

A Case of Generalized Granuloma Annulare That Contributed to the Diagnosis of Diabetes Mellitus and Regressed with Antidiabetic Therapy

Jeneralize Granüloma Anültre Nedeni ile Diabetes Mellitus Teşhis Edilen ve Antidiyabetik Tedavi ile Gerileyen Jeneralize Granüloma Anültre

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ABSTRACT A 45 year-old man attended with erythematous lesions for two years. On dermatological examination, annular, firm, scaleness, purple-red plaques on the forearms, posterior and lateral sides of neck were detected. The histopathological examination of the lesions confirmed the diagnosis of granuloma annulare (GA). In laboratory tests increased glucose level was detected, and diabetes mellitus (DM) was diagnosed. Antidiabetic therapy was started, and the GA lesions regressed after two months of therapy without specific treatment for GA. Granuloma annulare is a benign, self-limited, inflammatory skin disease with an unknown etiopathogenesis. Generalized GA occurs in 15% of GA patients. The relationship between GA and DM is still controversial. Our pateint was detected to have DM after the diagnosis of generalized GA. The lesions regressed after the regulation of serum glucose level. We think that this case can contribute to the information of relationship between GA and DM in etiopathogenesis of GA.

Key Words: Granuloma annulare, diabetes mellitus, hypoglycemic agents

ÖZET Kırk beş yaşında erkek hasta iki yıldır devam eden eritemli lezyonlarla kliniğimize başvurdu. Dermatolojik muayenede, her iki ön kolda ve boynun yan ve arka yüzlerinde annuler, sert, skuamlı ve mor kırmızı renkli plaklar izlendi. Lezyonların histopatolojik incelemesi granuloma annular (GA) tanısını doğruladı. Laboratuvar testlerinde açlık kan şekeri yüksekliği tespit edildi ve diabetes mellitus (DM) teşhisi kondu. Antidiyabetik tedavinin başlanmasından iki ay sonra GA için ek tedavi verilmesi gerekmezsin lezyonlar geriledi. GA benign, kendi kendini sınırlayabilen, etiolojisi bilinmeyen inflamatuvar bir deri hastalığıdır. Jeneralize GA, tüm GA'li hastaların %15'inde oluşur. GA ve DM ilişkisi halen tartışmalıdır. Olgumuzda jeneralize GA teşhisinden sonra DM teşhis edildi ve serum glukoz seviyesinin regülasyonundan sonra lezyonlar geriledi. Bu olgunun GA ve DM ilişkisine katkıda bulunacağını düşünüyoruz.

Anahtar Kelimeler: Granüloma annular; diabetes mellitus, antidiyabetik tedavi

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Granuloma annulare (GA) is a benign, inflammatory, self-limited skin disease. The etiology of the disease is unknown. Generalized GA is a rarely seen form of GA. Although some reports have been published about the relationship of generalized GA with DM, this association is still controversial.¹⁻⁵ We present a case with DM that was diagnosed while the patient was being investigated for GA, and his lesions improved after the regulation of serum glucose level.

CASE REPORT

The patient was 45-year-old man. He had erythematous lesions which had started on both forearms two years ago and spread to posterior and lateral sides of neck. There were no pathology in the history of himself and his family. He did not receive any treatment previously. His physical examination was normal except increased blood pressure levels. On dermatological examination firm, purple-red, annular plaques on the forearms extending from ankle to elbow were observed (Figure 1A). Similar lesions were detected on posterior and lateral sides of the neck (Figure 1B). The histopathological examination of the lesions that revealed palisadic arrangement of his-

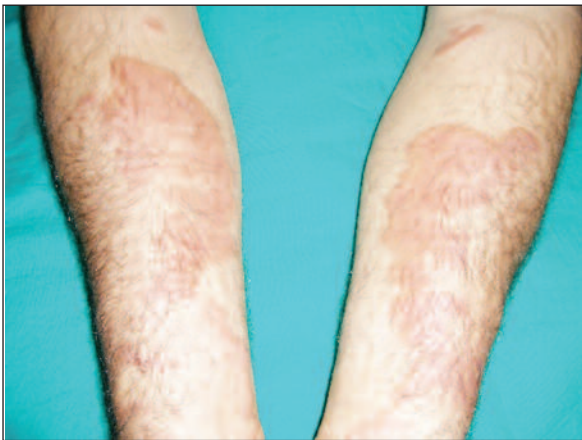


FIGURE 1A: Erythematous-purple, annular shaped plaques with peripheral activation on both of forearms.



FIGURE 1B: The lesions of GA on the lateral side of neck.

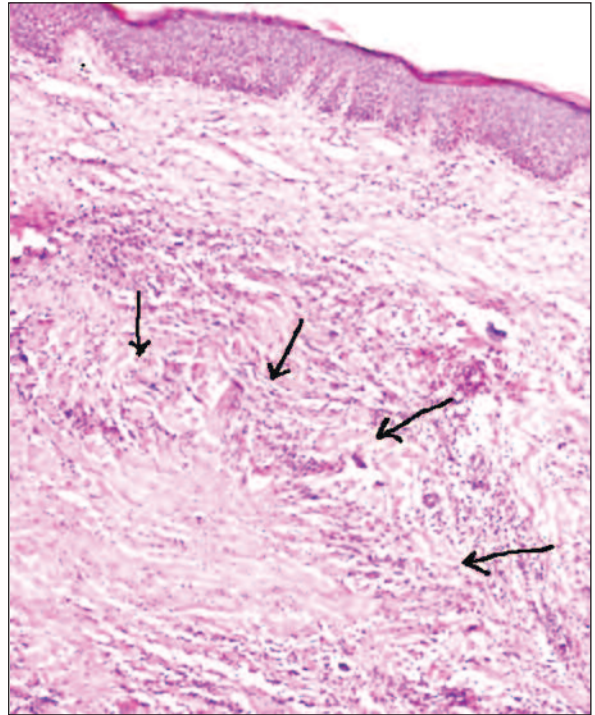


FIGURE 2: Necrobiotic focus in dermis was seen as pointed with arrows (H, E x 50).

tiocytes and multinuclear giant cells derived from histiocytes surrounding the necrobiotic focus in dermis confirmed the diagnosis of GA (Figure 2). Because of late age of onset, chronic course of lesions and involvement of both trunk and extremity, he was diagnosed as generalized GA.

For investigating the associated diseases with GA, routine laboratory examinations were performed. The pathologic findings were increased blood glucose level (350 mg/dL, N: 70-115 mg/dL), high total cholesterol 250 mg/dL (N: 112-200 mg/dL) and triglyceride levels in serum 1566 mg/dL (N: 50-179 mg/dL). VLDL was 231 mg/dL (N: 0-40 mg/dL). DM type 2 was diagnosed.

The therapies of hypertension (amlodipine besilate), DM (metformin HCL) and hypercholesterolemia (fenofibrate) were started. As a slight regression in the lesions were observed until the result of histopathological examination, the patient was followed once a month without any therapy for lesions of GA. Under antidiabetic therapy, the



FIGURE 3A: Regression of the lesions.



FIGURE 3B: The lesions on the neck were regressed after antidiabetic therapy.

lesions on the neck completely regressed and infiltration of the lesions on the forearms partially improved after the first month of treatment (Figure 3A, 3B). At the second month of therapy, the lesions on the forearms also improved with postinflammatory hyperpigmentation. The patient was still being followed up.

DISCUSSION

Granuloma annulare is an idiopathic, benign, granulomatous skin disorder. It presents flesh-colour or pinkish-violet, firm papules that are solitary or coalesced for annular configuration. The lesions are generally asymptomatic and localized on the trunk and extremities.^{2,6}

Six different types of GA were defined: Localized, subcutaneous, perforating, arcuate dermal, actinic and patch type.⁷ Generalized form is a rarely seen form of GA, occurring in only 15 % of GA patients.^{6,7} Although generalized GA is generally considered as a disseminated form of localized GA, it differs from the localized GA by a later age of onset, protracted course with only rare spontaneous resolution, poor response to treatments. The lesions of GA generally involve trunk, and one or both of extremities.⁸ The lesions of our patient showed late age of onset (43 years old) and extended progressively in two years period. GA lesions involved both upper extremities symmetrically, and posterior and lateral sides of neck.

The etiology of GA is unknown. However it has been reported that endogen and exogen factors such as localized trauma, insect bite, exposure to sunlight, viral infection, acquired immune deficiency syndrome, sarcoidosis, thyroiditis, malign disorders and DM may be associated with generalized GA.^{2,9}

The relation of GA with DM is still controversial.^{2,6,8} There are case reports and studies regarding the coexistence of GA with DM in the literature. In these studies the relation of DM and glucose intolerance with generalized form of GA were reported.^{4,6,8-10} In some reports, a relationship between GA and DM was demonstrated.¹¹ However in 2002, Nebessio et al studied the prevalences of DM in GA, and as control group, they selected the patients with psoriasis and they did not find any significant difference in the rates of DM between patients with GA and psoriasis.³ In our case, DM was diagnosed while he was being investigated for GA, and the lesions regressed after the oral antidiabetic therapy.

There are several hypothesis that were suggested, based on the detection of lymphocytic involvement, cytokines and cell products histopathologically in the pathogenesis of GA. These are: vasculitis that caused to necrotizing changes in dermal blood vessels, necrobiosis triggered by trauma, releasing of lysosomal enzymes caused to necrobiotic changes from monocytes and lymphocyte-mediated delayed-type of hypersensitivity reaction caused to degenerative changes.

The etiological factors such as insect bite, trauma, infections, DM and thyroiditis trigger the activation and chemotaxis, and the factors released from lymphocytes stimulates macrophages and causes to degenerative changes. This is the most frequent accepted theory.^{8,12}

How DM triggers GA is unknown. The increased serum glucose level or resistance of insulin may change the structure of dermal blood vessels. Another possibility is that it can trigger the disease onset by damaging the structure of dermal collagen. DM may contribute to development of generalized GA by another unestimated mechanism.

The generalized GA is usually has a protracted course. There may be also spontaneous resolution in the lesions.⁸ Although we can not exclude the possibility of spontaneous regression of the lesions of GA in our patient, and the effects of the other drugs on the disease course, we believe that the lesions were regressed by using antidiabetic therapy, as the lesions were persisting and deteriorating for two years time before attending to us. By this case, we suggest that DM may play a role in the etiopathogenesis of GA and the patients with generalized GA should be investigated or taken under observation for development of DM or glucose intolerance.

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