVS SRIVATSAV
(Resident , Department of General Medicine , Dr DY Patil medical college , hospital and research centre)
srivatsav00013@gmail.com

Dr.Nikitha Nimmagadda
Resident , General Medicine , Dr DY Patil medical college hospital and research centre , Pune)

ABSTRACT: There are several key observations on paraneoplastic myopathies: The risk of cancer associated with DM is very high, whereas risk of cancer associated with PM is mildly increased Most cancers develop within one year of the onset of myositis, although the risk remains high up to 5 years after diagnosis. The most common cancers associated with DM are adenocarcinoma, including lung, ovary, cervical, stomach, pancreas, colorectal and lymphoma, whereas PM is associated with a high risk of lymphoma. The clinical course of myopathy is closely linked with the course of cancer. Certain clinical features are associated with CAM including severe treatment resistant skin manifestations, severe muscle weakness, respiratory muscle weakness, and dysphagia, while some clinical features are protective such as arthritis, Raynaud, and ILD. Screening should be based on age, gender, ethnicity, and the geographic area of the patient; however, certain high-risk patients may require more extensive screening including tumor markers and thoracoabdominal-pelvic CT scans. Certain autoantibodies including anti-p155 and the absence of more common autoantibodies are associated with a higher risk of CAM, while the presence of antisynthetase autoantibodies lowers the risk for CAM. Although the pathogenesis of CAM is unclear, a plausible hypothesis is that immune responses generated against antigens commonly targeted in myositis are related to antitumor responses in affected individuals.

INTRODUCTION

Paraneoplastic myopathies are disorders of skeletal muscle or of the neuromuscular junctions which are not caused by direct infiltration by the tumor. The minimal criteria for these disorders are not well established.[1] Some authors use this term to describe nonspecific neurophysiological or morphological abnormalities without clinical symptoms or signs occurring in tumor patients. Others include only a few, often rare, diseases which are precisely defined. As a consequence, prevalence and incidence rates vary considerably.[2]

In clinical practice, problems differ from those in epidemiology. In a patient with a neoplastic disease suffering from the common symptom of muscular weakness, tumor progression must be considered, as well as some rare disorders which are potentially treatable.[3]

In neurological practice, precise knowledge of the potential risk of an underlying neoplastic disorder helps determine which investigations are necessary for adequate patient work-up.[4]

ISSN 2515-8260 Volume 10, Issue 01, 2023

Some of the paraneoplastic disorders are always linked to malignancy; in other diseases, however, only some of the patients suffer from a malignoma. Incidence of Paraneoplastic Mvopathies Due to the imprecise definition of paraneoplastic myopathies, data on incidence vary considerably.[5]

CASE PRESENTATION

A 44-year-old male patient had presented with chief complaints of fever and burning micturition since last 3 days. There was no history of hematuria, pain abdomen, and the complaints were not associated with early morning facial puffiness or pedal edema.

There was no previous history of tuberculosis, and the patient was not a known case of diabetes mellitus or hypertension. On further questioning, patient had given history of multiple similar episodes previously starting from 5 to 6 months before presentation to our hospital. He was treated in a local clinic with antibiotics and was not investigated further.
On examination, patient was moderately built, conscious and well oriented to time, place and person.

Vitals on admission were as follows:
Pulse rate: 108/min
Blood pressure: 150/100 mmHg
Oxygen saturation: 98% on room air
Temperature: 101-degree Fahrenheit.
Patient was evaluated for recurrent urinary tract infections and the investigations were as follows:

Hemoglobin- 9.6	Urea - 74
Platelet count -2,34,000	Serum Creatinine- 3.4
Total leukocyte count – 12,000	Serum procalcitonin –1.2
MCV- 88	CRP- 98
Total bilirubin – 1.07	Urine pus cells – 50-60 cells
SGOT- 46	Urine RBCs- 30-40
SGPT-65	Blood culture – NO GROWTH
ALP -72	Urine for acid-fast bacilli- negative

Urine report for culture and sensitivity showed growth of E. coli, sensitive to ciprofloxacin, meropenem and colistin

Ultrasound of abdomen and pelvis revealed aheterogenous mass lesion in the urinary bladder of size 66 X 86 X 87mm with vascularity within: to rule out neoplastic etiology
CECT abdomen pelvis could not be performed due to the presence of acute kidney injury.

Biopsy was done of the mass lesion in the bladder and his to pathological examination was suggestive of high grade invasive urothelial carcinoma.

PET-CT scan showed: Hypermetabolic wall thickening in urinary bladder suggestive of primary malignancy and metabolically active pelvic lymph nodes and retroperitoneal nodes-appear metastatic.

ISSN 2515-8260 Volume 10, Issue 01, 2023

Patient was started on chemotherapy with paclitaxel and gemcitabine and discharged after the first cycle with 48 hours of observation.

After 3 cycles of chemotherapy, patient had presented to OPD with complaints of bilateral lower limb weakness which was insidious onset and gradually progressive resulting in difficulty getting up from supine and sitting position. There was no history of trauma or loss of consciousness. These complaints were not associated with tingling, numbness or loss of sensations.
On examination: power in bilateral lower limbs was 1/5, associated with loss of reflexes
Bilateral plantars showed flexor response.

MRI brain with whole spine screening was done which showed no obvious abnormality.

Nerve Conduction Velocity studies also revealed no obvious abnormality.

MYOSITIS PANEL:

Myositis Profile-IgG(16 Antigen)

	Observed Value	Reference Range	Disease association
MI-2	Negative,2	Negative	Autoantibodies against MI-2α, one of two isoforms of MI-2, have largely the same serodiagnostic Significance as autoantibodies against MI-2,with prevalence in DM of around 20%.
MI-2ß	Negative,2	Negative	Serologically detected more frequently in DM Associated with neoplasia (e.g. colon or breast carcinoma). Prevalence 3-4%
MDA5	Negative,2	Negative	(melanoma differentiation-associated gene 5), synonym IFIH1 (interferon nduced with helicase C domain 1).Autoantibodies against MDA5 are detected in 13% to 26% of DM patients. They are highly specific for clinically amyopathic DM (95% of these patients are anti-MDA5-positive) or DM combined with interstitial lung disease.
SAE1	Negative,0	Negative	SUMO activating enzyme subunits 1 (40 kDa) and 2 (90 kDa). Anti-SAE1 antibodies are highly specific markers for DM in 8% of cases and for adult DM associated with interstitial lung diseases (ILD) in 5% of cases.
TIF1	Negative,2	Negative	(transcriptional intermediary factor 1-gamma) TIF1-gamma autoantibodies are detected in around 15% of DM patients and only in these persons. Hence, the detection of anti-TIF1-gamma antibodies is definitive for DM.In around 58% of anti-TIF1- gamma-positive patients, DM is associated with a malignant disease (e.g.pancreatic carcinoma).
NXP2	Negative,2	Negative	Autoantibodies against NXP2 are detected in 18% to 25% of cases of juvenile PM/DM (JDM) and in only around 1% of adult cases. This form of PM/DM is characterised by accompanying calcinosis and particularly severe and chronic disease courses. In adults the disease may be carcinoma-associated (breast, uterine or pancreatic carcinoma).
SRP	Negative,2	Negative	(signal recognition particle, ribonucleoprotein complex) Autoantibodies against SRP can be detected in around 5% of cases of polymyosit is (at a specificity of around 90%). Anti-SRP antibodies are a marker for necrolising myopathy (anti-SRP syndrome).The symptoms are acute,severe, proximal, symmetrical skeletal muscle weakness, and pain in muscles, including the heart muscle. Extramuscular signs of the disease can be interstitial lung diseases.
PL-12	Negative,1	Negative	(alanyl-tRNA synthetase) Autoantibodies against PL-12 are detected with a prevalence of up to 3% in myositis patients.
PL-7	Negative,2	Negative	(threonyl-tRNA synthetase) with a prevalence of around 3% to up to 6% in patients with myositis.
JO-1	Negative,0	Negative	found in polymyositis with a prevalence of 25% to 55% and a specificity of almost 100%.
EJ	Negative,1	Negative	(glycyl-tRNA synthetase) Autoantibodies against EJ are a diagnostic marker for polymyositis,occurring with a prevalence of 1% to 3%.
OJ	Negative,2	Negative	(isoleucyl-tRNA synthetase)Autoantibodies against OJ are associated with (poly) myositis (prevalence 3%).
PM-SCL75	Negative,2	Negative	Autoantibodies against the two main antigen-protein components PM-Scl100 and PM-Scl75 are classified by molecular masses. Anti-PM-Scl antibodies (antibodies against PM-Scl75 and PM-Scl100) are detected in 50% to 70% of patients with a so-called overlap syndrome. This combines the symptoms of polymyositis,dermatomyositis and systemic sclerosis (SSc). Patients with SSc exhibit mainly antibodies against PM-Scl75. Antibodies against PM-Scl75 can be detected in 3% of polymyositis cases,in 2% to 3% of patients with systemic sclerosis (SSc) and in 24% to 50% of patients with overlap syndrome.
PM-SCL100	Negative,1	Negative	Autoantibodies against the two main antigen-protein components PM-Scl100 and PM-Scl75 are classified by molecular masses. Anti-PM-Scl antibodies (antibodies against PM-Scl75 and PM-Scl100) are detected in 50% to 70% of patients with a so-called overlap syndrome. This combines the symptoms of polymyositis,dermatomyositis and systemic sclerosis (SSc). Patients with SSc exhibit mainly antibodies against PM-Scl75. Antibodies against PM-Scl75 can be detected in 3% of polymyositis cases,in 2% to 3% of patients with systemic sclerosis (SSc) and in 24% to 50% of patients with overlap syndrome
KU	Negative,1	Negative	Ku (DNA-binding,non-histone protein) were originally described in polymyositis-scleroderma overlap syndrome.They occur with a prevalence of up to 10% in systemic lupus erythematosus (SLE),40% of patients with antibodies against Ku show symptoms of myositis or systemic sclerosis (SSc), achronic autoimmune disease with fibrosis of the skin (scleroderma) on the joints and of inner organssuch as the oesophagus,lungs,heart and kidneys.Autoantibodies against Ku can also occur in Sjögren's syndrome.
RO-52	Negative,3	Negative	Antibodies against Ro-52 are detected in myositis patients with a prevalence of 25%. Anti-Ro-52 also occurs in some rheumatic and non-rheumatic diseases.

Interpretation :

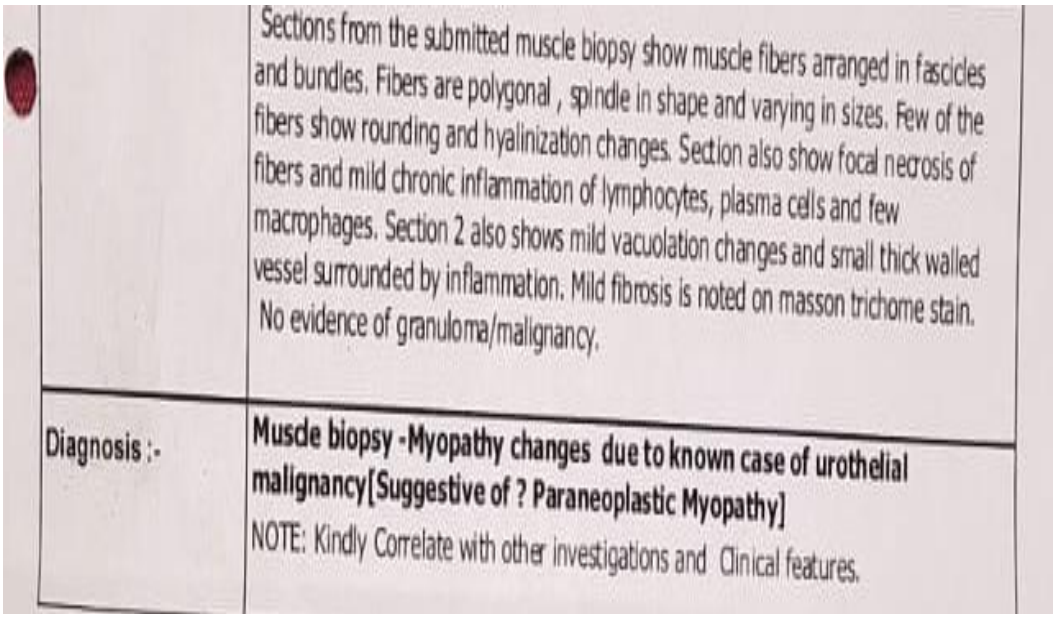
Intensity	Class	Result
0-7	0	Negative
8-14	(+)	Borderline
15-35	+	Positive
36-70	++	Positive
71-255	+++	Strong Positive

Method – Immunoblot (Autoimmune Inflammatory Myopathies 16 Ag (IgG) Sample screening dilution is 1:101)

-- End of Report --

ISSN 2515-8260 Volume 10, Issue 01, 2023

MUSCLEBIOPSY REPORT:



	Sections from the submitted muscle biopsy show muscle fibers arranged in fascicles and bundles. Fibers are polygonal , spindle in shape and varying in sizes. Few of the fibers show rounding and hyalinization changes. Section also show focal necrosis of fibers and mild chronic inflammation of lymphocytes, plasma cells and few macrophages. Section 2 also shows mild vacuolation changes and small thick walled vessel surrounded by inflammation. Mild fibrosis is noted on masson trichome stain. No evidence of granuloma/malignancy.
Diagnosis :-	**Muscle biopsy -Myopathy changes due to known case of urothelial malignancy[Suggestive of ? Paraneoplastic Myopathy]** NOTE: Kindly Correlate with other investigations and Clinical features.

Hence, a diagnosis of paraneoplastic myopathy was established in a known case of urothelial carcinoma.
Despite our best treatment measures, patient succumbed to the illness.

DISCUSSION

Myositis is one of the inflammatory conditions with a clinical presentation of proximal muscle weakness and characteristic skin findings of Gottron papules and heliotrope eruption. The most common subgroups of inflammatory myopathies are dermatomyositis, polymyositis, necrotizing autoimmune myopathy, and inclusion body myopathy.[6] The pathogenesis of inflammatory myopathies is not well understood; however, some theories have been described, including: type 1 interferon signaling causing myofiber injury and antibody-complement mediated processes causing ischemia resulting in myofiber injury. [7,8] The diagnoses of inflammatory myopathies may be suggested based on history, physical examination findings, laboratory values showing muscle injury (creatine kinase, aldolase, ALT, AST, LDH), myositis-specific antibodies (antisynthetase autoantibodies), electromyogram, and magnetic-resonance imaging. However, muscle biopsy remains the gold standard.[9]

The initial treatment of inflammatory myopathies begins with glucocorticoid therapy at 0.5-1.0 mg/kg. This regimen may be titrated down over 6 weeks to a level adequate to control symptoms.[10]

A paraneoplastic syndrome is a collection of symptoms that are observed in organ systems separate from the primary disease. This process is mostly caused by an autoimmune response to the tumor and nervous system.[8] Inflammatory myopathies, such as dermatomyositis, have been shown to be associated with a variety of malignancies as part of a paraneoplastic syndrome. The most common cancers associated with dermatomyositis are ovarian, lung, pancreatic, stomach, colorectal, and non-Hodgkin lymphoma.[9] Although an association between dermatomyositis and bladder cancer has been established, very few cases have been reported in the literature.[11]

ISSN 2515-8260 Volume 10, Issue 01, 2023

The risk of malignancy is highest in the first year after diagnosis, but may extend to 5 years after the diagnosis, so repeat screening should be performed 3-6 months after diagnosis, followed with biannual testing for 4 years. If a malignancy is present, then treatment should be tailored to the neoplasm to improve symptoms of myositis; however, response is generally worse than it would be with dermatomyositis in the absence of malignancy.[12]

Even though dermatomyositis is usually a chronic disease process, 87% of patients respond initially to corticosteroid treatment.[12] Therefore, treatment should be escalated with an agent such as azathioprine or methotrexate, or, like in this case, an underlying malignancy should be suspected. This case emphasizes the importance of screening patients appropriately and reveals the poor prognosis associated with this disease.

CONCLUSION

Cancer-associated myositis differs from primary myositis in many aspects. Prognosis and life-expectancy are determined by the underlying malignancy. Therefore, patient-specific examinations for detection of an underlying cancer are important in the management of patients. Recent clinical findings and new possibilities in immunoserological testing may result in the elaboration of an evidence-based recommendation for cancer screening programs in patients with IIM in the future.

REFERENCES

1. Greenberg, SA. Dermatomyositis and type 1 interferons. CurrRheumatol Rep. 2010;12(3):198-203.
2. Dalakas, MC, Hohlfeld, R. Polymyositis and dermatomyositis. Lancet. 2003;362(9388):971-982.
3. Dalmau J, Gultekin HS, Posner JB. Paraneoplastic neurologic syndromes: pathogenesis and physiopathology. Brain Pathol. 1999;9(2):275-284.
4. Hill CL, Zhang Y, Sigureirsson B, et al. Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. Lancet. 2001;357(9250):96-100.
5. Troyanov Y, Targoff IN, Tremblay JL, Goulet JR, Raymond Y, Senecal JL. Novel classification of idiopathic inflammatory myopathies based on overlap syndrome features and autoantibodies: analysis of 100 French Canadian patients. Medicine (Baltimore), 2005;84(4):231-240.
6. Zampieri S, Valente M, Adami N, et al. Polymyositis, dermatomyositis and malignancy: a further intriguing link. *Autoimmun Rev*. 2010;9(6):449–453.
7. [4] Meyer A, Meyer N, Schaeffer M, et al. Incidence and prevalence of inflammatory myopathies: a systematic review. *Rheumatology (Oxford)*. 2015;54(1):50–63.
8. Tan JA, Roberts-Thomson PJ, Blumbergs P, et al. Incidence and prevalence of idiopathic inflammatory myopathies in South Australia: a 30-year epidemiologic study of histology-proven cases. *Int J Rheum Dis*. 2013;16(3):331–338.
9. Ponyi A, Constantin T, Garami M, et al. Cancer-associated myositis: clinical features and prognostic signs. *Ann N Y Acad Sci*. 2005;1051:64–71.
10. Hill CL, Zhang Y, Sigurgeirsson B, et al. Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. *Lancet*. 2001;357(9250):96–100.

ISSN 2515-8260 Volume 10, Issue 01, 2023

11. Croce S, Guèye M, Korganow AC, et al. Paraneoplastic polymyositis associated with breast cancer: a therapeutic emergency. *Breast Cancer Res Treat*. 2011;126(3):811–814.
12. Merali N, Yousuff M, Pronisceva V, et al. Paraneoplastic polymyositis presenting as a clinically occult breast cancer. *Ann R Coll Surg Engl*. 2017;99(2):e40–e43.