Case Report

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Lenalidomide-related malar rash-like lesion in patient with 5q-syndrome

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Abstract:

It has become important to be careful in terms of side effects with the increased lenalidomide use. The most commonly reported adverse events with the use of lenalidomide were hematologic toxicities and less frequently peripheral edema, infections, gastrointestinal disorders, fatigue, and muscle cramps. In particular, the nonserious rash is the most common cause of permanent discontinuation of lenalidomide. Although morbilliform, urticarial, or acneiform rashes have been observed with lenalidomide, malar rash-like lesions have not been described previously. Our aim is to present here 71-year-old female myelodysplastic syndrome patient with deletion of 5q abnormality who should be discontinued lenalidomide due to recurrent skin reaction like a malar rash.

Keywords:

5q-syndrome, lenalidomide, malar rash, myelodysplastic syndrome, skin reaction

Introduction

Myelodysplastic syndrome (MDS) is a stem cell malignancy characterized by dysplasia and ineffective hematopoiesis with the risk of acute leukemia transformation. The MDS is classified into subgroups based on dysplastic lineages, cytopenia, ring sideroblasts as percent of marrow erythroid elements, the ratio of bone marrow and peripheral blood blast, and cytogenetic features according to conventional karyotype analysis.[1,2] Treatment is generally sequential and is performed according to the lower- and higher-risk category. Growth factors, lenalidomide, and azanucleosides are options in lower-risk MDS, while allogeneic hematopoietic stem cell transplantation, acute myeloid leukemia-like treatment, or azanucleosides may be considered in higher-risk MDS patients.[2]

Lenalidomide is a thalidomide analog immunomodulatory drug that inhibits tumor necrosis factor-alpha, angiogenesis and reduces serum vascular endothelial growth factor, basal fibroblast growth factor levels. It has been reported as a treatment option in MDS patients with deletion of 5q (del5q) abnormality, anemia, and lower-risk MDS.[3] It has become important to be careful in terms of side effects with the increased lenalidomide use. The most commonly reported adverse events with the use of lenalidomide were hematologic toxicities and less frequently peripheral edema, infections, gastrointestinal disorders, fatigue, and muscle cramps.[3,4] Lenalidomide may need to be discontinued in such side effects. In particular, the nonserious rash is the most common cause of permanent discontinuation of lenalidomide.[4,5] Although morbilliform, urticarial, or acneiform rashes have been observed with lenalidomide, malar rash-like lesions have not been described previously.[5]

Our aim is to present here 71-year-old female MDS patient with deletion of 5q abnormality who should be discontinued lenalidomide due to recurrent skin reaction like a malar rash.

Case Report

A 71-year-old female patient was admitted to

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our clinic with weakness and fatigue. She had a medical history of using losartan/hydrochlorothiazide (100/25 mg a day) due to arterial hypertension for 2 years. Physical examination was normal except for conjunctival pallor. Her general condition was stable with blood pressure of 115/60 mmHg, pulse rate of 78/min, and her temperature was 37.1°C. Her blood parameters were as follows: hemoglobin 10.7 g/dl, mean corpuscular volume 107.3 fL, leukocyte count 3.43 × 10^9/L, lymphocyte count 1.4 × 10^9/L, platelet count 105 × 10^9/L, urea 35 mg/dl, creatinine 1.07 mg/dl, and erythrocyte sedimentation rate 47 mm/h. The patient's liver/renal/thyroid function tests and electrolytes were within normal ranges. The urine test was negative for proteinuria; also hepatitis markers and autoantibodies were negative.

Peripheral blood smear examination revealed cytoplasmatic hypogranulated neutrophils and macrocytic erythrocytes. The bone marrow aspirate and biopsy were hypercellular with erythroid dysplasia and <5% blasts. The erythroid/myeloid ratio was 2: 3, reticular fiber grade was +1, and myeloid/megakaryocytic lineages and iron deposits were normal. Cytogenetic analysis showed del5q minus. Hence, diagnosis of MDS with isolated del5q was confirmed based on peripheral blood smear, bone marrow findings, and cytogenetic analysis.

Lenalidomide started with 10 mg on days 1–21 of a 28-day cycle. The rash observed on the 10th day of treatment. Lenalidomide was discontinued because no cause was found to explain the rash other than drug use. The rash disappeared with lenalidomide discontinuation, an oral antihistamine, and corticosteroid treatment. Lenalidomide was restarted 2 weeks (later) after the skin reaction-like malar rash disappeared. However, it was observed again on the 7th–10th days after lenalidomide [Figure 1]. The rash disappeared again after 1 week of lenalidomide discontinuation [Figure 2].

Discussion

There is an increased risk of developing all-grade rash with lenalidomide compared to control groups. The overall incidence of all-grade and Grade 3 rash associated with lenalidomide was reported to be 27.2% and 3.6%, respectively, in a heterogeneous population including MDS, lymphoma, multiple myeloma, and myelofibrosis.[6,7] There was no statistical difference in the incidence of rash compared with lenalidomide alone versus dexamethasone in combination with lenalidomide and 10 mg lenalidomide versus 25 mg lenalidomide.[7] The mechanism of lenalidomide associate skin rash remains uncertain and is not fully understood. It has been hypothesized that lenalidomide may lead to rash through affecting keratinocytes.[7] The rash is often characterized by a maculopapular or morbilliform pattern on the proximal extremities and trunk. Itching in the scalp, maculopapular erythema all over the body, and pustules similar to vasculitic lesions in the legs have been described.[8,9] In our case, the malar rash appeared on the face which is an area had not been previously described. Furthermore, the higher-grade lesions such as vasculitis-like lesions, exfoliative skin lesions, Stevens–Johnson syndrome, and toxic epidermal necrolysis have been less frequently reported with lenalidomide.[4,5] Lenalidomide-induced high-grade lesions are important because they may cause morbidity and mortality.

Lenalidomide is discontinued in patients with moderate symptoms, and it can be started after the rash resolution. However, treatment may be discontinued or dose reduced due to the presence of rash in some cases. In our case, lenalidomide was discontinued when the rash appeared 7 days after starting therapy. Patients with severe or persistent rash need to be interrupted for 7–14 days until the symptoms disappear.[8,10] Topical or short courses of oral steroid and oral antihistamines

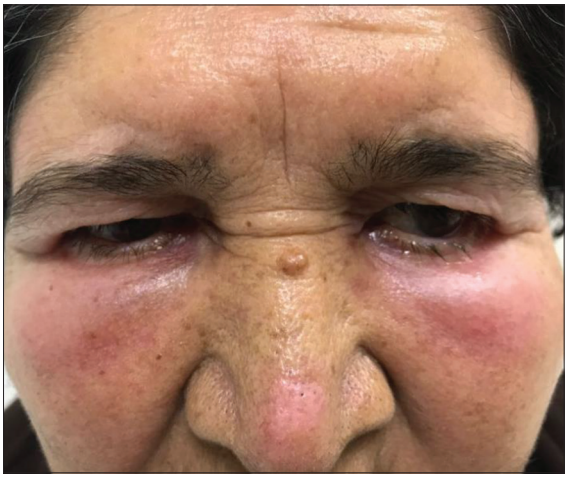

Figure 1: Malar rash-like lesions over the dorsum of the nose and maxillary area in myelodysplastic syndrome patients with 5q syndrome

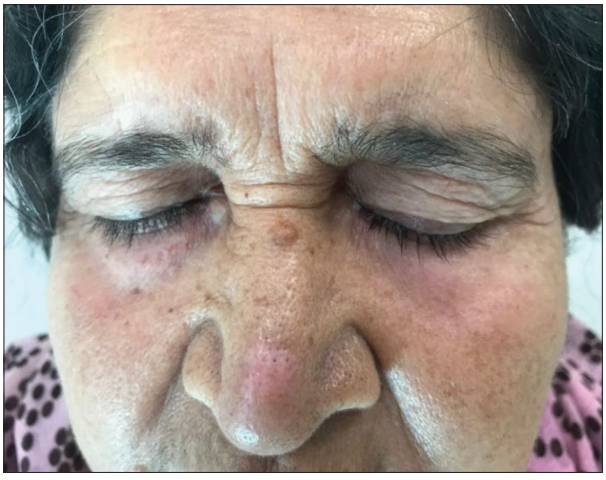

Figure 2: Disappear rash with the lenalidomide discontinuation

are treatment options for nonlife-threatening lesion as in our case topical and oral steroid therapy started with continuation of lenalidomide. If there is no response to medical treatment and the lesions are Grade 2 and Grade 3, interruption or discontinuation of lenalidomide should be considered. Grade 4 lesions such as Stevens–Johnson syndrome and toxic epidermal necrolysis may have life-threatening consequences and require urgent intervention.[4,5]

It may be difficult to predict in which subgroup of MDS will develop dermatological reactions with lenalidomide. As our case, malar rash-like lesion may develop in MDS patients with del5q syndrome on the face and maxillary area. Early diagnosis, recognize resistant lesions, atypical presentations, and also effective treatment are important for lenalidomide-related skin lesions.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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