Colon Cancer: An Unusual Presentation with a Paraneoplastic Syndrome

Reham Almasouda  Rasha Allousha  Labib Al-Ozaibib

aRashid Hospital, Dubai, UAE; bGeneral Surgery Department, Rashid Hospital, Dubai, UAE

Keywords
Colon adenocarcinoma · Dermatomyositis · Microangiopathic hemolytic anemia · Paraneoplastic syndrome · Surgery

Abstract
Dermatomyositis (DM) is a rheumatological disorder characterized by proximal myositis and distinctive dermatological manifestations. It can be an isolated clinical syndrome or, in rarer cases, can be the initial presentation for an underlying malignancy as a part of a paraneoplastic syndrome. In this case report, we describe a case of a 51-year-old lady who presented with proximal myopathy, typical DM skin rash, dysphagia, and markedly elevated creatine kinase. She was diagnosed with a seronegative DM and her malignancy screening revealed a mass in the ascending colon. During her hospital course, she also developed microangiopathic hemolytic anemia, another paraneoplastic disorder typically associated with late stages of malignancy, manifested as hemolytic anemia, thrombocytopenia, and low fibrinogen. The patient received intravenous corticosteroids and underwent tumor resection with following resolution of her both rheumatological and hematological manifestation. Unfortunately, due to her general poor health, she developed sepsis and died in the hospital.

Introduction
Paraneoplastic syndromes are immune-mediated processes triggered by an underlying malignancy affecting <1/10,000 patients with cancer. They present with a wide variety of manifestations affecting the nervous and musculoskeletal systems among others, often acting as the initial and sole symptoms in cancers originating from different organs in the body [1]. Dermatomyositis (DM), in less than a third of its cases, as well as microangiopathic hemolytic anemia (MAHA) is thought to be a part of a paraneoplastic syndrome, which prompts the need to screen for an underlying malignancy. Management of these cases presents a challenge due to the lack of official guidelines on treatment and their poor response to typical myositis therapy.

Case Presentation
A 51-year-old female, with a known history of hypertension and dyslipidemia, presented to the emergency department with a 2-month history of fever, severe body aches, muscle weakness, skin rash along with recent onset of dysphagia. On examination, the patient was ill looking but vitally stable. Further, inspection revealed a wide distribution of skin rash: bilateral periorbital pink-violaceous patches with edema (heliotrope rash); malar rash over the chest (shawl sign), arms, and lateral aspect of the thighs (Holster sign). Examination
of muscle power showed overall weakness in the upper and lower limbs, along with profound weakness at the shoulder and hip girdles. Cardiovascular, pulmonary, and abdominal examinations were within normal. Blood investigations showed raised creatine phosphokinase (CPK) at 1,359 U/L (normal 0–167 U/L), as well as mildly elevated C reactive protein and erythrocyte sedimentation rate. Serological tests were positive for antinuclear antibodies (ANA); however, the other antibodies investigated were negative.

Based on the findings above, a diagnosis of seronegative DM was made and screening for an underlying malignancy was initiated. Tumor markers (CA 19-9, CA 125, carcinoembryonic antigen) were within normal. A systemic survey of malignancy was conducted, including a CT scan, esophagoduodenoscopy, and a colonoscopy, which led to the diagnosis of ascending colon adenocarcinoma. During her admission, she developed Coombs-negative hemolytic anemia and thrombocytopenia with schistocytes on blood film, which was diagnosed as malignancy-induced MAHA.

Her management plan included intravenous corticosteroids for the management of her DM and MAHA along with mass resection. She underwent an open right-sided hemicolectomy with end ileostomy, and histopathology showed cecal adenocarcinoma (T3N1M0). She had an unstable prolonged stay in the intensive care unit after her operation. Despite her CPK levels dropping back to normal, her hematological profile correcting and the improvement in her skin rash during that time, she was unable to regain full muscle power. Unfortunately, the patient’s low albumin, poor nutritional status, and medical condition impaired her wound healing causing her to develop wound infection requiring drainage and multiple antibiotics courses. She continued to deteriorate further, developing sepsis with disseminated intravascular coagulopathy and died.

Discussion

DM is an idiopathic myositis with characteristic cutaneous findings. Its incidence is estimated to be 1 in 100,000 population [2], peaking at the ages of 45–60 years in adults with females affected almost twice as much as males [3, 4].

The diagnosis of DM is done based on the constellation of distinctive skin manifestations (Table 1) [3–5], presence of skeletal muscle weakness (mainly the proximal muscles), elevated levels of serum muscle enzymes, and confirmation are done by muscle biopsy [3, 5]. Our patient was clinically diagnosed with DM as she presented with bilateral proximal weakness, typical heliotrope rash, V sign and holster sign, and significantly elevated levels of CPK. As her presentation was typical, muscle biopsy was not done to confirm the diagnosis.

DM is considered a part of paraneoplastic syndrome [3, 6, 7], meaning it is a clinical syndrome associated with an underlying malignancy owing to the production of antibodies [6]. Paraneoplastic syndromes affect any part of the nervous system, neuromuscular junction, and muscles. The antibodies which indicated a higher risk of malignancy were: transcription intermediary factor 1γ (TIF-1γ) [5], and nuclear matrix protein NXP-2 [3, 5, 8, 9]. About a third of patients diagnosed with DM are diagnosed with cancer during its clinical course [6], with adenocarcinomas of the lung, stomach, pancreas, colon, and pelvis being most common [2, 4, 6, 10]. The malignancy is most likely diagnosed simultaneously with or shortly after the diagnosis of myopathy has been made [10–12]. In our case, investigations revealed cecal adenocarcinoma which we believe to be the cause of her paraneoplastic DM as well as her MAHA. Cancer-related MAHA is another paraneoplastic syndrome usually present in cases of late stage or metastatic cancers. It is characterized by Coombs-negative hemolytic anemia with thrombocytopenia and schistocytes on blood film [13]. It is uncommon to find in early stages of cancer and to be accompanied by the presentation of DM such as in our case.

Limited information is available in regards to the management of DM associated with malignancy as most clinical trials exclude these patients from their research [3]. The first line of therapy in DM is systemic glucocorticoids; hence, it was started for our patient. Methotrexate or azathioprine is among other possible therapeutic options [2, 8–11] with consequent intravenous immunoglobulin in refractory disease [2, 10]. This regimen is not easily implemented in the presence of malignancy [3] as it is based on immunosuppression.
Colon Cancer Presenting as a Paraneoplastic Syndrome

It is assumed that, because DM is paraneoplastic in origin, antitumoral treatment would also help treat the myositis [3, 10, 11] and a survey reported an improvement in about 40% of patients with surgically resected tumors [11]. Nonetheless, malignancy remains a factor affiliated with poor prognosis in myositis [12] with about 30% of patients remaining severely disabled despite treatment [11]. This is supported by the clinical and biochemical improvement of the patient from her DM symptoms after resection of the adenocarcinoma. However, her poor nutritional status as well as her comorbidities leads to her deterioration and unfortunate outcome.

Conclusion

DM can be associated with malignancy as a paraneoplastic syndrome. Some features increase the likelihood of the presence of an underlying malignancy like specific antibodies, severe presentation with involvement of esophageal muscles and cardiac muscle as well as association with other features of paraneoplastic syndrome such as MAHA as in our case scenario. The management of malignancy-induced DM is by targeting the underlying malignancy with the concomitant use of steroids for symptomatic therapy of DM as well as other associated rheumatological paraneoplastic disorders such as MAHA.

We have noted a lack of case studies in the United Arab Emirates regarding the prevalence of DM or its correlation to malignancy. We recommend that researchers give this condition the necessary attention to deepen our understanding of this phenomena and its management.

Statement of Ethics

A written consent was obtained from the patient to publish the case. Ethical approval was not required for publishing this case report.

Conflict of Interest Statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding Sources

The authors have not declared a specific grant for this research from any funding agency in the public, commercial, or non-for profit sectors.

Author Contributions

All authors were involved in the acquisition and interpretation of the data, the article’s conception and design, and the final approval of the version to be published.

Data Availability Statement

All data generated or analyzed during this case report are included in this article. Further enquiries can be directed to the corresponding author.

References

1. Honnorat J, Antoine JC. Paraneoplastic neurological syndromes. Orphanet J Rare Dis. 2007 May 4 [cited 2020 Dec];2(1).
2. Chu LL, Rohekar G. Dermatomyositis. Can Med Assoc J. 2019 Mar;25191(12):E340.
3. Aussy A, Boyer O, Cordel N. Dermatomyositis and immune-mediated necrotizing myopathies: a window on autoimmunity and cancer. Front Immunol. 2017;8:992.
4. Yang SH, Chang C, Lian ZX. Polymyositis and dermatomyositis: challenges in diagnosis and management. J Transl Autoimmun. 2019 [cited 2020 Dec];2:100018.
5. Schmidt J. Current classification and management of inflammatory myopathies. J Neuromuscul Dis. 2018 [cited 2020 Dec];5(2):109–29.
6. Kamiyama H, Niwa K, Ishiyama S, Takahashi M, Kojima Y, Goto M, et al. Ascending colon cancer associated with dermatomyositis which was cured after colon resection. Case Rep Gastroenterol. 2016 [cited 2020 Dec];10(2):338–43.
7. Cassius C, Le Buanc H, Bouaziz JD, Amode R. Biomarkers in adult dermatomyositis: tools to help the diagnosis and predict the clinical outcome. J Immunol Res. 2019 [cited 2020 Dec];2019:9141420.
8. Jakubaszek M, Kwiatkowska B, Maślińska M. Polymyositis and dermatomyositis as a risk of developing cancer. Reumatologia. 2015 [cited 2020 Dec];53:101–5.
9. Hu T, Vinik O. Dermatomyositis and malignancy. Can Fam Physician. 2019 Jun [cited 2020 Dec];65(6):409–11. Available from: https://www.cfp.ca/content/65/6/409.
10. Chung JH, So MW, Kim S-G. Paraneoplastic dermatomyositis presenting myopathy combined with synchronous cervical and sigmoid colon cancer. Korean J Intern Med. 2016 Mar [cited 2020 Dec];31(2):413–6.
11. Zerdes I, Tolia M, Nikolaou M, Tsoukalas N, Velentza L, Hajiioannou J, et al. How can we effectively address the paraneoplastic dermatomyositis: diagnosis, risk factors and treatment options. J BUON. 2017 [cited 2020 Dec];22(4):1073–80.
12. Marie I, Hachulla E, Hatron PY, Hellot MF, Levesque H, Devulder B, et al. Polymyositis and dermatomyositis: short term and long-term outcome, and predictive factors of prognosis. J Rheumatol. 2001 [cited 2020 Dec];28(10):2230.
13. Lechner K, Obermeier HL. Cancer-related microangiopathic hemolytic anemia: clinical and laboratory features in 168 reported cases. Medicine. 2012 [cited 2020 Dec];91(4):195–205.