# Generalized and patch granuloma annulare in a patient with psoriasis and multiple sclerosis after treatment with fingolimod

Funda Tamer[1], Belgin Kocer[2], Betul Ogut[3], Ozlem Erdem[3]

[1]Department of Dermatology, School of Medicine, Gazi University, Ankara, Turkey
[2]Department of Neurology, School of Medicine, Gazi University, Ankara, Turkey
[3]Department of Pathology, School of Medicine, Gazi University, Ankara, Turkey

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Granuloma annulare is an inflammatory cutaneous disorder which may present with localized, generalized, patch, perforating and subcutaneous forms. Granuloma annulare has been associated with diabetes mellitus, hyperlipidemia, malignancy, bacterial and viral infections. In addition, various medications such as tumor necrosis factor-α (TNF-α) inhibitors, allopurinol, amlodipine, paroxetine and tocilizumab have been implicated in the development of granuloma annulare. It has been suggested that activation of T helper (Th) 1 and the Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathways might play a role in the etiopathogenesis of granuloma annulare. However, the pathogenesis of drug-induced granuloma annulare has not been clearly understood yet [1]. Hereby, we report a 32-year-old Caucasian female patient with psoriasis and multiple sclerosis who developed both generalized and patch granuloma annulare at the same time 2 months after the initiation of oral fingolimod for the treatment of multiple sclerosis.

A 32-year-old female patient was admitted with a 10-month history of asymptomatic erythematous macules and plaques on the trunk and extremities. The lesions first appeared in the inframammary fold and then increased in size and number gradually. The patient stated that the lesions occurred 2 months after the initiation of oral fingolimod 0.5 mg/day for the treatment of multiple sclerosis. The patient was previously treated with 0.1% mometasone furoate and 1% terbinafine hydrochloride cream twice daily for 8 weeks. However, no clinical response was achieved. Fingolimod was discontinued 2 months ago due to skin lesions. The past medical history was remarkable for multiple sclerosis, psoriasis and asthma. The patient revealed that she was diagnosed with psoriasis vulgaris at the age of 9. She was treated with topical medications with complete clearance. However, she reported a psoriasis plaque that recently developed on her arm. The family history was remarkable for psoriasis in her sister. Dermatological examination revealed erythematous round-shaped macules and plaques with distinct borders on the breasts, inframammary fold and intermammary region. In addition, erythematous macules and slightly elevated plaques were detected on the right arm, dorsum of the right hand, leg, feet and abdominal region. On the other hand, the erythematous and squamous plaque which was detected on the extensor surface of the right forearm indicated psoriasis clinically (fig. 1).

Among laboratory tests, complete blood count revealed an increased blood eosinophil count ($0.9 \times 10^9$/l, range: 0.01–0.4 × $10^9$/l). Biochemistry panel was normal except for increased serum levels of alkaline phosphatase (120 U/l, range: 33–98 U/l) and γ-glutamyl transferase (81 U/l, range: 0–38 U/l). A skin biopsy was performed from the lesion on the abdomen to reach a definitive diagnosis. Histopathological examination revealed annular granulomatous inflammation composed of histiocytes and mild mucin deposition (fig. 2). Therefore, the diagnosis of granuloma annulare was made based on clinical and histopathological findings. The patient was initiated on tacrolimus 0.1% ointment and hydrocortisone 17-butyrate 0.1% cream twice daily.

Granuloma annulare is a granulomatous cutaneous disorder with unknown etiology. Localized, generalized, subcutaneous, perforating and patch forms of granuloma annulare have been reported [1, 2]. Generalized granuloma annulare describes lesions on the trunk and extremities [3]. Patch granuloma annulare is a rare form of the disease that presents with erythematous patches [4]. Diabetes mellitus, hyperlipidemia, autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus, human immunodeficiency virus infection and various medications such as TNF-α inhibitors, allopurinol, amlodipine, paroxetine and tocilizumab have been asso-

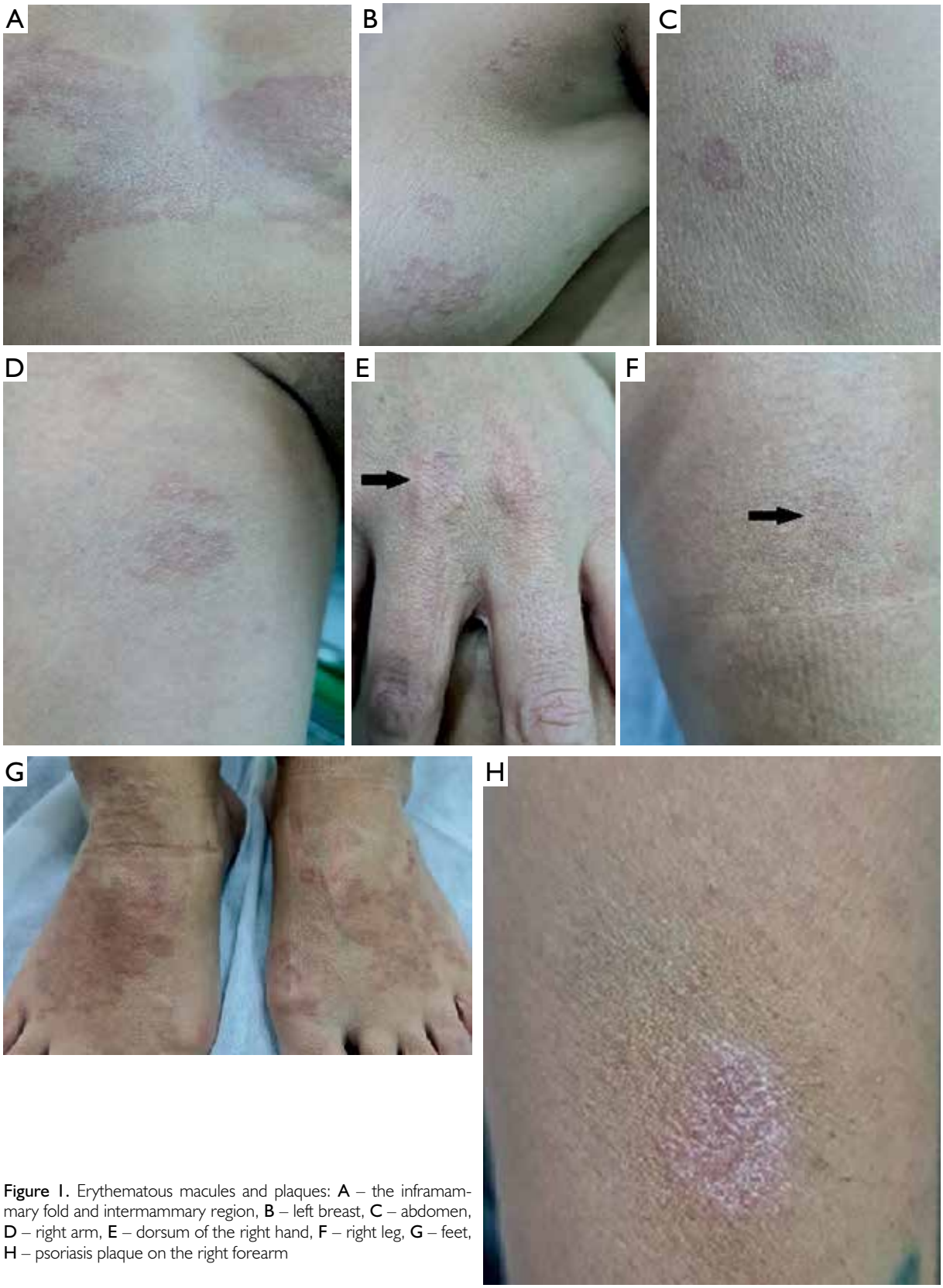


**Figure 1.** Erythematous macules and plaques: **A** – the inframammary fold and intermammary region, **B** – left breast, **C** – abdomen, **D** – right arm, **E** – dorsum of the right hand, **F** – right leg, **G** – feet, **H** – psoriasis plaque on the right forearm

ciated with granuloma annulare. The mechanism of drug-induced granuloma annulare remains unknown as well as complicated. For instance, granuloma annulare can be triggered by TNF-α inhibitors and also treated with them [1]. To the best of our knowledge, the patient we presented is the first case who devel-

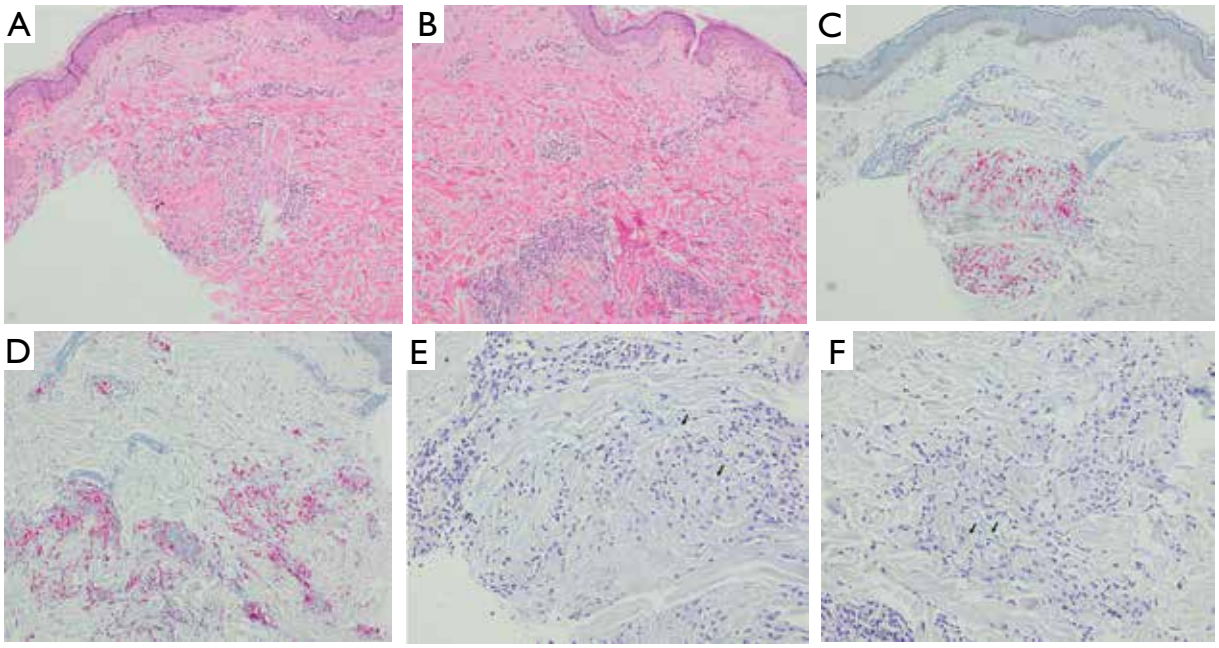


Figure 2. A – Annular granulomatous inflammation composed of histiocytes was observed in the dermis at the biopsy margin (hematoxylin and eosin ×100). B – Histiocytic inflammation scattered in the dermis (hematoxylin and eosin ×100). C, D – Immunohistochemically, histiocytes with CD68 expression in annular granulomatous inflammation and scattered histiocytes were observed, respectively (CD68--red chromogen, ×100). E, F – mild mucin deposition was observed in the same areas with alcian blue (×100, arrows)

oped granuloma annulare following fingolimod treatment for multiple sclerosis. Since fingolimod affects lymphocyte functions through sphingosine 1-phosphate (S1P) receptor subtype S1P1 [5], T lymphocytes may have a potential role in the development of fingolimod-induced granuloma annulare. In addition, our case is unique as the patient had psoriasis and developed both generalized and patch granuloma annulare at the same time. Hopefully, our case will contribute to the literature on this extremely rare topic.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## References

1. **Joshi T.P., Duvic M.:** Granuloma annulare: an updated review of epidemiology, pathogenesis, and treatment options. Am J Clin Dermatol 2022, 23, 37-50.
2. **Salzmann M., Rendon A., Toberer F., Hassel J.C.:** Generalized perforating granuloma annulare: a case report. J Dtsch Dermatol Ges 2021, 19, 585-587.
3. **Lee J.H., Cho S.:** Resolution of refractory generalized granuloma annulare after treatment with alitretinoin. JAAD Case Rep 2022, 24, 38-41.
4. **Khanna U., North J.P.:** Patch-type granuloma annulare: an institution-based study of 23 cases. J Cutan Pathol 2020, 47, 785-793.
5. **Chun J., Hartung H.P.:** Mechanism of action of oral fingolimod (FTY720) in multiple sclerosis. Clin Neuropharmacol 2010, 33, 91-101.

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**Address for correspondence:**
Assoc. Prof. Funda Tamer
Department of Dermatology
School of Medicine
Gazi University
Ankara, Turkey
Phone: +90 5455611881
E-mail: fundatmr@yahoo.com

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