Development of B-cell non-Hodgkin lymphoma in a Patient of untreated Psoriasis Vulgaris: A case report and Literature Review

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Abstract

Psoriasis is a chronic skin disease. The frequency of non-Hodgkin lymphoma among psoriasis patients has dramatically increased globally in recent decades. This is a male patient of chronic psoriasis vulgaris which is not treated for about 15 years ago, he is discovered accidently of having elevated white blood cells count (WBC), after routine investigations done for him due to slight feeling of fatigue and fever. The case was investigated to identify the cause of elevated WBC in the blood, and after complete work up, he is diagnosed as a case of psoriasis vulgaris developing B cell non-Hodgkin lymphoma. The objective of this case report is to inform dermatologist and physicians about the risk of developing malignancies in psoriasis to facilitate early detection and treatment. This study reviewed literature regarding the development of lymphoproliferative cancers in psoriasis.

Keywords: psoriasis vulgaris, lymphoma, B cell non-Hodgkin lymphoma.

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تطور ليمفوما الخلايا البائية غير هودجكينية لدى مريض مصاب بالصدفية الشائعة غير المعالجة: تقرير حالة ومراجعة للأبحاث

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الملخص:

يعتبر مرض الصدفية من الأمراض الجلدية المزمنة. يوجد تزايد عالمي في ظهور حالات سرطان الغدد الليمفاوية لدي المرضى المصابين بالصدفية في العقود الحديثة. ولدينا حالة من تلك الحالات وهو شخص ذكر وكبير في السن مصاب بمرض الصدفية في الجلد لم يتم علاجها لمدة خمسة عشر سنة وتم إكتشاف مصادفة ارتفاع عدد كرات الدم البيضاء أثناء فحص روتيني عند شعوره بتعب وحمى في الجسم .بعد ذلك خضع المريض لكافة الفحوصات والاشعة والعينات اللازمة من الدم والجلد وتم أكتشاف إصابته بسرطان الغدد الليمفاوية المسمي بنوع غير الهودجكين (بي). الهدف من هذا البحث الذي يدور حول سرطان الغدد الليمفاوية وظهورها في مرضى الصدفية وكذلك الهدف من نشر هذه الحالة هو تنبيه أطباء الجلدية وأطباء العموم حول إمكانية ظهور أورام الغدد الليمفاوية وغيرها من الاورام في مرضى الصدفية لذلك يجب المتابعة والتشخيص المبكر لأخذ العلاج في وقت مبكر. وخلال هذه الدراسة تم البحث عن حالات وأبحاث مماثلة في العالم حول ظهور الأورام وسرطان الغدد الليمفاوية وكذلك سبب ظهوره في مرضى صدفية الجلد.

الكلمات المفتاحية: الصدفية الشائعه ، الليمفوما، الليمفوما البائيه غير الهودجكينية.

Introduction:

Psoriasis is a prevalent and persistent skin disease. Psoriasis affects a wide range of body surface areas, from mild disease in 80-85% of patients to more severe skin involvement in 15-20% of individuals (1). Research indicates that individuals with psoriasis have an elevated chance of acquiring malignancies, particularly those with severe manifestations of the disease (2-3). Studies published demonstrates that the patients with psoriasis are at a greater risk of developing non-Hodgkin lymphoma (NHL) (4), and despite its dramatic worldwide rise in incidence, the etiology remains largely unexplained (5-6). Antigen-driven lymphocyte proliferation in psoriasis-induced chronic inflammation could be one explanation for the rise in these cancers (antigenic stimulation theory) (7).

Due of the increased incidence of lymphoma among psoriasis patients, this case report aimed to aware dermatologist and physicians about this potential comorbidity during clinical diagnosis of cases of psoriasis whose are untreated for a long duration.

Case Presentation:

Sixty years old male patient, driver, not hypertensive nor diabetic, and no history of any drug intake, he came to my private clinic with history of psoriasis for 20 years ago, not under treatment for 15 years and before that he was treated with only topical creams and ointments. During physical examination of the patient, there are silvery plaques and scattered in the scalp, trunk and upper and lower limb, this type is called psoriasis vulgaris (Figure 1), chest, back and abdomen. There are deformities seen in some joints of the hands. Lastly the patient gave history of fever and fatigue and the general practitioner request for him complete blood cells (CBC) test, which revealed an increased WBC count. We also repeated the test and requested more investigations to get the real cause of increased WBC count and to reach the final diagnosis.

The results revealed an increased WBC count more than 44 thousands (92% are lymphocytes), and slight decrease in platelets, elevated ESR, and elevated S. uric acid. Ultrasonography revealed; mild bright hepatomegaly, marked splenomegaly, and cervical, axillary and inguinal lymphadenopathy. Blood film was requested and showed; normocytic normochromic cells, lymphocytic leukocytosis (the majority are small mature with many smear cells), and mild thrombocytopenia.

Immunophenotyping on peripheral blood sample was ordered and showed: lymphocyte constitutes about 85% of the cells, the majority of these lymphocytes are monoclonal B-cells expressing CD19, HLADR, CD79b, CD20, CD22, FMC7, CD52, CD11c with lambda light chain restriction, these lymphocyte as negative for CD5, CD10, CD25, CD38, CD23, and CD103, these result was consistent with that of B-cell Non-Hodgkin lymphoma. Skin biopsy from the skin lesions was taken for histopathological evaluation and the result was confirming of psoriasis vulgaris with no evidence of mycosis fungoids (Figure 2). The patient underwent chemotherapy treatment sessions for the B-cell Non-Hodgkin lymphoma, in addition to topical treatment for psoriasis, there is improvement of the condition, and he was advised to follow up regularly.

Discussion:

Psoriasis is a chronic, inflammatory, and proliferative disease of the skin and joints characterized by a typical relapsing and remitting pattern, affecting around 1%-2% of the population (3-8). In psoriasis, there is an increased activity of T cells, antigen-presenting (e.g., dendritic) cells, and Th-1 cytokines these represent the hallmarks of the aberrant immune response that underlies the pathophysiology of this disease (9). Additionally, some researchers have shown that psoriasis patients had higher B cell activity, indicating widespread immunological activation (10-12). This immunologic nature of psoriasis has sparked worries that its pathophysiology may be linked to an elevated risk of lymphoma as has been shown for other Th-1 mediated diseases like rheumatoid arthritis (13-14).

According to a systematic meta-analysis study conducted by Pouplard *et al.* (2013), individuals with psoriasis were more likely to develop lymphoma, keratinocyte cancer, and some solid malignancies (15). Male patients showed the greatest increase in risk (2, 16).

Lymphoma is a type of immune system malignant tumor that is originating from the lymph nodes and extralymphatic tissues. Its incidence is believed to be related to lymphocytes proliferation and differentiation during immune responses (17). Non-Hodgkin's lymphoma (NHL) and Hodgkin's lymphoma (HL) are the two main types of lymphomas (18). Non-Hodgkin's lymphoma arises from the division of mature B, T, and natural killer (NK) cells into many clones at various phases of development (19). Approximately 90% of all lymphomas are NHL (20–21). B cell origin accounts for around 85% of NHL (22). NHL may be associated with a number of variables, including infections, environmental factors, immunodeficiency states, and chronic inflammation (23).

It is believed that immunosuppressive therapy and chronic inflammation are the causes of psoriasis patients' elevated risk of lymphoproliferative cancers (24).

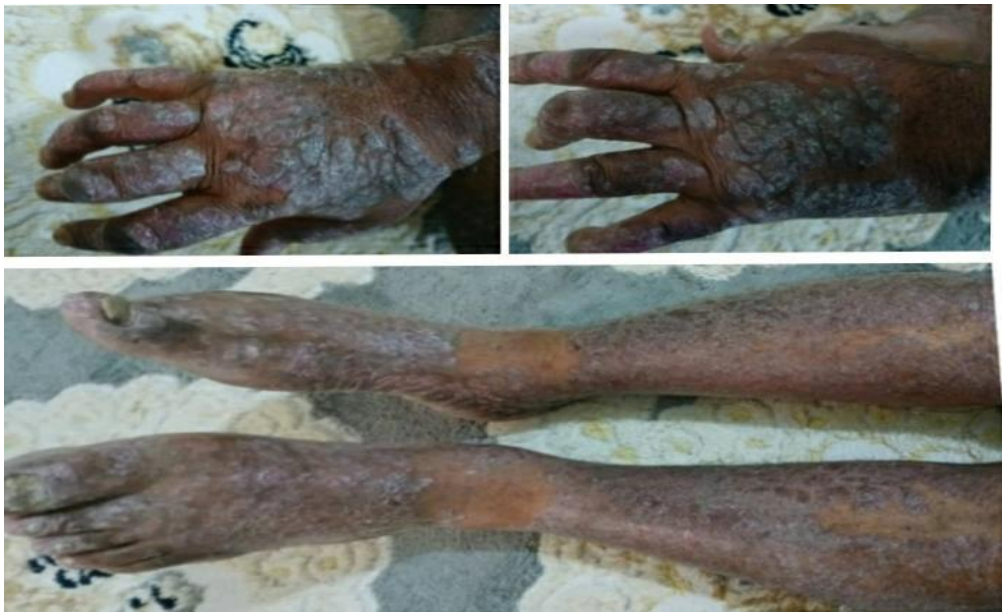

Figure 1: Silvery scaly psoriatic plaques in the upper and lower extremities with deformities in some finger joints.

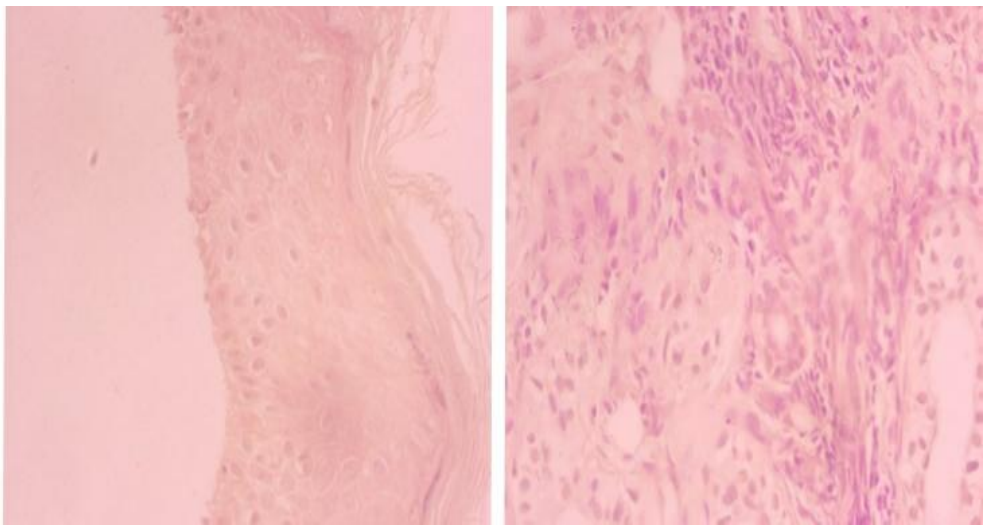

Figure 2: Microscopic examination revealed the presence of thick parakeratosis, mild elongation of the rate ridges, spongiosis in the upper spinous layer and loss of the granular layer. No evidence of mycosis fungoids could be detected.

Systemic treatments such methotrexate and cyclosporine may be used to treat people with severe psoriasis; however, these drugs have been linked to the development of lymphoma in these patients (25–27). According to a cohort research conducted by Margolis *et al.*, people with psoriasis who took systemic therapy had a greater overall risk of lymphoproliferative malignancies than those who did not (2).

It has been found by several earlier studies that psoriatic patients had a higher risk of NHL (28–29). Yuan *et al.* a meta-analysis discovered that patients with psoriasis had a greater likelihood of developing NHL after an average of ten years of follow-up (4). Although the exact relationship between NHL and psoriasis is unknown, earlier research suggested that tumor necrosis factor-alpha (TNF-α) may be a major player in the pathophysiology of both conditions. Psoriasis patients had higher serum levels of cytokines, and TNF-alpha promotes keratinocyte proliferation and cytokine production (30-31). B-cell activating factor, which is a member of the TNF superfamily, has been demonstrated in numerous studies to preferentially activate B lymphocytes and encourage their proliferation (32).

It's interesting to note that a case-control research done by Tavani *et al*, revealed that older psoriasis patients might be more susceptible to lymphoma than younger ones (33). Also studies showed that the risk of developing NHL were 1.8 times higher for adults with moderate-to-severe psoriasis and 1.5 times higher for those with mild psoriasis (34-35).

According to this case study and the literature analysis, it is critical to monitor psoriatic patients in order to detect any non-Hodgkin lymphoma or other cancers early on.

References:

1. Gelfand JM, Wang X, Qing L, Neimann AL, Weinstein R, Margolis D, *et al.* Epidemiology and treatment patterns of psoriasis in the general practice research database (GPRD). Pharmacoepidemiol Drug Saf 2005; 14: S23.
2. Margolis D, Bilker W, Hennessy S, Vittorio C, Santanna J, Strom BL. The risk of malignancy associated with psoriasis. Arch Dermatol 2001; 137: 778-783.
3. Quéreux G, Renaut JJ, Peuvrel L, Knol AC, Brocard A, Dréno B. Sudden onset of an aggressive cutaneous lymphoma in a young patient with psoriasis: role of immunosuppressants. Acta Derm Venereol 2010; 90: 616-620.
4. Yuan HZ, Yuan T, Jiang C. Incidence of non-Hodgkin lymphoma among patients with psoriasis: a meta-analysis. International Journal of Dermatology and Venereology 2018; 1(1); 21-23.
5. Ekström SK, Vajdic CM, Falster M, Engels EA, Martínez-Maza O, Turner J, *et al.* Autoimmune disorders and risk of non-Hodgkin lymphoma subtypes: a pooled analysis within the InterLymph Consortium. Blood 2008; 111: 4029-4038
6. Oh JK, Weiderpass E. Infection and cancer: global distribution and burden of diseases. Ann Glob Health 2014; 80: 384-392.
7. Soderberg KC, Jonsson F, Winqvist O, Hagmar L, Feychting M. Autoimmune diseases, asthma and risk of haematological malignancies: a nationwide case-control study in Sweden. Eur J Cancer 2006; 42: 3028–33
8. Parisi R, Symmons DP, Griffiths CE, Ashcroft DM; Identification and Management of Psoriasis and Associated ComorbidiTy (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol. 2013; 133(2):377-85. doi: 10.1038/jid.2012.339. PMID: 23014338.
9. Krueger JG, Bowcock A. Psoriasis pathophysiology: current concepts of pathogenesis. Ann Rheum Dis 2005; 64(Suppl 2): ii30–6.
10. Muller KM, Rocken M, Joel D, Bonnefoy JY, Saurat JH, Hauser C. Mononuclear cell-bound CD23 is elevated in both atopic dermatitis and psoriasis. J Dermatol Sci 1991; 2: 125–33.
11. Jeffes EW III, Lee GC, Said S, Sabahi M, McCullough JL, Herrod R, *et al.* Elevated numbers of proliferating mononuclear cells in the peripheral blood of psoriatic patients correlate with disease severity. J Invest Dermatol 1995; 105: 733–8.
12. Mahmoud F, Abul H, al Saleh Q, Hassab-el Naby H, Kajeji M, Haines D, *et al.* Elevated B-lymphocyte levels in lesional tissue of non-arthritic psoriasis. J Dermatol 1999; 26: 428–33
13. Gridley G, McLaughlin JK, Ekbom A, Klareskog L, Adami HO, Hacker DG, *et al.* Incidence of cancer among patients with rheumatoid arthritis. J Natl Cancer Inst 1993; 85: 307–11.
14. Ekstrom K, Hjalgrim H, Brandt L, Baecklund E, Klareskog L, Ekbom A, *et al.* Risk of malignant lymphomas in patients with rheumatoid arthritis and in their first-degree relatives. Arthritis Rheum 2003; 48: 963-770.

15. Pouplard C, Brenaut E, Horreau C, *et al.* Risk of cancer in psoriasis: a systematic review and meta-analysis of epidemiological studies. J Eur Acad Dermatol Venereol 2013; 27(suppl 3): 36-46.
16. Brauchli YB, Jick SS, Miret M, Meier CR. Psoriasis and Risk of Incident Cancer: An Inception Cohort Study with a Nested Case–Control Analysis. Journal of Investigative Dermatology 2009; 129: 2604–2612.
17. Campo E, Swerdlow SH, Harris NL, *et al.* The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. Blood 2011; 117(19):5019-5032.
18. Fisher SG, Fisher RI. The epidemiology of non-Hodgkin's lymphoma. Oncogene 2004; 23: 6524-6534.
19. Swerdlow SH, Campo E., Pileri SA. *et al.* The 2016 Revision of the World Health Organization Classification of Lymphoid Neoplasms, Blood. 2016; 127(20): 2375–2390.
20. Alsaadi M, Khan MY, Dalhat MH, Bahashwan S, Khan MU, Albar A, Almehdar H, Qadri I. Dysregulation of miRNAs in DLBCL: Causative Factor for Pathogenesis, Diagnosis and Prognosis. Diagnostics (Basel). 2021; 11(10):1739. doi: 10.3390/ diagnostics11101739. PMID: 34679437; PMCID: PMC8535125.
21. Arita A., McFarland DC, Myklebust JH, *et al.* Signaling Pathways in Lymphoma: Pathogenesis and Therapeutic Targets, Future Oncology 2013; 9(10): 1549-1571,
22. Bierman PJ, Harris NL, Armitage JO. Non-Hodgkin's lymphoma. In: Cecil textbook of medicine (Goldman L, Ausiello D, eds), 22nd edn, Philadelphia, PA: WB Saunders Co, 2004: 1174-1184.
23. Rajendran R, Sivapathasundharam B, editors. Benign and malignant tumors of oral cavity. In: Shafers Textbook of Oral Pathology. 6th ed. Netherlands: Elsevier; 2009. p. 173-178.
24. Gelfand JM, Shin DB, Neimann AL, Wang X, Margolis DJ, Troxel AB. The risk of lymphoma in patients with psoriasis. J Invest Dermatol 2006; 126(10): 2194-2201.
25. Cliff S, Pettengell R, Gharge S, Marsden RA. B-cell lymphoma developing in a patient on cyclosporin for recalcitrant psoriasis. Br J Dermatol 1999; 140: 763–765.
26. Mahe E, Descamps V, Grossin M, Fraitag S, Crickx B. CD30+ T-celllymphoma in a patient with psoriasis treated with ciclosporin and infliximab. Br J Dermatol 2003; 149:170173.
27. Lelievre JD, Sacre K, Adle-Biassette H, Molinier-Frenkel V, Gaulard P, Papo T. Epstein-Barr virus-associated lymphoproliferative disease after long-standing cyclosporine therapy for psoriasis: a case of spontaneous regression. J Am Acad Dermatol 2005; 52: 24-27.
28. Hannuksela-Svahn A, Pukkala E, Läärä E, *et al.* Psoriasis, its treat- ment, and cancer in a cohort of Finnish patients. J Invest Dermatol 2000; 114(3): 587-90.,
29. Fallah M, Liu X, Ji J, Försti A, Sundquist K, Hemminki K. Autoimmune diseases associated with non-Hodgkin lymphoma: a nationwide cohort study. Ann Oncol. 2014; 25(10):2025-2030. doi: 10.1093/annonc/mdu365. PMID: 25081899.
30. Pietrzak A T, Zalewska A, Chodorowska G, *et al.* Cytokines and anticytokines in psoriasis. Clinica Chimica Acta 2008; 394(1-2): 7-21.
31. Hui E, Xu A, Hong BY, *et al.* Obesity as the common soil of non-alcoholic fatty liver disease and diabetes: Role of adipokines. J Diabetes Investig 2011; 4(5): 413-425.
32. Moore PA, Belvedere O, Orr A, *et al.* BLyS: member of the tumor necrosis factor family and B lymphocyte stimulator. Science 1999; 285, 260-263.
33. Tavani A, La Vecchia C, Franceschi S, Serraino D, Carbone A. Medical history and risk of Hodgkin's and non-Hodgkin's lymphomas. Eur J Cancer Prev 2000; 9:59-64.
34. Chiesa FZC, Shin DB, Ogdie BAA, Gelfand JM. The risk of cancer in patients with psoriasis: a population-based cohort study in the health improvement network. JAMA Dermatol 2016; 152 (3):282-290.
35. Diaz MJ, Haq Z, Tran JT, Abdi P, Motaparthi K, Grant-Kels JM, *et al.* Psoriasis and non-Hodgkin's lymphoma in a diverse sample of U.S. adults: a propensity matched case-control study. J Am Acad Dermatol. 2024;91(1):104-107. doi: 10.1016/j.jaad.2024.02.040. PMID: 38452818.

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