CLINICAL VIGNETTE

Carbohydrate Antigen 19-9 as a Marker of Disease Activity in a Patient with Dermatomyositis

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Case Report

Dermatomyositis (DM) is an idiopathic inflammatory myopathy with characteristic cutaneous manifestations and it is strongly associated with malignancy.[1] DM has been noted to improve after the treatment of malignancy, and its recurrence has been reported to signal a relapse of malignant disease.[2]

Inflammation is closely linked to cancer, and diseases such as inflammatory bowel disease and Sjogren's syndrome may predispose patients to cancers including colorectal cancer and lymphoma, respectively.[3,4] While DM has been reported to be a harbinger of malignant disease, less data exists on whether DM itself may predispose patients to malignancy. This case highlights the potential interplay between so-called "tumor antigens" and DM, and poses the question of whether chronic inflammation from active DM predisposes patients to malignancy.

A 73-year-old female with a history of uterine cancer presented with a 1-month history of proximal muscle weakness, shortness of breath, and a rash. Physical examination revealed a heliotrope rash, an erythematous rash involving the face, chest, scalp and neck, and gottron's papules. She had marked proximal muscle weakness and chest exam revealed bibasilar crackles.

Laboratories showed elevation of muscle enzymes: CK =2313 U/L (24-182), aldolase =17.4 U/L (1.9-7.3), AST = 172 U/L (7-36), and ALT =100 U/L (4-48). Erythrocyte Sedimentation Rate (ESR) was elevated at 51mm/hr. Myositis antibody testing revealed a positive Mi-2 antibody as well as unidentified bands on S35 immunoprecipitation consistent with the presence of one or more unidentified autoantibodies. Electromyogram suggested an irritable myopathy and muscle biopsy demonstrated a focal zone of perifascicular atrophy, fiber degeneration, increased MHC class 1 expression, and increased membrane attack complex reactivity within microvessels consistent with DM. Malignancy work-up revealed an elevated CA19-9 level at 143 U/mL (0-35) and normal CA-125 and carcinoembryonic antigen (CEA) levels. Computed tomography (CT) scans revealed mild lower lobe pulmonary fibrosis and two enlarged aortal caval lymph nodes, the largest measuring 1.8 cm, which on biopsy was negative for malignancy. Colonoscopy revealed 2 non-malignant polyps. Upper endoscopy revealed non-malignant ulcerations and H. Pylori-associated pan-gastritis. On follow-up endoscopy, one gastric biopsy suggested suspicion for low grade gastric MALT lymphoma. Gastric mapping following H. Pylori eradication failed to reveal evidence of malignancy.

Following treatment for DM with corticosteroids and mycophenolate mofetil (MMF), the patient improved clinically, her labs normalized (see graph) and her lymph nodes decreased. Prednisone was tapered off and she remained on MMF. Two years later, she had a flare of her disease with recurrence of rash, but muscle enzymes and inflammatory markers remained normal. Her CA 19-9 level increased to 279 U/ml with the flare, but CT imaging remained unchanged. The CA 19-9 level normalized (graph) with low dose prednisone as the patient improved. The patient is doing well currently on 5mg of prednisone and 2000mg of MMF daily nearly 3 years following her diagnosis without evidence of malignancy.

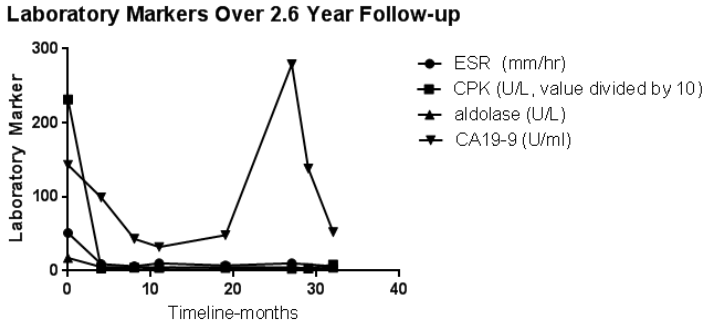
Discussion

Cancer may occur before the onset of myositis, concurrently, or afterwards. Many of the malignancies are occult and the clinical investigation may include both laboratory and imaging studies. Screening for serum tumor markers is often included, although the value in cancer detection in inflammatory myositis is still unclear.[5] In 1916, Stertz was the first to describe a patient with biopsy-proven DM and stomach adenocarcinoma.[6] In work by Amoura and colleagues, CA-125 and CA 19-9 levels were useful in prediction of tumor risk for patients with PM and DM; the risk of developing cancer was highest during the first year following the increased CA-125 and CA 19-9 levels.[5]

We present a patient with DM with a positive Mi-2 antibody and a markedly elevated CA 19-9 level. CA 19-9 is a predominantly carbohydrate antigen, which was defined from the culture medium of a colorectal cancer cell line.[7] While this marker can be elevated in a number of benign pancreatobiliary inflammatory disorders, its elevation has not previously been reported in association with DM. In the current case, although one gastric biopsy showed the presence of H. Pylori with suspicion for gastric MALT lymphoma, this was not confirmed on repeat gastric mapping following H. Pylori treatment. Furthermore, no cases have reported any association of CA 19-9 levels with MALT lymphoma. The significance of the CA 19-9 elevation in our patient remains unclear. It appears to be a

more sensitive marker of her clinical disease activity then traditional laboratory assays including muscle enzymes and inflammatory markers.

This case poses the question whether chronic inflammation from active DM may predispose patients to malignancy as has been reported for other inflammatory conditions. Cross-expression of similar antigens in tumors and regenerating muscle has previously been suggested as a potential mechanism to explain the association between cancer and inflammatory myositis.[8] Interestingly, our patient did have a remote history of uterine cancer and had an antibody detected to the Mi-2 antigen. Mi-2 has previously been reported as among the most commonly mutated proteins in patients with certain endometrial tumors.[8] Further research may lead to better understanding of the association between DM and cancer as well as better biomarkers of malignancy risk and disease activity.



REFERENCES

1. **Chow WH, Gridley G, Mellemkjaer L, McLaughlin JK, Olsen JH, Fraumeni JF Jr.** Cancer risk following polymyositis and dermatomyositis: a nationwide cohort study in Denmark. *Cancer Causes Control.* 1995 Jan;6(1): 9-13. PubMed PMID: 7718740.
2. **Hill CL, Zhang Y, Sigurgeirsson B, Pukkala E, Mellemkjaer L, Airio A, Evans SR, Felson DT.** Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. *Lancet.* 2001 Jan 13;357(9250):96-100. PubMed PMID: 11197446.
3. **Gallinger ZR, Weizman AV.** Colorectal cancer in inflammatory bowel disease: a shift in risk? Expert Rev Anticancer Ther. 2014 Jul;14(7):847-56. doi: 10.1586/ 14737140.2014.895936. Epub 2014 Mar 13. Review. Erratum in: *Expert Rev Anticancer Ther.* 2014 Jul; 14 (7): 856. PubMed PMID: 24621115.
4. **Risselada AP, Kruize AA, Bijlsma JW.** Clinical features distinguishing lymphoma development in primary Sjögren's Syndrome--a retrospective cohort study. *Semin Arthritis Rheum.* 2013 Oct;43(2):171-7. doi: 10.1016/j. semarthrit.2013.03.001. Epub 2013 May 7. PubMed PMID: 23664530.
5. **Amoura Z, Duhaut P, Huong DL, Wechsler B, Costedoat-Chalumeau N, Francès C, Cacoub P, Papo T, Cormont S, Touitou Y, Grenier P, Valeyre D, Piette JC.** Tumor antigen markers for the detection of solid cancers in inflammatory myopathies. *Cancer Epidemiol Biomarkers Prev.* 2005 May;14(5):1279-82. PubMed PMID: 15894686.
6. **Steitz G.** Polymyositis. *Berl Klin Wochenshr*; 1916. p. 489
7. **Goonetilleke KS, Siriwardena AK.** Systematic review of carbohydrate antigen (CA 19-9) as a biochemical marker in the diagnosis of pancreatic cancer. *Eur J Surg Oncol.* 2007 Apr;33(3):266-70. Epub 2006 Nov 9. Review. PubMed PMID: 17097848.
8. **Mohassel P, Rosen P, Casciola-Rosen L, Pak K, Mammen AL.** Expression of the dermatomyositis auto-antigen transcription intermediary factor 1γ in regenerating muscle. *Arthritis Rheumatol.* 2015 Jan;67 (1): 266-72. doi: 10.1002/art.38863. PubMed PMID: 25186009; PubMed Central PMCID: PMC4280343.

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