

The First Report of Erythroderma as the First Manifestation of Myelodysplastic Syndromes that responded to 5-azacytidine

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Case report

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Abstract

Background:

Erythroderma is an uncommon and severe dermatological manifestation of a variety of diseases, and identifying its potential cause is challenging. Additionally, erythroderma is exceedingly rare as the first manifestation of myelodysplastic syndromes (MDS).

Case presentation:

We report the case of a 67-year-old male patient with MDS that initially presented with erythroderma. The patient was dependent upon steroid treatment to control the erythroderma when he was treated with decitabine. When we converted decitabine to 5-azacytidine, the patient achieved complete remission of both erythroderma and MDS and was relieved of his dependency on the steroid treatment. The patient continued to be steroid-independent 13 months after treatment with 5-azacytidine.

Conclusions:

This is the first report of erythroderma as the first manifestation of MDS. When screening the potential causes of erythroderma, MDS should be considered in addition to common cutaneous T-cell lymphoma. Based on our case report and a review of the published literature, 5-azacytidine appears to be a more effective treatment option for MDS-related autoimmune and inflammatory dermatoses. On the other hand, various cutaneous adverse events can be induced by 5-azacytidine. Since MDS-related autoimmune and inflammatory dermatoses may occur prior to the diagnosis of MDS, concomitantly with it or even during the illness, it is important to distinguish whether the dermatoses is MDS-related or 5-azacytidine-induced.

Background

Erythroderma presents as widespread erythema with a variable degree of scaling, and is distributed over 90% of the body surface. It has multiple causes with the most common reasons being underlying dermatoses, medication, and underlying malignancy. The most common hematological system disease associated with the etiology of erythroderma is cutaneous T-cell lymphoma[1].

MDS is a heterogeneous and clonal disorder of hematopoietic stem cells marked by dysplasia in myeloid cells, ineffective hematopoiesis, and refractory hemocytopenia with a risk of leukemic transformation. Cutaneous manifestations of MDS are common, especially Sweet's syndrome [2].

It is important to identify the cause of erythroderma in order to provide targeted treatment. Herein, we report the case of a patient with erythroderma as the first manifestation of MDS prior to diagnosis. By switching the patient from decitabine to 5-azacytidine treatment, the patient achieved relief of erythroderma.

Case Presentation

A 67-year-old male patient with whole-body scaling erythema was diagnosed with general eczema and took cetirizine hydrochloride and rupatadine fumarate intermittently for about six months to control the itchy rash. However, his erythema became aggravated gradually and he was obsessed with the swelling of limbs and fever. He was hospitalized in the Department of Dermatology of the First Affiliated Hospital of China Medical University and was diagnosed with erythroderma by skin biopsy. The patient received intravenous administration of 40mg/d methylprednisolone for 12 days and continuous oral administration of 28mg/d methylprednisolone. His skin lesions improved gradually and the dose of methylprednisolone was tapered regularly.

Routine blood examination revealed anemia and thrombocytopenia (hemoglobin 99g/L, platelet $62 \times 10^9/L$). A bone marrow aspirate was performed and a diagnosis of unclassifiable MDS (MDS-U) was made according to the 2016 WHO classification of MDS with normal karyotype. The results of a PCR screening assay for 41 recurrent fusion genes in acute leukemia were negative. Next generation sequencing (NGS) revealed gene mutations in *ASXL1*, *DNMT3A*, and *TET2*.

Based on the patient's low International Prognostic Scoring System (IPSS) risk score, the patient received supportive care, including thalidomide and erythropoietin. Thereafter, the patient's platelet levels declined progressively to $10 \times 10^9/L$ and he received platelet transfusions twice a week in the emergency ward. As such, he was hospitalized in our department for further treatment. At that time, he was administered 18 mg/d methylprednisolone as the erythroderma was still covering his limbs (Fig. 1A) and he complained of aggravated erythroderma when the dose of methylprednisolone was reduced. To address the patient's condition, treatment with decitabine was started, and two cycles later, the patient's platelet level returned to $244 \times 10^9/L$. During the treatment, there were several events of infection due to agranulocytosis and methylprednisolone, so we attempted to reduce the dose of methylprednisolone. As expected, the patient's rash became aggravated when the dose of methylprednisolone was reduced to 8 mg/d (Fig. 1B). Therefore, we altered his treatment from decitabine to 5-azacytidine, once a month. After two cycles of 5-azacytidine, the patient's erythroderma was relieved (Fig. 1C), we ceased administration of methylprednisolone, and re-examination of the patient's bone marrow indicated complete remission. Just before the sixth cycle of 5-azacytidine, the patient's platelet levels decreased to $63 \times 10^9/L$ and, according to the morphology and immunophenotype studies on bone marrow, his MDS-U progressed to MDS with excess blasts-1 (MDS-EB-1) with no relapse of erythroderma. Two more cycles of 5-azacytidine were administered and his platelet levels continued to decline progressively. Due to the influence of the coronavirus disease 2019 outbreak, the patient had to suspend treatment for 3 months; when he returned to our hospital, his platelet level was $19 \times 10^9/L$ and was accompanied with the relapse of erythroderma. Upon further examination, bone marrow aspirate indicated acute leukemia. Due to financial reasons the patient rejected ongoing treatment with 5-azacytidine, so we prescribed decitabine and venetoclax. Presently, his platelet levels have stabilized around $30 \times 10^9/L$ and 4 mg/d methylprednisolone is needed to control the erythroderma.

Discussion

Erythroderma, or generalized exfoliative dermatitis, is a rare inflammatory disorder of the skin characterized by erythema with scaling on 90% or more of the body surface[3]. A study from India reported that the incidence of erythroderma is 35 per 100000 dermatologic outpatients [4], but the actual incidence worldwide is unclear. The etiology of erythroderma includes several general groups, including preexisting dermatoses, medication, malignancies, connective tissue diseases, and idiopathic disorders. Erythroderma can be urgent or even life-threatening and the response to therapy varies by the underlying etiology. As such, it is crucial to identify the cause of erythroderma in order to provide the proper treatment[5].

Malignancy-associated erythroderma may be more progressive[6]. The most common malignancy associated with erythroderma is cutaneous T-cell lymphoma. Other hematological system diseases associated with the etiology of erythroderma include acute and chronic leukemia, lymphoma, and MDS[7–9], as in the case reported in this study. Various cytokines, antibodies and immunocytes play an important role in the cause of paraneoplastic dermatoses associated with malignancy, rather than the direct invasion of the tumor cells[10]. Although paraneoplastic dermatoses are frequently seen in MDS, erythroderma was first reported.

It has been reported that the prognosis of the malignancy and dermatosis progress in parallel; as the malignancy is treated successfully or recurs, the dermatosis follows a similar course. In our case, the patient was initially treated with methylprednisolone to control erythroderma. When the patient was diagnosed with MDS, decitabine was then administered. However, methylprednisolone dependency caused the patient to develop repeated pulmonary infections. Since several studies reported that 5-azacytidine was an effective treatment for MDS-related autoimmune and inflammatory dermatoses, especially Sweet's syndrome[11, 12], we switched the patient from decitabine to 5-azacytidine. After two cycles of 5-azacytidine, the patient's erythroderma was relieved along with the cessation of methylprednisolone. While it is unclear why 5-azacytidine appears to be more effective for treating MDS-related autoimmune and inflammatory dermatoses than decitabine, we hypothesize that erythroderma can be relieved by dealing with the potential malignancy. Interestingly, 5-azacytidine can also lead to cutaneous adverse events, such as Sweet's syndrome, maculopapular erythematous eruption, and urticarial rash[13]. Since MDS-related autoimmune and inflammatory dermatoses may occur prior to the diagnosis of MDS, concomitantly with it or even during the illness, it is important to distinguish whether the dermatoses is caused by 5-azacytidine. 5-azacytidine-induced cutaneous adverse events always follow each cycle of 5-azacytidine and can be relieved by corticosteroids and/or discontinuation of 5-azacytidine administration.

Conclusion

The most common causes of erythroderma are preexisting dermatoses and drugs use. When these causes have been excluded, careful screening for an underlying malignancy should be undertaken. In

addition to cases of common cutaneous T-cell lymphoma, MDS should also be considered. Steroid therapy can increase the risk of infection in patients with hematological diseases, and early diagnosis of underlying malignancy and early targeted treatment can prevent the erythroderma-associated morbidity and mortality. Therefore, 5-azacytidine should be regarded as a more effective treatment option for patients with MDS with related autoimmune and inflammatory dermatoses. And pay attention to whether the dermatoses is MDS-related or 5-azacitidine-induced.

Abbreviations

MDS: myelodysplastic syndromes; MDS-U: MDS, unclassifiable; IPSS: International Prognostic Scoring System;

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Written informed consent was obtained from the patient for publication.

Availability of data and materials

All data and material were presented in this published article.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

All authors were involved in the clinical care on the patient. Danyang Wu performed the literature review and were the major contributors in writing the manuscript. All authors read and approved the final manuscript.

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Figures

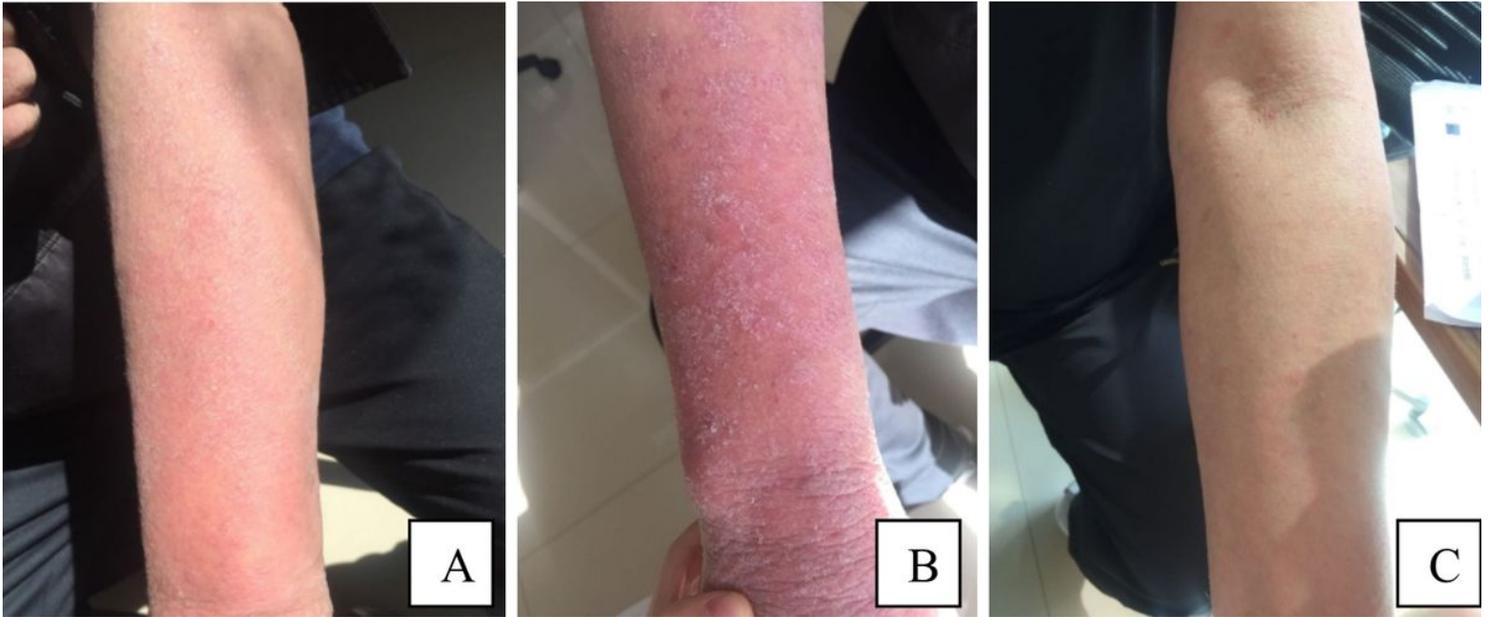


Figure 1

Changes in cutaneous symptoms during the treatment of the patient. A. Condition of the patient when he was admitted to our department and was treated with 18 mg/d methylprednisolone by oral. B. After two cycles of decitabine, the patient's rash aggravated after the dose of methylprednisolone was reduced to 8mg/d orally. C. After two cycles of 5-azacytidine the patient's cutaneous symptoms were relieved.