Journal of Pathology of Nepal (2023) Vol. **13**, 2114 -2118

Journal of
PATHOLOGY
of Nepal
www.acpnepal.com

Case Report

Leukemia cutis: A rare manifestation of underlying primary plasma cell leukemia

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Keywords:

Leukaemia cutis; Leukemia; Multiple myeloma; Plasma cell; Plasmacytoma

ABSTRACT

Plasma cell leukaemia is the rarest yet most aggressive plasma cell disorder characterized by a malignant proliferation of plasma cells in the blood and bone marrow. Leukaemia cutis includes cutaneous manifestation of any type of leukaemia, and is defined as skin infiltration by malignant leukocytes or their precursors, resulting in clinically detectable cutaneous lesions. Plasma cell leukaemia cutis is a rare clinical presentation with an adverse prognosis which makes the index case an unusual entity. We hereby report a case of primary Plasma cell leukaemia, who presented with multiple cutaneous scalp nodules. Fine-needle aspiration cytology performed on these scalp nodules revealed cellular smears exhibiting both mature and immature plasma cells dispersed singly and arranged in small clusters. The total leucocyte count was 25,800/cu mm, with differential count of 18% polymorphonuclear cells, 20% lymphocytes, and 62% abnormal plasmacytoid cells. The diagnosis of primary PCL with cutaneous involvement was subsequently rendered through histology and immunophenotyping.

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Received : December 20th 2022; **Accepted :** April 22th 2024

Citation: Dixit N,Trivedi S,Bansal VK,Jain P, Raina A, Agarwal S. Leukemia cutis: A rare manifestation of an underlying primary plasma cell leukemia. J Pathol Nep 2023;13(2): 2114-8. DOI: 10.3126/jpn.v13i2.50422

INTRODUCTION

Plasma cell leukaemia (PCL) is the rarest yet most aggressive plasma cell disorder characterized by a malignant proliferation of plasma cells in the blood and bone marrow.[1] PCL is defined by an absolute plasma cell (PC) count of more than 2×10^9/L in the peripheral blood (PB) or more than 20% circulating clonal PCs.[2] It accounts for around 2-4% of all plasma cell malignancies.[3] Primary PCL (p PCL) presents with leukemic phase at initial diagnosis in the absence of a prior history of multiple myeloma (MM), whereas secondary PCL (sPCL) manifest as leukemic

progression in the background of pre-existing or concurrent MM. As per historical data, 60-70% cases are p PCL, and approximately 40% cases are reported as s PCL.[1,4] However, with the availability of more effective and targeted therapies, the incidence of s PCL is rising due to improved survival and clonal selection over time.[4]

Leukaemia cutis includes the cutaneous manifestations of any type of leukaemia and is defined as skin infiltration by malignant leukocytes or their precursors, resulting in clinically detectable cutaneous lesions. PCL cutis is a rare clinical presentation with an adverse prognosis.[5] We hereby report a case of p PCL, who presented with multiple cutaneous scalp nodules.

CASE REPORT

A 41-year-old female was admitted to our hospital for evaluation of fever, lethargy, and severe lower back pain of two months duration along with multiple scalp nodules for 4 months. Her previous medical history was unremarkable. Systemic examination revealed only moderate pallor. Cutaneous examination revealed multiple firm, erythematous, non-tender, and smooth nodules ranging in size from 9 mm to 1.8 cm in diameter.

FNAC performed on these scalp nodules revealed cellular smears exhibiting both mature and immature plasma cells dispersed singly and arranged in small clusters against the haemorrhagic background, binucleate and multinucleate forms were also present along with occasional plasmablasts (fig. 1). Plasma cells showed prominent eccentric nuclei, condensed nuclear chromatin with some showing prominent nucleoli, basophilic cytoplasm, and perinuclear hof, while plasmablasts cells had a high N: C ratio, fine reticular nuclear chromatin, prominent nucleoli without perinuclear hof.

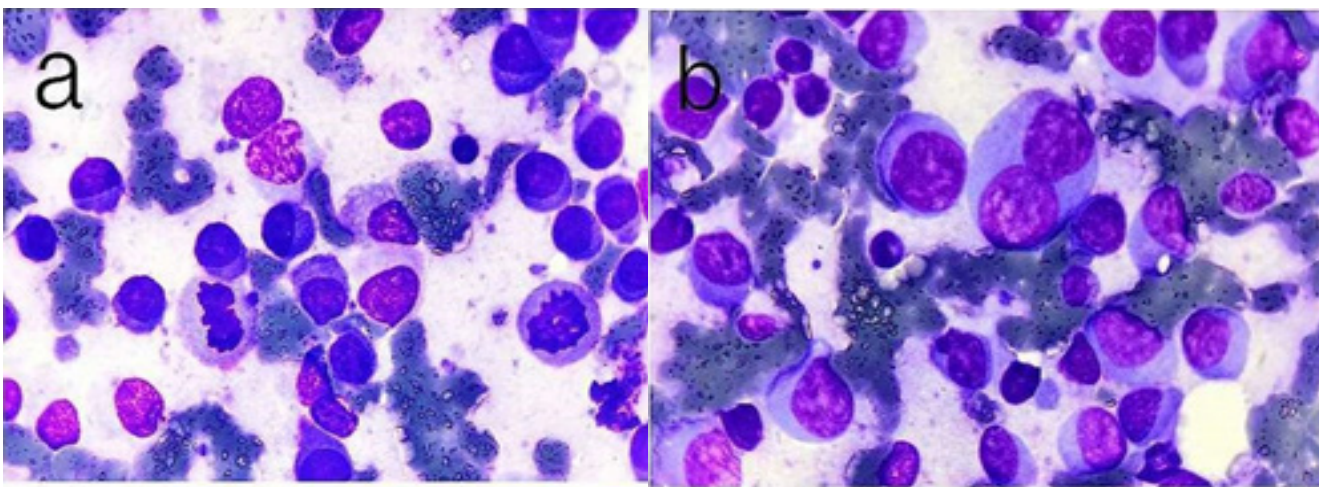

Figure 1: *FNAC of a skin lesion showing mature and immature plasma cells including atypical mitotic figures in (a) and binucleate cell in (b) (MGG, ×100)*

Her hemogram performed revealed haemoglobin of 7.2 gm /dl with normocytic normochromic red blood cells (RBCs) and platelet count of 60,000 /cu mm. Her total leucocyte count was 25,800 /cu mm, with a differential count of 18 % polymorphonuclear cells, 20% lymphocytes, and 62% abnormal plasmacytoid cells including plasmablasts along with rouleaux formation in peripheral smear (fig. 2).

DOI : 10.3126/jpn.v13i2.50422

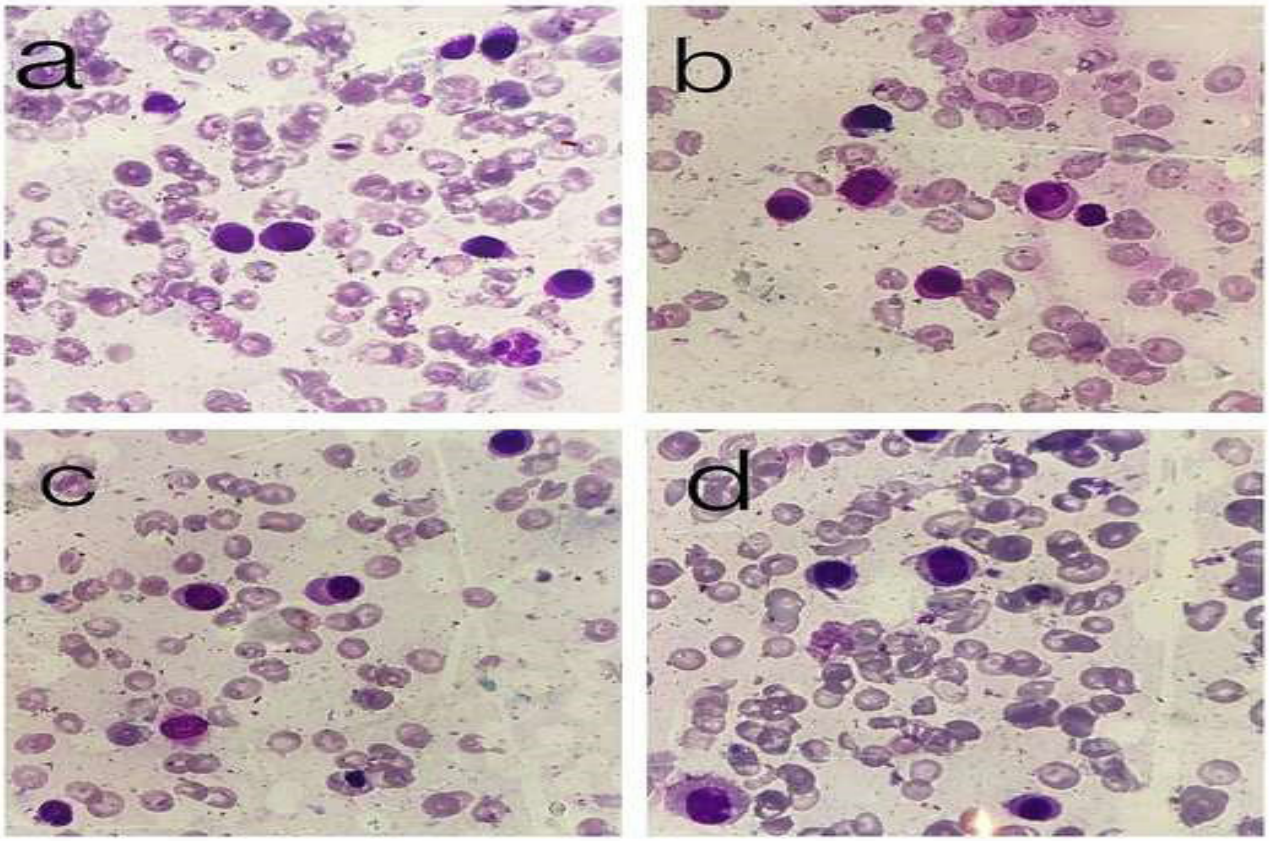

Figure 2: *Peripheral blood smears showing abnormal plasmacytoid cells including immature plasma cells and plasmablasts (MGG, × 40)*

Bone marrow aspiration was hyper cellular revealing 62% plasma cells including plasmablasts. Bone marrow trephine biopsy showed marked infiltration by atypical plasma cells comprising >50% of total bone marrow cellularity with suppression of all three normal hematopoietic lineages (fig.3). The neoplastic cells were immunoreactive for CD138 and Lambda light chain antibodies and nonreactive to CD56, CD45, CD3, CD19, kappa light chain, and CK AE1/AE3 (fig. 4). Flow cytometric analysis of the marrow revealed the cells to be positive for CD138, CD38, and lambda light chain and negative for CD19, CD45, CD56, and kappa light chain. Serum protein electrophoresis and immunofixation revealed IgG lambda paraproteinemia of 48 g/L in the gamma region with severe immunoparesis.

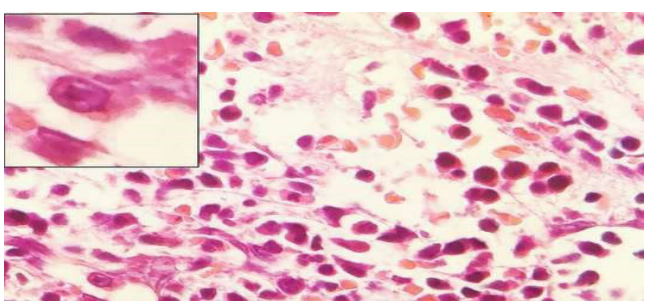

Figure 3: *Bone marrow biopsy showing a diffuse infiltration by atypical plasma cells. Inset shows a plasmablast having a central large nucleus, high N/C ratio, reticular chromatin, and prominent nucleoli. (H and E stain , × 40)*

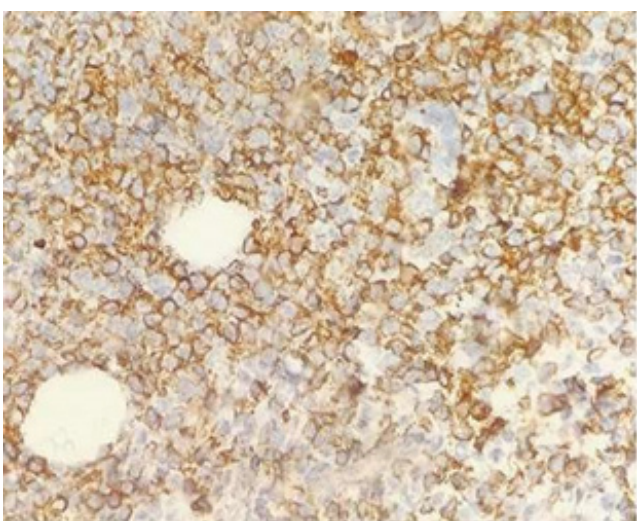

Figure 4: *Cells showing diffuse positivity for CD 138 (IHC, ×40)*

Punch biopsy from scalp nodules showed diffuse infiltration of plasmacytoid cells in the reticular dermis, with remarkable sparing of papillary dermis and epidermis. The neoplastic cells were monotonous in appearance with occasional cells showing distinctive features of myeloma cells. The immunohistochemical (IHC) findings were similar to those mentioned above for bone marrow biopsy. Based on the above findings, the diagnosis of primary plasma cell leukaemia with cutaneous involvement was rendered.

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Biochemical parameters were: blood urea 102 mg/dl, serum creatinine: 1.6 mg/dl, serum calcium and phosphorus: 9.8 and 3.5 mg/dl, total protein: 7.1 gm/dl with albumin: globulin ratio of 1.32 respectively. Serum bilirubin and liver enzymes were within normal limits. Non-contrast computed tomography (NCCT) abdomen and pelvis revealed lytic lesions in multiple vertebrae and iliac bone, ill-defined hypodense areas in the right lobe of liver probably secondaries, and, mild splenomegaly. The patient is currently on systemic chemotherapy and recuperating now. The patient provided informed consent to the publication of this case.

DISCUSSION

The present case described above had leukaemia cutis associated with p PCL. Leukaemia cutis is the infiltration of malignant leukocytes or their precursors into the epidermis, dermis, or subcutaneous tissue, developing a clinically recognizable cutaneous lesion. Leukaemiacutis usually occurs in association with systemic leukaemia, but can also appear abruptly, prior to leukemic cells showing up in peripheral blood or bone marrow. It is frequently seen in patients suffering from acute myelogenous leukemia, but can also occur in association with other haematological malignancies.[6] Accurate diagnosis of leukaemia cutis has immense prognostic implications as it can establish a diagnosis in cases where leukaemia cutis is the predecessor of systemic leukemic development. It usually portends a poor prognosis with the survival of fewer than 12 months after being diagnosed.[6, 7]

Plasma cell neoplasms encompass the following entities-classic MM, extra medullary plasmacytoma without MM, solitary plasmacytoma of bone, and PCL. PCL accounts for 2-4% of patients with MM and 0.3% of leukemias.[3] It is an unusual and aggressive disease that can occur de novo (p PCL) or as a secondary leukemic transformation of a formerly diagnosed MM (s PCL).[4]

p PCL has some distinct biological and clinical features compared to MM. The average age at diagnosis of p PCL is 61 years, about 10 years younger than the mean age of detection in a typical MM patient.[8] p PCL has a higher prevalence of significant anaemia, thrombocytopenia, hypocalcaemia, renal impairment, elevated lactate dehydrogenase, and β2-microglobulin, along with pronounced bone marrow (BM) plasma cell infiltration. Light chain and nonsecretory subtypes are also more frequently noted in p PCL.[4] p PCL tend to invade extra medullary sites more commonly (lymphadenopathy, hepatomegaly, splenomegaly, skin, pleural effusion, and central nervous system involvement) in contrast to MM which shows predominant bone involvement resulting in osteolytic lesions, bony tenderness, and pathological fractures.[9] The immunophenotypic expression patterns found in p PCL are distinct from MM. Both express CD38 and CD138, however, p PCL cells exhibit increased prevalence of CD20, CD28, CD27, and CD45 and lower CD56, CD117, CD9, and HLA-DR as opposed to MM. Extra medullary involvement in p PCL may be attributed to tumor cells showing lower expression of adhesion molecules (CD56, LFA-1, LFA-3, VLA-5), which impairs the confinement of PCs within the BM.[4]

Although p PCL is known to involve extra medullary sites more commonly, cutaneous infiltration of p PCL is a very rare phenomenon. Leukaemia cutis lesions in patients with underlying PCL are commonly described as extra medullary plasmacytomas of the skin or cutaneous plasmacytomas.[10] Plasmacytomas are the clonal expansion of PCs in tissues that can be extra osseous or extra medullary.[6] Cutaneous plasmacytomas constitute around 4% of all extra medullary sites of plasmacytomas. These lesions (solitary or multiple) may occur simultaneously with soft-tissue plasmacytomas involving the other organs or be a part of the clinical manifestations of MM.[10] The cutaneous plasmacytomas usually presents clinically as single or multiple, slowly growing violaceous dermal or subcutaneous nodules with no predisposition for any specific site.[6] The differences between s PCL and p PCl are described in Table No. 1.

Table No.1: Comparison between Primary Plasma Cell leukemia and Secondary Plasma Cell Leukaemia

Type of Plasma cell dyscrasia	Primary Plasma Cell leukemia	Secondary Plasma Cell Leukaemia
Incidence	60% of PCL cases.[1]	1% of MM patients, 40% of PCL cases[11]
Age/Sex of patients	M: F: 3:2[12] Median age :55 Years[3]	M: F: 3:2[12] Median age: 66Years3
Clinical Presentation	It is predecessor of MM. Prevalence of osteolytic lesions is 18%[12] Extramedullary deposits (Liver, Spleen, Lymph nodes) and bleeding tendencies.[13]	Extra medullary disease, bone marrow failure, advanced stage disease. Prevalence of osteolytic lesions & elevated LDH, β2-microglobulin and decreased serum albumin. is 53%[12,13] Untreated multiple myeloma may lead to sPCL within 20–22 months[9]
Laboratory Markers	Increased incidence of hypodiploidy, 17 p deletion, TP53 and DIS3 mutations, t(11;14), t(4;14) and t(14;16).[3]	--
Prognosis/Survival	11.2months[12]	1.3 months[12]

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PCL cutis can be a consequence of a phenomenon termed pathergy which is the development of skin lesions or ulcers at a previous site of trauma.[14] Locally immunocompromised cutaneous areas, resulting from burns, herpes zoster viral infections, recent surgeries, intramuscular injections, and trauma may also be a trigger for the establishment of the cutaneous leukemic infiltrates.[6]

The diagnosis of leukaemia cutis can prove to be challenging in the absence of established systemic leukaemia. In all cases, a rigorous correlation between clinical features, cyto-histopathological findings, and immunophenotyping is required. Regardless of prior history of leukaemia, a skin biopsy for pathology and tissue cultures along with immunohistochemical (IHC) stains or immunophenotyping must be performed in all suspected patients. Bacterial, fungal, and mycobacterial cultures should also be retrieved to exclude any possible infectious etiology.[7] A complete blood count and peripheral smear must be analysed to evaluate the abnormalities in cell counts (cytopenias usually seen) and the presence of circulating leukemic cells. A bone marrow biopsy is also imperative along with IHC, cytogenetics, and flowcytometry studies for the definitive diagnosis of systemic leukaemia.

The therapeutic management of plasma cell leukaemia cutis should be directed at eradicating the underlying systemic disease which may be accomplished by systemic chemotherapy, as well as local therapy such as radiation or surgery. Overall, the development of leukaemiacutis usually portends a poor prognosis.[7]

CONCLUSION

PCL is a rare plasma cell disorder characterized by a malignant proliferation of plasma cells in the blood and bone marrow. It can occur de novo or as a secondary leukemic transformation of a formerly diagnosed multiple myeloma. Leukaemia cutis associated with p PCL, as confirmed in our patient, is very rare and usually portends a poor prognosis. The diagnosis can prove to be challenging in the absence of established systemic leukaemia. In all the cases, a rigorous correlation between clinical features, cyto-histopathological findings, and immunophenotyping is required.

Conflict of Interest: None

REFERENCES

1. Pagano L, Valentini CG, De Stefano V, et al. Primary plasma cell leukemia: a retrospective multicenter study of 73 patients. Ann Oncol. 2011; 22(7): 1628-35. Crossref
2. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th edn. (WHO, 2017).
3. Swaminathan N, Varadi G. Secondary Plasma Cell Leukemia: A Case Report. Cureus. 2020; 12(6): e8693. Crossref
4. Tuazon SA, Holmberg LA, Nadeem O, Richardson PG. A clinical perspective on plasma cell leukemia; current status and future directions. Blood Cancer J. 2021; 11:23. Crossref
5. Ballester-Martínez MA, González-García C, Fleta-Asín B, Burdaspal-Moratilla A, SantónRoldán A, Jiménez-Gómez N, Martín-González MM, Olasolo P. Cutaneous nodules as a diagnostic clue in multiple myeloma. Am J Dermatopathol. 2013; 35: 377-80. Crossref
6. Demartinis NC, Brown MM, Hinds BR, Cohen PR. Leukemia Cutis Associated with Secondary Plasma Cell Leukemia. Cureus. 2017; 9(5): e1235. DOI:10.7759/cureus.1235 7.Cho-Vega JH, Medeiros LJ, Prieto VG, Vega F. Leukemia cutis. Am J ClinPathol. 2008; 129: 130–42. Crossref
7. Gundesen MT, Lund T, Moeller HEH, Abildgaard N. Plasma cell leukemia: definition, presentation, and treatment. CurrOncol Rep. 2019; 21(1): 8. Crossref
8. Ngu S, Asti D, Valecha G, Thumallapally N, Pant M, Bershadskiy A. Primary plasma cell leukemia: A case report and review of the literature. Clin Case Rep. 2019; 7: 1702–08. Crossref
9. Gupta R, Nath AK, Subbian M, Basu D, Hamide A, D'Souza M. Hemorrhagic Skin Nodules and Plaques: A Diagnostic Clue to Underlying Primary Plasma Cell Leukemia. Indian J Dermatol. 2016; 61(2): 203-05. Crossref
10. International Myeloma Working Group. Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders: a report of the International Myeloma Working Group. Br J Haematol. 2003;121:749–757.
11. Miguel Ángel Flores-Caballero, Dania Lizet Quintanilla-Flores, René Rodríguez-Gutiérrez; Secondary plasma cell leukemia in a patient with light chain multiple myeloma in post- chemotherapy remission phase. Journal of Applied Hematology. 2014;5(3):111-4. Website
12. Alessandra GM, Almeida JG, de Araujo RC, et al. Plasma Cell Leukemia Remains Like an Incurable Disease? A rare presentation of an aggressive case of secondary plasma cell leukemia. J Leuk 2015;3: 157. Crossref
13. Kim JE, Kim MY, Kim HO, Park YM. Plasma cell leukaemia cutis preferentially localized to recent puncture sites. Br J Dermatol. 2004; 151(1): 237-8. Crossref