

# Disseminated Granuloma Annulare Associated with Acute Myelogenous Leukemia: Case Report

## Akut Myelojen Lösemiyle İlişkili Dissemine Granüloma Anulare

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**ABSTRACT** Granuloma annulare (GA) is a benign, usually self-limited dermatosis of unknown cause, characterized by necrobiotic dermal papules that often assume an annular configuration. Disseminated GA was reported in association with numerous systemic disorders including thyroid autoimmune disease, human immunodeficiency virus infection, and diabetes mellitus. Among the haematologic malignancies, malignant lymphoma is among the most common. Disseminated GA has a tendency to present with atypical clinical features, especially when associated with malign lymphoma or AIDS. In this report, we described a 38-year-old female patient with disseminated GA in association with acute myelogenous leukemia (AML). To our knowledge, it is the second reported case which is associated with AML.

**Key Words:** Granuloma annulare; leukemia, myelocytic, acute

**ÖZET** Granüloma anulare (GA) iyi huylu, genellikle kendini sınırlayan, sıklıkla anuler şekilde olan nekrobiyotik dermal papüllerle karakterize bir dermatozdur. Dissemine GA'nın tiroid otoimmün hastalığı, "human immunodeficiency virus" enfeksiyonu ve diabetes mellitus gibi çok sayıda sistemik bozuklukla ilişkili olduğu gösterilmiştir. Hematolojik malignensiler içerisinde malign lenfoma sıklıkla bildirilmiştir. Dissemine GA'nın, özellikle malign lenfoma veya AIDS ile ilişkili olduğunda atipik klinik özellikler göstermeye meyilli olduğu belirtilmiştir. Bu makalede, akut myelojen lösemi (AML) ile ilişkili dissemine GA olan 38 yaşında kadın hasta sunmaktayız. Bilgimize göre bu olgu AML ile ilişkili bildirilen 2. olgudur.

**Anahtar Kelimeler:** Granüloma anulare; akut myelojen lösemi

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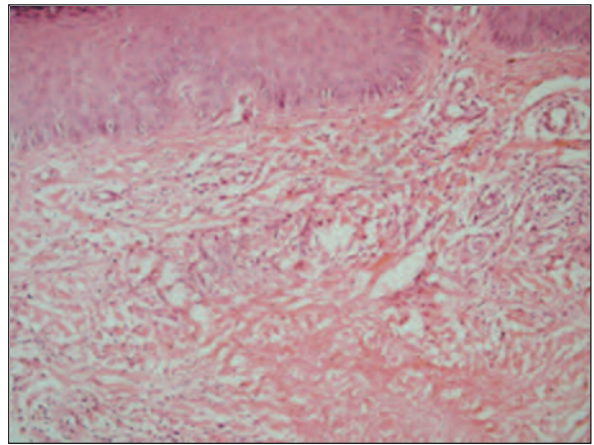
Granuloma annulare (GA) is a benign, usually self-limited dermatosis of unknown cause, characterized by necrobiotic dermal papules that often assume an annular configuration. Clinically, GA can be divided into four distinct forms: localized, disseminated, perforating and subcutaneous.<sup>1</sup> Disseminated GA is known to have associations with numerous systemic disorders, including hematopoietic malignancies, and has a tendency to present with atypical clinical features, especially when associated with malign lymphoma or AIDS.<sup>2-5</sup> We described a case of disseminated GA in association with AML.

## CASE REPORT

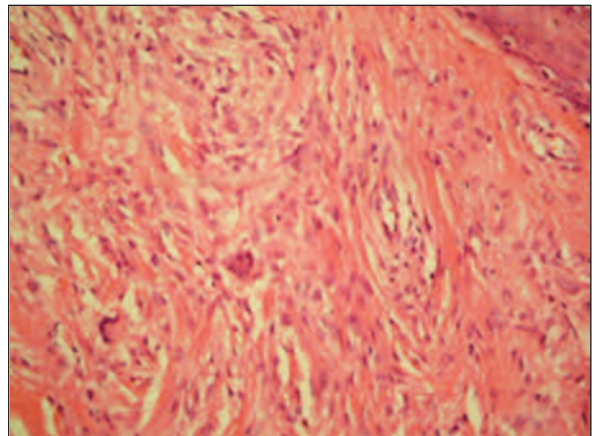
A 38-year-old woman hospitalized with fever, back pain, weakness and multiple erythematous papules and plaques involving the upper extremities and face. Constitutional symptoms had started a month before hospitalization and the skin eruption has been present for 3 weeks. On physical examination, splenomegaly and high fever (38.5°C) were detected. Dermatologic examination revealed multiple, discrete papules and plaques with annular configuration on the upper extremities, hands and face (Figure 1). Although some lesions had annular configuration, many, especially those on the hands were in the form of erythematous plaques, patches, and papules of different sizes. There were also crusted and hemorrhagic lesions probably due to scratching. The majority of the lesions were on the forearms. Laboratory investigations were as follows: hemoglobin: 6.3 g/dL, white blood cells: 17000/mL with a differential count of 57% neutrophils, 35% lymphocytes, 0.3% eosinophils, and platelets: 10000/mL. In addition, 25 blasts were detected on the blood smear. Bone marrow aspirate showed a hypercellular marrow with blastic infiltration consistent with AML. The serum chemistry studies were all within normal limits, including fasting blood glucose level. Autoimmune markers and thyroid function tests were also normal. The urinalysis and chest X-ray disclosed no abnormali-



**FIGURE 1:** Multiple, discrete erythematous papules and plaques on the arms and hands.



**FIGURE 2:** Two separate granulomatous foci presenting with necrobiotic collagenous centers, surrounded by a wall of palisaded histiocytes (HE x 100).



**FIGURE 3:** Multinucleated giant cells (HE x 400).

ties. No organism grew in cultures. She was diagnosed with AML and was started on chemotherapy with cytosine arabinoside plus intravenous antibiotics. A punch biopsy was obtained from an erythematous plaque located on the arm. The epidermis was normal and in the dermis, there were two separate granulomatous foci presenting with necrobiotic collagenous centers, surrounded by a wall of palisaded histiocytes (Figure 2). In these areas multinucleated giant cells were obvious (Figure 3). These findings were consistent with those of GA. Because she had more than 10 lesions, a diagnosis of disseminated GA was made. We treated her with group 4 topical steroids and the skin lesions cleared after 3 weeks. She is still

under the follow-up of the haematology and dermatology departments and no recurrence of the lesions is observed.

## DISCUSSION

Disseminated GA is characterized by numerous skin-colored to erythematous papules, usually on the trunk and extremities, that tend to coalesce in a circular configuration.<sup>6</sup> It has a marked tendency to occur in late middle life and a female sex preponderance of 2.2:1. The trunk, arm, and thigh are the most commonly involved sites; involvement of the face, scalp, palm and sole are infrequent. Interestingly, the lesions were located on the face as well as upper extremities and hands in our patient. We cannot present a photo of her facial lesions since the patient refused to give consent for this. Patients with GA usually have no associated symptoms, but interestingly, our patient had pruritic lesions.<sup>1</sup> Disseminated GA was reported in association with numerous systemic disorders including thyroid autoimmune disease, human immunodeficiency virus infection, and diabetes mellitus.<sup>2,4,5,7</sup> Among the haematologic malignancies, malignant lymphoma is among the most common. Disseminated GA develops occasionally in leukaemia patients. In 1993, Vestey et al. presented a patient with disseminated GA who developed AML secondary to a background myelodysplastic syndrome.<sup>8</sup> In 1994, Huilgol et al presented a patient of disseminated GA associated with chronic myelomonocytic leukemia and myelodysplasia.<sup>9</sup> In 2002 Granjo et al reported a patient with disseminated GA associated with large granular lymphocytic leukemia.<sup>10</sup> In 2003, Jee et al. presented a patient with disseminated GA associated with chronic myelogenous leukemia.<sup>11</sup> Fullen et al reported the first case of cutaneous lesions resembling GA with concomitant involvement by B-cell chronic lymphocytic leukemia.<sup>12</sup> To our knowledge, our case is the sixth case of disseminated GA associated with leukemia, and the second case that is associated with AML. In all reported cases, the lesions of disseminated GA and the hematologic malignancies did not occur concurrently,

whereas in our patient the skin lesions were present as soon as the constitutional symptoms of AML had started.

It is still controversial whether there is a causal relationship between disseminated GA and hematologic malignancies. Some researchers suggested that there was no causal relationship due to the wide variation of the interval between two events.<sup>2</sup> In our patient, there was no interval between the occurrence of disseminated GA and AML, so we think that a correlation is likely. Some authors suggested that hematologic malignancies or AIDS, which lead to disordered immune states, such as immunodeficiency could cause a generalized granulomatous reaction and that disseminated GA might be a part of such a reaction.<sup>3-5</sup>

In addition to the concurrent occurrence of disseminated GA and AML, our case is of interest because of unusual facial location, severe pruritus, and clinical course of rapid onset and easy resolution with only topical steroid. In our patient, the time between the constitutional symptoms of AML and GA was only one week. Reports indicate that treatment of disseminated GA is difficult. Treatment recommendations are based on the pathophysiology of the disease, expert opinion, and case reports only. Liquid nitrogen, injected steroids, or topical steroids under occlusion were recommended for the treatment of localized disease. There are case reports defining the success of some therapies in treating disseminated GA such as PUVA, isotretinoin, topical vitamin E, dapsone, niacinamide, antimalarials, fumaric acid esters, tacrolimus, and pimecrolimus.<sup>13-19</sup> Although treatment is unsatisfactory, our patient responded dramatically to group 4 topical corticosteroids. According to McGregor et al, underlying disorders that affect the immune system may modify the disease process and lead to atypical presentations.<sup>5</sup> Our case also seems to support this possibility.

In conclusion, we presented an unusual case of disseminated GA with leukemia, which is a rare condition.

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