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CASE REPORT

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Can erythrodermic psoriasis be considered a paraneoplastic syndrome in patients with metastatic occult gastric cancer?

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Abstract

Introduction. Erythrodermic psoriasis is a relatively rare form of psoriasis. It has many etiologies including infection, inflammatory skin diseases, malignancy, and systemic drug reactions. It may be seen more frequently in hematological malignancies. To our knowledge, this is the first reported case of paraneoplastic erythrodermic psoriasis in gastric cancer.

Case report. A 59-year-old male patient, who was diagnosed with psoriasis 5 years earlier, presented with severe erythroderma resistant to both local and immunosuppressive treatments. During treatment, he was diagnosed with pathological and radiological metastatic occult gastric cancer and treated with a modified FOLFOX-6 chemotherapy protocol that was planned every 14 days. After six cycles of chemotherapy, a clinically significant benefit was observed in control examination. Extensive skin lesions almost completely resolved after chemotherapy. Erythroderma and pruritus symptoms completely regressed. The patient continues his treatment.

Conclusions. Erythrodermic psoriasis may be considered a paraneoplastic syndrome associated with malignant disorders, and therefore paraneoplastic syndrome should be considered in the treatment of these patients.

Keywords: erythrodermic psoriasis, occult gastric cancer, paraneoplastic syndrome, chemotherapy

Introduction

Erythrodermic psoriasis (EP) is a clinical form that patients with psoriasis may experience at any time in their lives. It is characterized by diffuse erythema and varying degrees of desquamation, which may be accompanied by general malaise, fever, lymphadenopathy, and protein loss. It can be caused by various factors including infection, inflammatory skin conditions, malignancy, and systemic drug reactions [1]. Paraneoplastic syndromes are defined as signs and symptoms that may appear when substances released by tumor cells alter normal functions of nearby cells or tissues. Their incidence is not well defined although they are more frequent in hematologic cancers. Moreover, they can appear either at the beginning or during the course of the disease [2]. We present a case of a 59-year-old man with a new onset of erythrodermic psoriasis and concurrent metastatic occult gastric cancer (GC). To our knowledge, this is the first reported case of paraneoplastic EP with metastatic occult GC.

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Case

A 59-year-old male who had been followed up with a diagnosis of psoriasis vulgaris for about five years presented to the dermatology outpatient clinic with signs of peeling skin, diffuse redness, chills, and

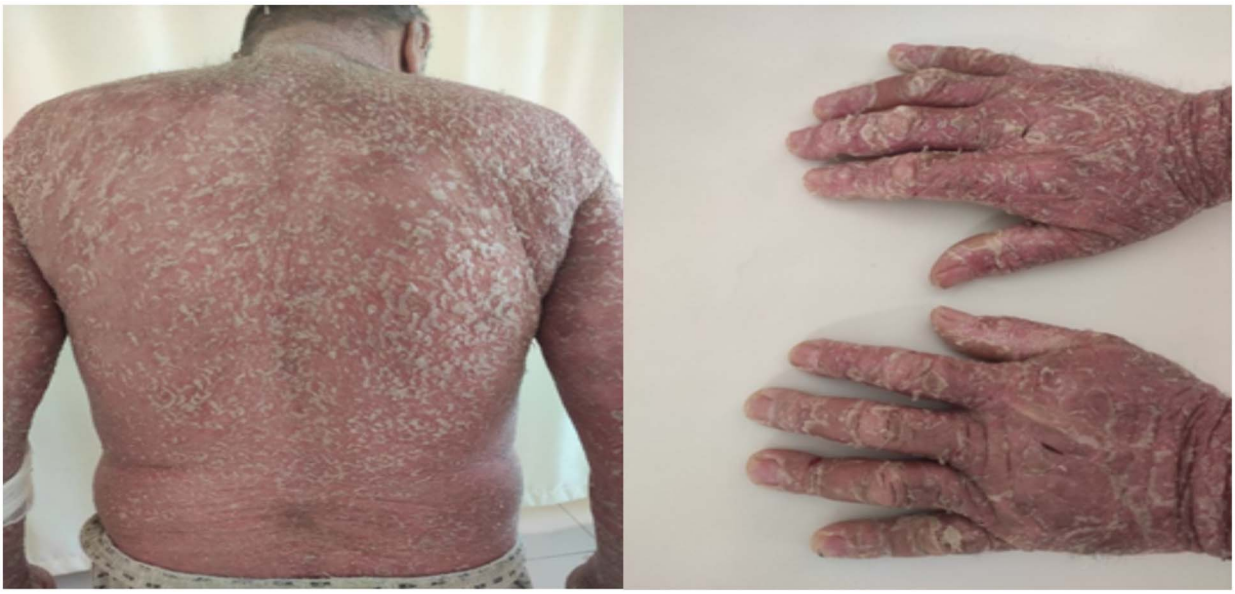

Figure 1. Dermatological lesions at the time of diagnosis

shivering. The patient stated that the skin changes that had started on his hands and feet spread rapidly all over his body and were accompanied by joint pain. Dermatological examination revealed diffuse erythema and desquamation including the scalp (Fig. 1). No significant dystrophy was found in the fingernails of the hands and feet, but pitting was observed in the fingernails of the hands.

Firstly, topical treatment was initiated. The initial Psoriasis Area Severity Index (PASI) score was 15. The patient was evaluated for moderate-severe plaque psoriasis. He was treated with betamethasone plus calcipotriol, but there was no improvement in the PASI score. The conventional treatment with acitretin was started at 25 mg once daily before a biological agent. Acitretin has been added as an emollient and topical corticosteroid treatment as a topical treatment.

The patient was evaluated in terms of treatment effectiveness in the 12th week of his conventional treatment. The PASI score was calculated as 33. The patient did not have a PASI50 response in the induction phase, and the dose of acitretin was changed to 35 mg once daily.

After further 12 weeks, the results of using acitretin 35 mg once daily were evaluated. The PASI score was calculated at 31.2. Systemic acitretin treatment was considered unsuccessful due to failure to obtain a PASI50 response after 24 weeks of acitretin use.

Systemic treatment was started with acitretin and adalimumab, and an anti-tumor necrosis factor-alpha (anti-TNF) agent was initiated. The patient's baseline PASI score was calculated at 23.7. The patient received 80 mg of what? at the first application and 40 mg after 1 week, and then the treatment was continued with 40 mg of adalimumab administered subcutaneously every 2 weeks at regular intervals. Although we recommended the continuation of adalimumab, it was discontinued due to the patient's decision.

The patient presented at the dermatology clinic 4 months later, and diffuse psoriatic plaques and erythroderma were observed throughout the body. The patient, whose general condition was moderate, was hospitalized and followed up.

Additional systemic diseases, trauma, drugs, infections, or other similar trigger factors were questioned in the patient's history, but these were not ascertained. With a history of psoriasis vulgaris, diffuse erythroderma, desquamation, arthritis and secondary malnutrition, fever, chills and shivering on dermatological examination, the patient was diagnosed with severe EP. A punch biopsy was taken from the lesion on the right knee to support the current clinical diagnosis with histopathological examination (Fig. 2 and 3). The pathology result was reported as psoriasis form dermatitis. The patient had a history of using acitretin, a conventional systemic treatment, and adalimumab, an anti-TNF antibody. For this reason, standard treatment with secukinumab (300 mg loading dose), an anti-interleukin-17 antibody was started. Following induction treatment at 0, 1, 2, 3, and 4 weeks, monthly maintenance treatment was planned. Although there was some regression in diffuse skin erythema and desquamation in the 4th week of secukinumab treatment (Fig. 4), skin lesions continued to be prominent. The patient received a total of five loadings and two maintenance doses of secukinumab.

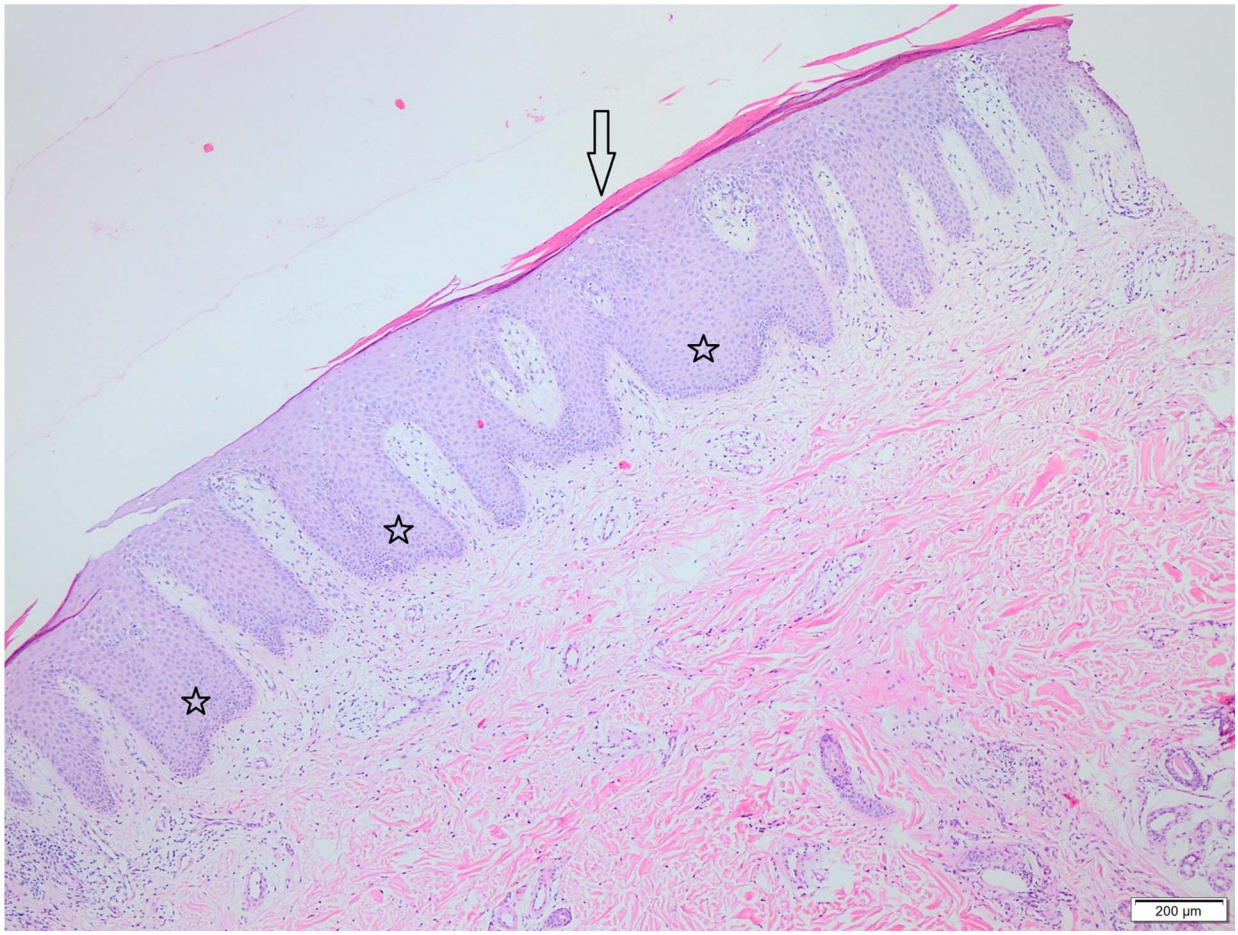

Figure 2. Hyperkeratosis on the surface, parakeratosis (arrow), acanthosis, retinal elongation and some have confluence (stars) at the lower ends, hypogranulosis (Hematoxylin/Eosin, 40×)

The patient was referred to the gastroenterology department due to dyspepsia, loss of appetite, and weight loss during treatment. An upper gastrointestinal system endoscopy was performed, and a biopsy was taken from a nodular edematous lesion in the corpus mucosa extending to the cardia along the level of the small curvature (Fig. 5). The pathology report indicated chronic gastritis.

The patient underwent whole-body imaging, and abdominal computer tomography (CT) revealed malignant wall thickening and minimal contrast enhancement starting from the cardia of the stomach and extending along the small curvature (Fig. 6). Lymphadenopathies were present in the root of the mesentery, starting around the celiac trunk and extending to the periportal, paraaortic and aortic bifurcations, with the largest lymphadenopathy having a short diameter of up to 2.5 cm, and there are also lymphadenopathies with a short diameter of less than 1 cm in the peripancreatic area. No malignant mass was detected in the pancreas and the biliary tract. Hypodense nodular lesions suggestive of metastasis were found in both adrenal glands, measuring 2.7 × 3.5 cm on the right and 3 × 2.7 cm on the left, with a Hounsfield unit of more than 20 HU. No evidence of metastasis was found on the thorax CT. Liver dynamic magnetic resonance imaging revealed a 7.5 cm lesion in the posterior superior part of the right lobe of the liver (Fig. 7), which did not have a typical appearance in terms of metastasis since no signal intensity loss was observed in the arterial portal and late phase sections after intravenous contrasting. No malign cells or tissue were observed in the rebiopsy taken from the stomach. It was reported as benign. A liver wedge biopsy was performed by an interventional radiologist for diagnostic purposes. In the pathology report, it was interpreted as carcinoma metastasis subtype unclassified, CDX-2, TTF-1; and HEPAR were negative, while cytokeratin 7 and 20 were positive. No loss of expression was observed for MLH1, MSH2, MSH6, and PMS2 proficient mismatch repair (pMMR). CERBB2 was positive (score 3) and PDL-1 TPS negative (Dako Clone 22C3). Due to these findings, we investigated the stomach and the pancreatobiliary system as the primary focus.

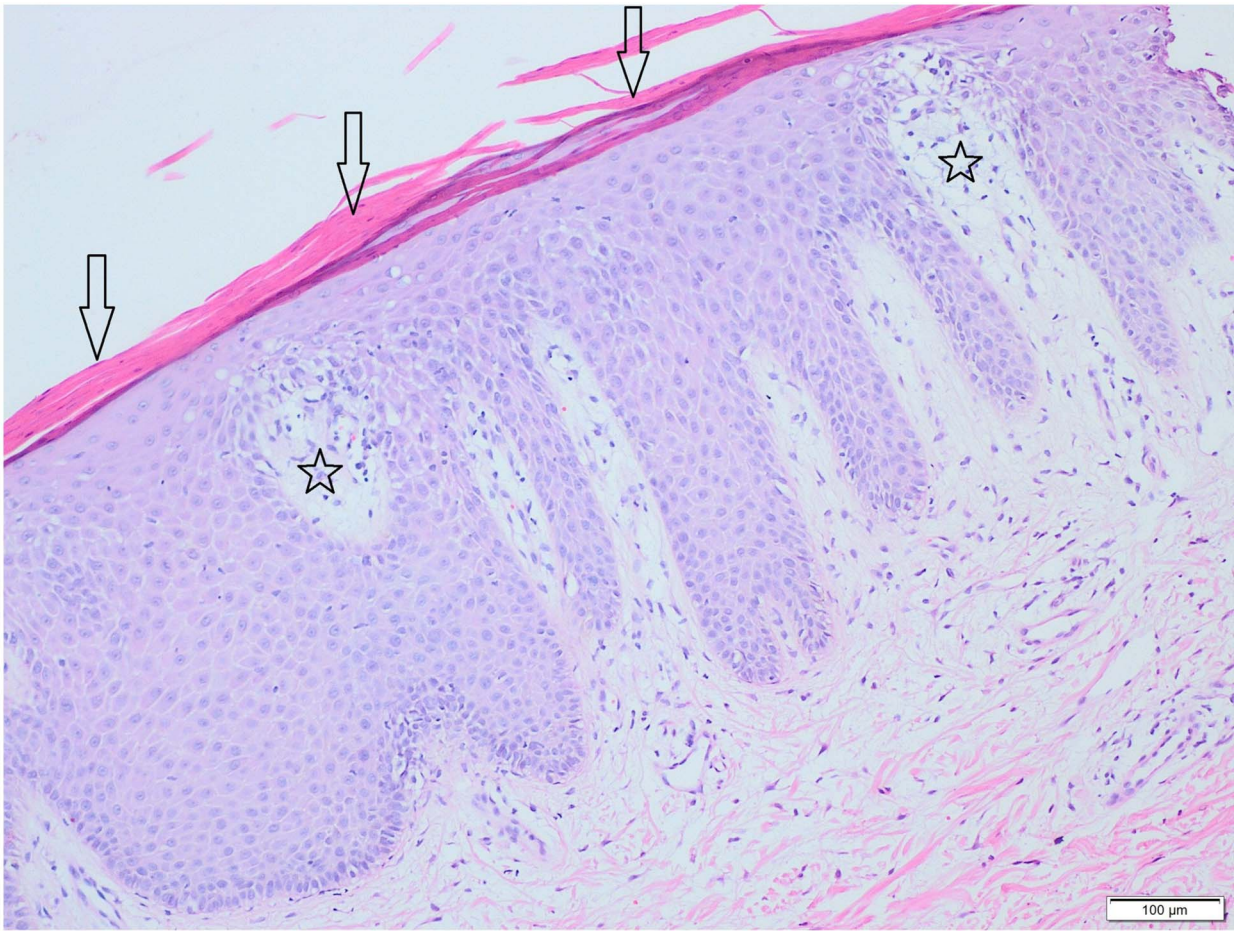

Figure 3. Closer view of skin texture. Persistent parakeratosis (arrows), edema of the papillary dermis, dilated capillaries (stars), and few perivasciluar lymphocytes are seen (Hematoxylin/Eosin, 100×)

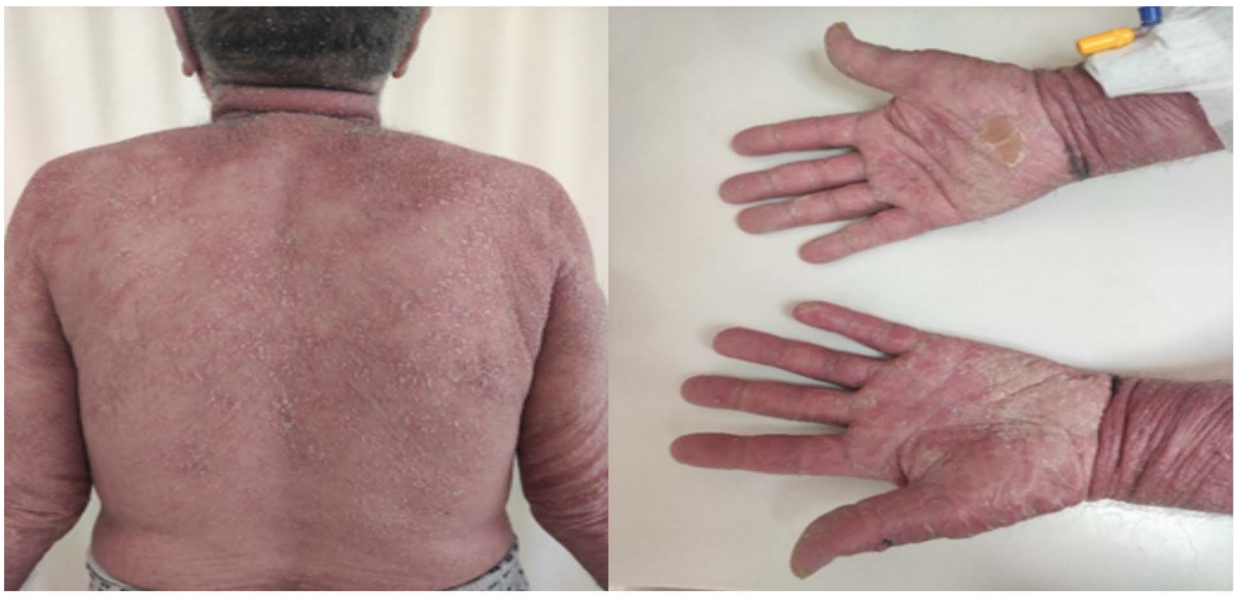

Figure 4. After secukinumab 4th week loading dose treatment

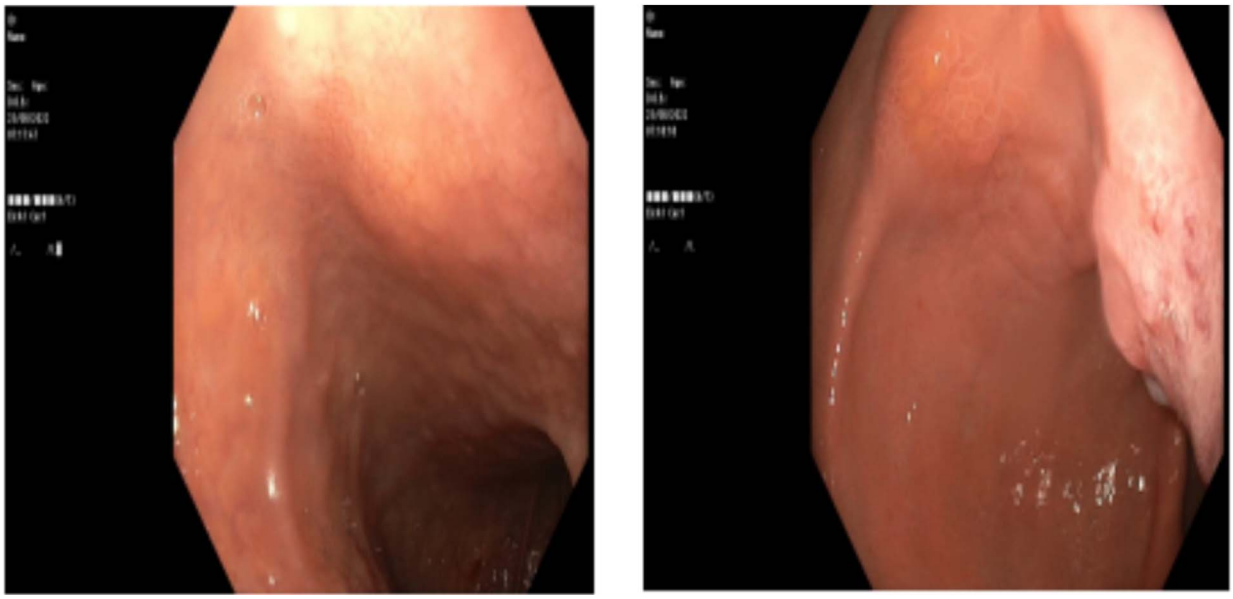

Figure 5. Endoscopic Image at diagnosis

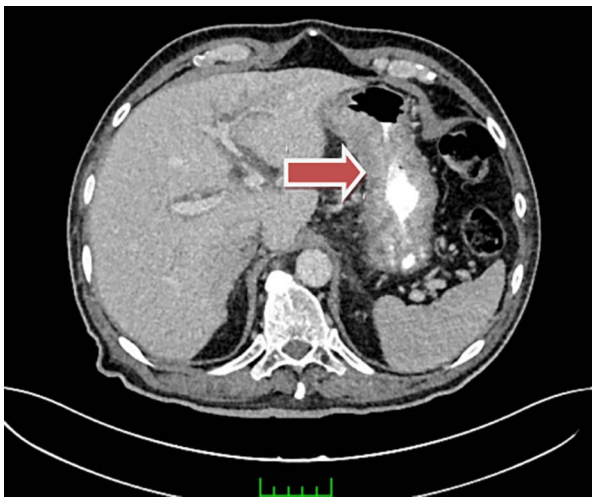

Figure 6. Thickness of the gastric wall

The clinical and radiological diagnosis was metastatic occult GC, and the patient was treated with a modified FOLFOX-6 chemotherapy protocol [oxaliplatin 85 mg/m^2, folic acid 400 mg/m^2, 5-fluorouracil 400 mg/m^2 intravenous (IV) injection and 2400 mg/m^2 46-hour infusion]. The protocol was planned every 14 days. After 6 cycles of chemotherapy, a clinically significant benefit was observed in the control examination. Extensive skin lesions almost completely resolved after chemotherapy. Erythroderma and pruritus completely regressed (Fig. 8). A CT scan of the thorax and abdomen, which was performed to evaluate the response to treatment, showed that the size and number of hepatic lesions and paraaortic and mesenteric root lymphadenopathies decreased, which we considered a partial response to treatment. The patient continues this treatment.

Discussion

Erythrodermic psoriasis is a relatively rare form of psoriasis but represents a fairly common etiology for erythrodermic phenotypes. Erythroderma is a diffuse erythema involving more than 90% of the body surface and may be exfoliative and exudative and involve hair and nail changes. It has many etiologies including infection, inflammatory skin diseases, malignancy, and systemic drug reactions [3]. However, the relationship between malignancy and psoriatic disease has not been clearly established. Studies in patients with psoriasis have documented increased rates of lymphoma and non-melanoma skin cancer, but results for other solid malignancies have not been significant [4]. Less commonly, acute myeloid leukemia and solid tumors (e.g., lung, prostate, thyroid, liver, ovaries, rectum, or skin) are associated with paraneoplastic erythroderma [5] A review of the literature identified two cases associated with EP. Both were hematological malignancies. Thus, the case of EP published by Chen et al. in 2017 [6] was accompanied by monoclonal B-cell lymphocytosis. In another study published in 2021, Li et al. [7] mentioned that B-cell chronic lymphocytic leukemia precipitated EP.

While rates of GC have been falling, over 100 000 new cases occur in Europe each year [8]. It remains one of the leading causes of cancer-related death and therefore a major health problem [9]. Patients are usually diagnosed at an advanced stage, which explains

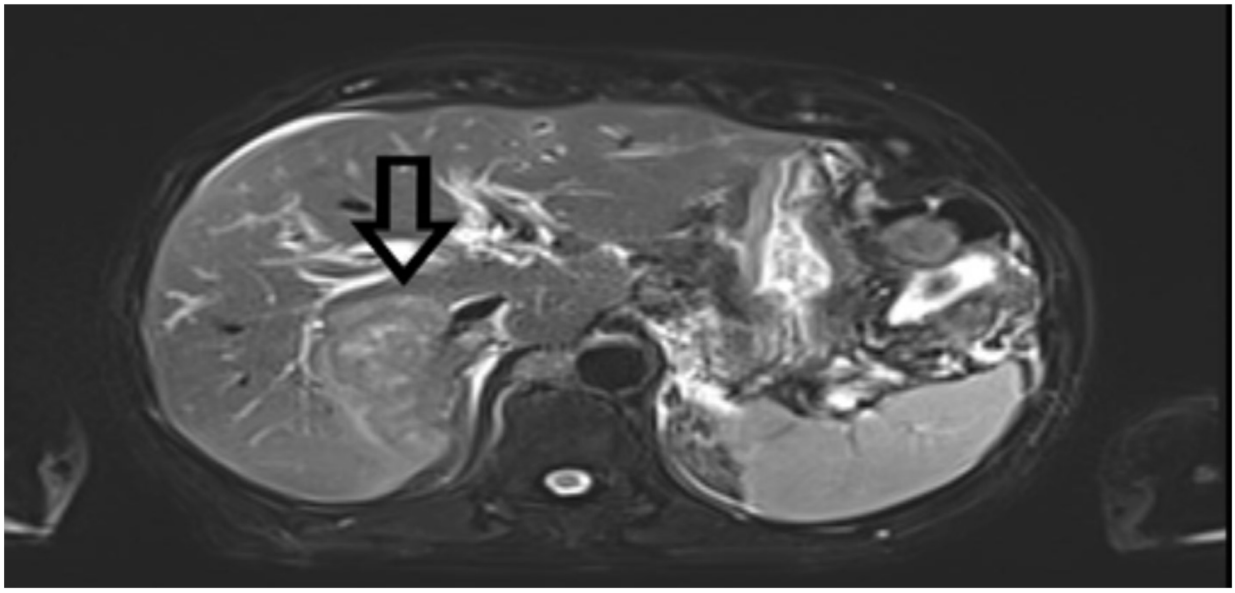

Figure 7. Magnetic resonance imaging of a metastatic lesion in the liver

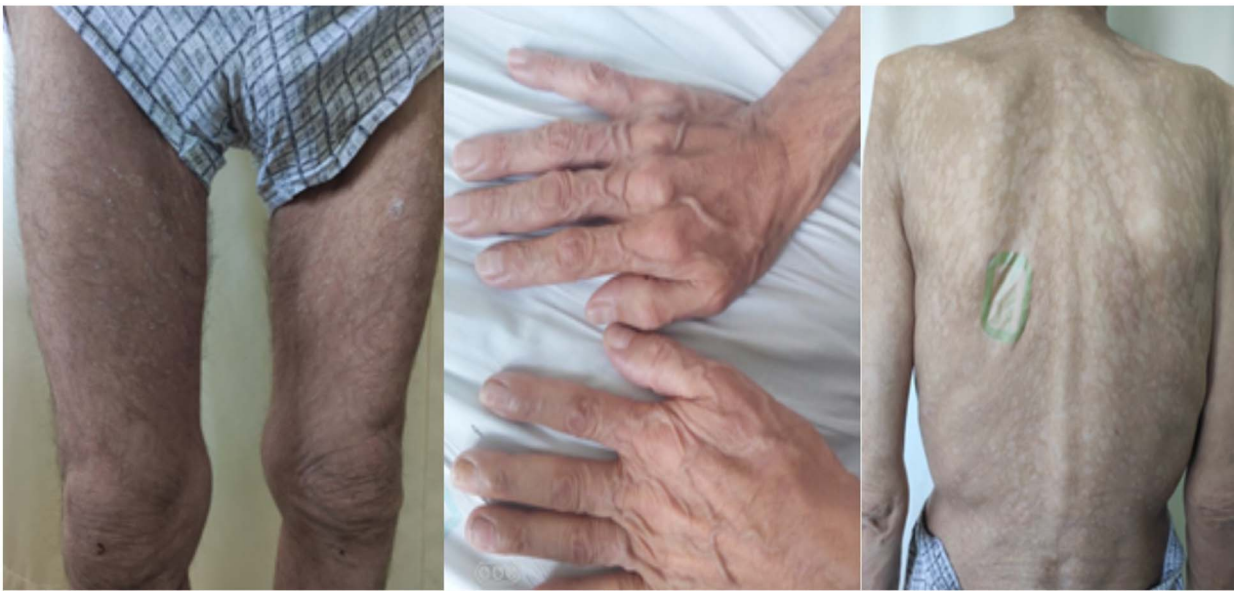

Figure 8. Post-chemotherapy dermatological lesions

the poor survival rate. Several dermatological paraneoplastic syndromes precede the diagnosis of GC and may therefore aid the clinician in the early detection of malignancy. In a prospective study by Tatsuat et al. [10], the frequency of false negative gastric wall biopsies in advanced gastric tumors was found to be 5.7%. The obtained results were negative because this type of tumor tissue is typically covered with gastric mucosa, and there is no apparent ulcer tissue. As a result, the biopsy is very small and superficial. Similarly, the two gastric wall biopsies performed in our case were not diagnosed as malignant as there was no obvious ulcer tissue [10].

Secukinumab is a humanized anti-IL-17A monoclonal antibody indicated for psoriasis treatment. It is indicated in moderate-to-severe psoriasis cases, psoriatic arthritis, and axial spondyloarthritis. It shows rapid responses and a safe profile in all psoriatic manifestations [11]. Although a recent case-control study in psoriasis suggested a possible increased risk of malignancy in patients using anti-TNF-alfa blockers for more than 12 months [12], studies with secukinumab failed to show an increased risk of malignancy [13, 14]. In a multicenter study of secukinumab using real-life data, 42 patients with psoriasis and a history of malignant diagnosis did not develop recurrence

or progression during a mean 56-week secukinumab treatment period [15]. In our case, we did not consider the malignancy risk due to secukinumab use because the patient had taken secukinumab for only five weeks and the treatment had been completed very recently.

The patient reported that he had experienced skin eruptions similar to psoriasis approximately 10 months before the diagnosis of GC. In fact, many dermatological paraneoplastic syndromes tend to occur as a prodrome of the underlying malignancy [16]. The severity of psoriasis in our patient was graded as a severe disease (PASI score 15) according to the clinical picture. There was no significant change in skin appearance after using topical glucocorticoids and acitretin, which is the standard treatment of psoriasis according to current guidelines in German-speaking countries [17]. Adalimumab, an anti-TNF agent, was used only for a short time. As a consequence of that ineffective treatment, our patient discontinued the therapy. After receiving 5 doses of secukinumab when the disease started to flare up again during treatment he was diagnosed with metastatic occult GC. Interestingly, within 3 months of starting chemotherapy, the lesions disappeared without any specific treatment after induced remission of gastric cancer under cytotoxic therapy. Although not confirmed, the close association between the development of lesions and cancer tumor burden is highly suggestive of paraneoplastic EP in this case. It is expected that any form of psoriasis, whether paraneoplastic or not, will improve with cytotoxic chemotherapy.

In our case, improvement of the disease was observed neither after glucocorticoid or after acitretin treatment, nor after anti-tnf and biological agents. Moreover, different temporal aspects of the disease support the hypothesis of paraneoplastic genesis. The first manifestations of EP were closely temporally related to the first diagnosis of GC. Moreover, during the first GC remission, EP also remained in remission without the need for any specific treatment.

Conclusions

Our patient's diagnosis of metastatic occult GC occurred concurrently with a severe, new, and atypical development of EP. Whether the two conditions occurred independently as coincidental events or as a paraneoplastic syndrome with related pathogenesis remains to be established, and additional reports may be helpful to elucidate if there is a connection between these conditions. We believe that EP may be a paraneoplastic syndrome associated with malignant disorders and therefore such a possibility should be considered in the treatment of these patients.

Article Information and Declarations

Ethics statement

Written informed consents were obtained from patient.

Author contributions

A.F.G.: conception, data collection, writing, editing and approval of the final draft; M.Araz: conception, data collection, editing and approval of the final draft; Fatih Kılıç: study design, writing, editing and approval of the final draft; O.Y.: study design, editing and approval of the final draft; M.U.: writing, editing; M.K.E.: editing and approval of the final draft; Fahriye Kılınç: data collection; M.Artaç: editing and approval of the final draft.

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Conflict of interest

The authors declare no conflict of interest.

Supplementary material

None.

References

1. Tomasini C, Aloi F, Solaroli C, et al. Psoriatic erythroderma: a histopathologic study of forty-five patients. Dermatology. 1997; 194(2): 102–106, doi: 10.1159/000246075, indexed in Pubmed: 9094455.
2. Gethi.org. Madrid: Grupo Español Tumores Huérfanos e Infrecuentes (GETHI). http://www.gethi.org/Portals/0/libro_digital_oncologia-V2.pd.
3. Mistry N, Gupta A, Alavi A, et al. A Review of the Diagnosis and Management of Erythroderma (Generalized Red Skin). Adv Skin Wound Care. 2015; 28(5): 228–236, doi: 10.1097/01.asw.0000463573.40637.73, indexed in Pubmed: 25882661.
4. Prizment AE, Alonso A, Folsom AR, et al. Association between psoriasis and incident cancer: the Iowa's Women's Health Study. Cancer Causes Control. 2011; 22(7): 1003–1010, doi: 10.1007/s10552-011-9773-0, indexed in Pubmed: 21553077.
5. King LE, Dufresne RG, Lovett GL, et al. Erythroderma: review of 82 cases. South Med J. 1986; 79(10): 1210–1215, doi: 10.1097/00007611-198610000-00005, indexed in Pubmed: 2945258.
6. Chen SX, Hinds BR, Goodman AM, et al. Erythrodermic Psoriasis in a Man with Monoclonal B-cell Lymphocytosis. Cureus. 2017; 9(12): e1936, doi: 10.7759/cureus.1936, indexed in Pubmed: 29464143.
7. Li Y, Wen Y, You R, et al. Erythrodermic psoriasis precipitated by B-cell chronic lymphocytic leukemia. Dermatol Ther. 2021; 34(3): e14904, doi: 10.1111/dth.14904, indexed in Pubmed: 33611837.
8. Keighley MRB. Gastrointestinal cancers in Europe. Aliment Pharmacol Ther. 2003; 18 Suppl 3: 7–30, doi: 10.1046/j.0953-0673.2003.01722.x, indexed in Pubmed: 14531737.
9. Comella P, Franco L, Casaretti R, et al. Emerging role of capecitabine in gastric cancer. Pharmacotherapy. 2009; 29(3): 318–330, doi: 10.1592/phco.29.3.318, indexed in Pubmed: 19249950.
10. Tatsuta M, Iishi H, Okuda S, et al. Prospective evaluation of diagnostic accuracy of gastrofiberscopic biopsy in diagnosis of gastric cancer. Cancer. 1989; 63(7): 1415–1420, doi: 10.1002/1097-0142(19890401)63:7<1415::aid-cncr2820630731>3.0.co;2-9.
11. Gottlieb AB, Deodhar A, Mcinnes IB, et al. Long-term safety of secukinumab in patients with moderate-to-severe plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis: integrated pooled

clinical trial and post-marketing surveillance data. Arthritis Res Ther. 2019; 21(1): 111, doi: 10.1186/s13075-019-1882-2, indexed in Pubmed: 31046809.
12. Lee JW, Jung KJ, Kim TG, et al. Risk of malignancy in patients with psoriasis: a 15-year nationwide population-based prospective cohort study in Korea. J Eur Acad Dermatol Venereol. 2019; 33(12): 2296–2304, doi: 10.1111/jdv.15783, indexed in Pubmed: 31287593.
13. Valenti M, Pavia G, Gargiulo L, et al. Biologic therapies for plaque type psoriasis in patients with previous malignant cancer: long--term safety in a single- center real-life population. J Dermatolog Treat. 2022; 33(3): 1638–1642, doi: 10.1080/09546634.2021.1886231, indexed in Pubmed: 33555951.
14. Bellinato F, Gisondi P, Maurelli M, et al. IL-17A inhibitors in patients with chronic plaque psoriasis and history of malignancy: A case series with systematic literature review. Dermatol Ther. 2021; 34(2): e14889, doi: 10.1111/dth.14889, indexed in Pubmed: 33595861.
15. Pellegrini C, Esposito M, Rossi E, et al. Secukinumab in Patients with Psoriasis and a Personal History of Malignancy: A Multicenter Real-Life Observational Study. Dermatol Ther (Heidelb). 2022; 12(11): 2613–2626, doi: 10.1007/s13555-022-00797-9, indexed in Pubmed: 36169883.
16. Pelosof LC, Gerber DE. Paraneoplastic syndromes: an approach to diagnosis and treatment. Mayo Clin Proc. 2010; 85(9): 838–854, doi: 10.4065/mcp.2010.0099, indexed in Pubmed: 20810794.
17. Nast A, Altenburg A, Augustin M, et al. Deutsche S3-Leitlinie zur Therapie der Psoriasis vulgaris, adaptiert von EuroGuiDerm - Teil 2: Therapiemonitoring, besondere klinische Situationen und Komorbidität. J Dtsch Dermatol Ges. 2021; 19(7): 1092–1117, doi: 10.1111/ddg.14507_g, indexed in Pubmed: 34288473.