







Eduardo Escario Travesedo: Effective participation in the research guidance, intellectual participation in the propaedeutic and/or therapeutic conduct of the studied cases, final approval of the final version of the manuscript.

Conflicts of interest

None declared.

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A case of psoriasiform eruption developed during imatinib therapy[☆]



Dear Editor,

Imatinib is the standard first-line systemic treatment for chronic myeloid leukemia and Gastrointestinal Stromal Tumor (GIST), targeting BCR-ABL and c-KIT tyrosine kinases, respectively. Imatinib-induced eruptions can present with a variety of skin manifestations, but cases with psoriasis/psoriasiform eruptions are rare. We herein report one such case with a review of the literature.

A 69-year-old man was referred to our department with a psoriasiform eruption. He had been treated with imatinib for GIST for the previous 2 years. Two months after the start of imatinib treatment at 400 mg/day, a rash appeared. Physical examination revealed red papules with scales of 2–4 mm in size on the trunk and limbs. In addition, the buttocks had a number of scaly erythema resembling psoriasis (Fig. 1A). A skin biopsy was performed from the scaly erythema of the lower leg (Fig. 1B). Histological findings revealed mild

epidermal proliferation with parakeratosis, and subepidermal dilatation of capillaries with perivascular infiltration of mononuclear cells, containing eosinophils (Fig. 1C). Blood test revealed that the patient's eosinophils were elevated between 10% and 15%. Based on the course of the disease, a diagnosis of drug eruption caused by imatinib was made. Treatment was begun with oral antihistamine and topical corticosteroids, and the skin rash improved (Fig. 1D). During the treatment period, imatinib was continued without dose reduction.

Cutaneous reactions are the most commonly reported nonhematological side effects, occurring in 9.5%–69% of patients.¹ Maculopapular or erythematous eruptions, edema, and periorbital edema are the most common adverse events observed. Severe drug eruptions such as Stevens-Johnson syndrome and toxic epidermal necrolysis have also been reported. Imatinib potentially affects immune cells directly, and several cases showed improvement in psoriasis after the introduction of imatinib.^{2,3} By contrast, exacerbation of psoriasis or *de novo* development of psoriasiform rash have rarely been reported. As a pathogenetic mechanism, it has been reported that imatinib treatment reduced CD4+CD25+FoxP3+ regulatory T-cell (Treg) frequency and decreased immunosuppressive function.⁴ Therefore, reduced activation of Tregs by imatinib may contribute to the development of psoriasis or

[☆] Study conducted at the Fukushima Medical University, Fukushima, Japan.

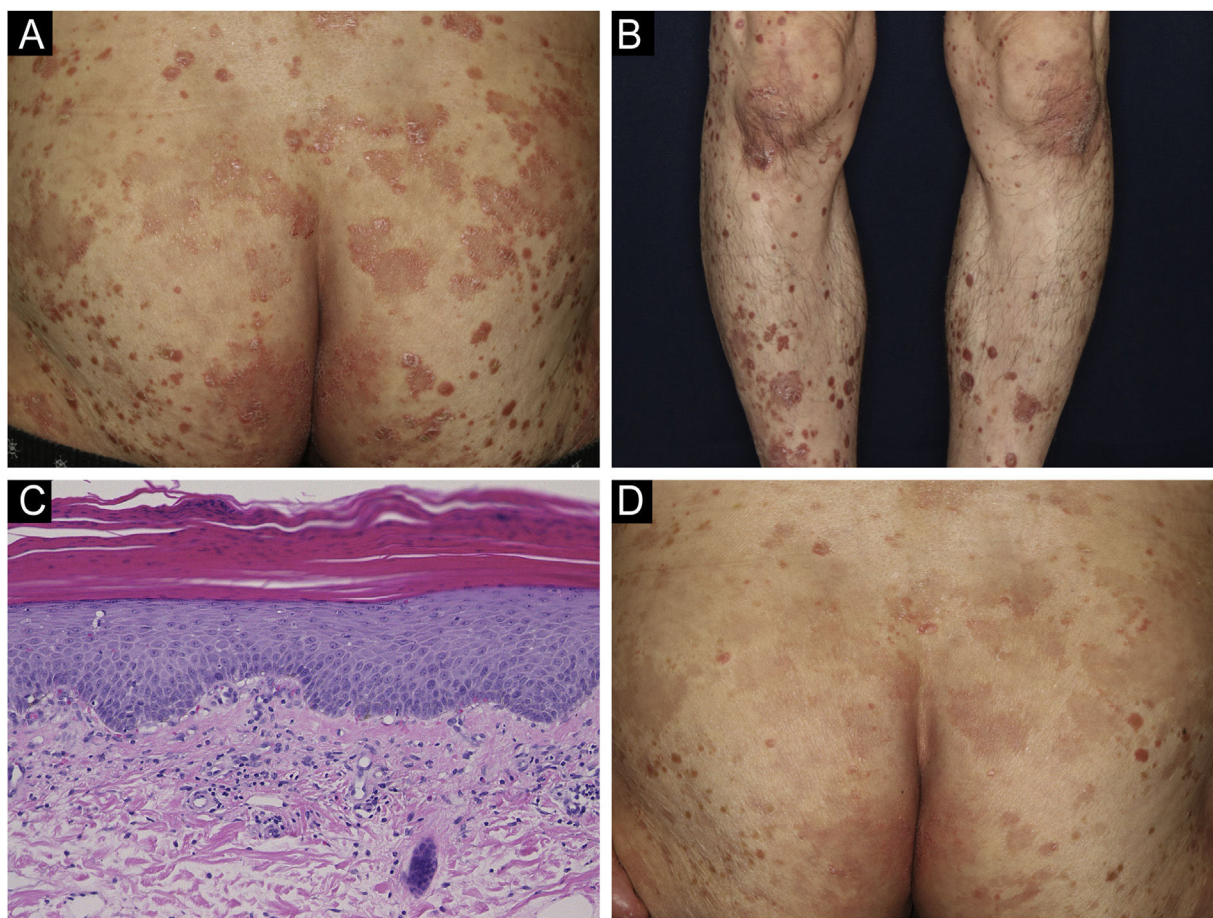


Fig. 1 (A) Psoriasiform lesions on the buttocks. (B) Similar lesions on the lower legs. (C) Histological findings revealed slight parakeratosis with a slightly flattened epidermis. Inflammatory cell infiltration was observed around blood vessels and stroma in the superficial dermis, accompanied by red blood cell extravasation. The inflammatory cells were eosinophils as well as lymphocytes and histiocytes. (Hematoxylin & eosin, $\times 200$). (D) After treatment, the skin rash was partially improved.

psoriasiform eruptions. It has also been reported that psoriasis/psoriasiform eruptions are generally less severe, due to effector T-cell inhibition by imatinib.²

We reviewed the English literature on PubMed from 2002 to 2022, using the keywords "imatinib" and "psoriasis". The results of our search revealed eight cases,^{2,3,5-10} the details of which are summarized in Table 1. Eight cases were reported to date in which imatinib caused psoriasis exacerbation, new onset, or even improvement. The average age at occurrence was 51.1 years old, with a male predominance (6:2 men to women ratio). The duration of onset ranged from a few weeks to several months. There were seven patients with pre-existing psoriasis, and the remaining patients had newly onset psoriasiform symptoms. Since the present case was also a new onset psoriasiform eruption, we focused on the previous case of the same type. There were differences in histological findings and the course of the disease. The histopathological features in the previous case were neutrophilic scale crust and loss of the granular cell layer.⁵ By contrast, the histopathological features in the present case were atypical for psoriasis, in that slight parakeratosis,

no clear epidermal proliferation, and the absence of neutrophilic microabscess below the corneal layers. The patient in the previous case was switched to a different drug,⁵ but the patient in the present case was able to continue with imatinib.

In the present report, we described a rare case of de novo development of psoriasiform eruption under imatinib treatment. Imatinib-induced psoriasis/psoriasiform eruption takes several months to develop and appears dose-dependent. Consequently, it is thought to be related to pharmacological effects rather than an allergic mechanism. In the present case, it had taken 2 months for the rash to develop. However, the rash improved without dose-reduction of imatinib. Furthermore, the patient's eosinophils were elevated after the start of imatinib but had improved after the end of imatinib. Also, eosinophil infiltration was marked in the histological findings. Thus, we suggested that an allergic mechanism or other pharmacological effects may be involved.

Table 1 Case of imatinib and psoriasis associated.

	Age, Sex	Imatinib dose	Rash	History of psoriasis	Duration	Therapy	Treatment outcome
1 ⁶	52, M	400 mg/day	Exacerbation	+	2 months	Topical corticosteroid, calcipotriol ointment, Resumption of imatinib at 200 mg/day	Improved
2 ⁷	55, M	400 mg/day	Exacerbation	+	2 months	Topical corticosteroid and vitamin D analogues, continued on imatinib.	Persisted
3 ⁸	62, F	400 mg/day	Exacerbation	+	4 weeks	Discontinuation of imatinib, resumption of imatinib at 400 mg/day, MTX12.5 mg/week	Improved
4 ⁹	63, M	400 mg/day	Exacerbation	+	3 weeks	Discontinuation, narrow-band UVB	Improved
5 ¹⁰	57, M	400 mg/day	Exacerbation	+	Unknown	Discontinuation, resumption of imatinib at 200 mg/day, vitamin D3 ointment	Improved
6 ⁵	21, M	400 mg/day	New onset	–	5 months	Discontinuation, narrow-band UVB	Improved
7 ²	35, M	400 mg/day	Improvement	+	1 month	Undescribed	Undescribed
8 ³	64, M	400 mg/day	Improvement	+	2 weeks	Undescribed	Undescribed
Present case	69, M	400 mg/day	New onset	–	2 months	Reduction of imatinib to 300 mg/day, topical corticosteroid	Improved

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Authors' contributions

Yukina Watanabe: Approval of the final version of the manuscript; preparation and writing of the manuscript.

Tomoko Hiraiwa: Approval of the final version of the manuscript; intellectual participation in propaedeutic and/or therapeutic management of studied cases.

Mikio Ohtsuka: Approval of the final version of the manuscript; intellectual participation in propaedeutic and/or therapeutic management of studied cases.

Toshiyuki Yamamoto: Manuscript critical review; approval of the final version of the manuscript.

Conflicts of interest

None declared.

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Acquired ichthyosis as a messenger to gastric diffuse large B-cell lymphoma[☆]



Dear Editor,

A 50-year-old male patient presented with recurrent bloody vomiting. In the endoscopic examination, a tumoral lesion was detected in the gastric antrum. Immediate gastrectomy was performed due to perforation. Histopathological examination diagnosed a triple-expressor gastric Diffuse Large B-Cell Lymphoma (DLBCL) [Bcl-2 focal (60%), Bcl-6 focal (40%), C-Myc (10%), CD10 focal (70%)]. The Ki-67 index was positive at 60%. A stool examination of the *Helicobacter pylori* antigen was negative. PET-CT demonstrated no involvement at the operation (gastrectomy) site.

The patient had been complaining of itchy, polygon-shaped brown, gray, and white scales on the whole-body skin, more prominently on the extremities, for 2 years. At the same time, the skin was very dry and thickened (Fig. 1). There was no similar history in the patient's family. The patient was started on R-CHOEP (Rituximab, Doxorubicin, Vincristine, Etoposide, Cyclophosphamide, and Prednisolone) chemotherapy. Also, a skin biopsy was performed. In the skin tissue hyperkeratosis, papillomatosis, mild acanthosis, and absent granular layer were noted. Perivascular mononuclear cell infiltration was observed in the superficial dermis (Fig. 2). At the end of chemotherapy, skin findings improved (Fig. 1).

Ichthyosis presents as rough, dry, skin with a large plate-like scale, and it can either be hereditary or acquired. Acquired Ichthyosis is defined in neoplastic disorders (Hodgkin's lymphoma, anaplastic large cell lymphoma, multiple myeloma, mycosis fungoides, POEMS [polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes] syndrome, Kaposi's sarcoma, leiomyosarcoma, etc). Also, it is known to be associated with malnutrition, infections (HIV, Human T-lymphotropic virus), hypothyroidism, celiac disease, autoimmune conditions, sarcoidosis, graft-versus-host disease, and drug intake (hydroxyurea, allopurinol, vemurafenib, cholesterol-lowering medications, etc.). It is assumed that ichthyosis can be caused by impaired epidermal lipogenesis and production of transforming growth factor- α by tumor cells and impaired vitamin A metabolism.^{1,2} According to the best of our knowledge, our case is the first ichthyosis as a precursor to gastric DLBCL.

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Authors' contributions

İrfan Yavaşoğlu: Design and planning of the study; Data collection, or analysis and interpretation of data; Drafting and editing of the manuscript or critical review of important intellectual content; Collection, analysis, and interpretation of data; Critical review of the literature; Approval of the final version of the manuscript.

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Ali Zahit Bolaman: Design and planning of the study; Data collection, or analysis and interpretation of data; Drafting and editing of the manuscript or critical review of important

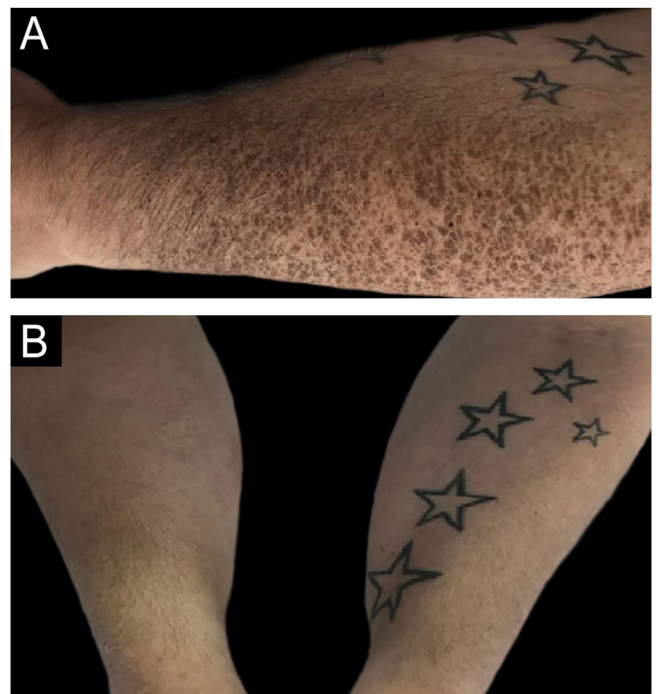


Figure 1 (A) Polygon-shaped brown, grey, or white scales on the forearm. (B) Resolution after the treatment.

[☆] Study conducted at the Aydin Adnan Menderes University Medical Faculty, Aydin, Turkey.