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Sezary syndrome with peripheral neuropathy - A rare neuropathic syndrome

[1]Dr. Sanjay Kumar Kannaujia, Assistant Professor Department of Pathology, UPUMS, Saifai.

[2]Dr. Neha Yadav, Senior Resident,SGPGI, Lucknow.

[3]Dr. Hanuman Prasad, Assistant Professor, Department of Neurosurgery, UPUMS, Saifai.

[4]Dr. Sanjeev Kumar Singh, Professor Junior grade Department of Pathology, UPUMS, Saifai.

[5]Dr. Geeta Maurya, Associate Professor, Department of Pathology, UPUMS, Saifai.

[6]Dr. Seema Dayal, Professor Junior grade, Department of Pathology, UPUMS, Saifai.

Corresponding Author: Dr. Sanjeev Kumar Singh, Professor Junior grade Department of Pathology, UPUMS Saifai.

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Abstract

Sezary syndrome is a rare cause of generalized exfoliative dermatitis with peripheral neuropathy. It is the leukemic counterpart of mycosis fungoid is. It is a malignancy of $CD4^+$ central memory T lymphocytes. We report a rare case of Sezary syndrome with peripheral neuropathy in a 65 years old male who presented with complaints of increasing breathlessness, cough with expectoration of 8 months duration and symptoms of peripheral neuropathy and numbness in bilateral hand and feet from last 5 months. On examination patient was conscious and oriented to time place and person. His CNS examination was normal except sensory loss in bilateral hand and feet. He had multiple papules and plaques over the trunk and lower limbs, bilateral pedal edema and generalized lymphadenopathy involving axillary, cervical and inguinal nodes. A diagnosis of Sezary syndrome with peripheral neuropathy was made due to presence of characteristic of erythroderma, lymphadenopathy, circulating atypical lymphoid cells on blood films and immunophenotypic positivity for T helper subtype.

Keywords: Sezary syndrome, Peripheral neuropathy, Lymphadenopathy, Exfoliative dermatitis.

Introduction

Sezary syndrome is an uncommon form of cutaneous T cell lymphoma. It was first described by Besnier and Hallopeau as a severe variant of cutaneous T cell lymphoma[1]. It was later defined as a classical triad of pruritic erythroderma, lymphadenopathy and abnormal hyperconvulated monstrous cells in peripheral blood by Sezary and Bouvrain[2]. Males are most commonly

affected than females with male to female ratio of 2:1[3.] The most commonly affected age group is between 55 and 60 years of age[3,4]. The Co-occurrence of Sezary syndrome and peripheral neuropathy was first reported in 1978 by Bargman and Coupe[5]. The other case of Sezary syndrome and neurolymphomatosis was reported by Bezier etal[6].The etiology of Sezary syndrome is unclear, though environmental factors and retroviral (HTLV-1) infections have been suggested. It is characterized by monoclonal proliferation of neoplastic T helper cells with cerebriform nuclei (Sezary cells), with immunophenotyping showing typical positivity for CD4 and negativity for CD7 and CD26[7]. Presence of T cell receptors (TCR) gene rearrangement is seen in many cases along with abnormalities in PTEN gene[8].In Sezary syndrome there occurs loss of skin homing of cutaneous lymphocytes antigens resulting in circulation of malignant cells in peripheral blood and predominant secretion of T helper type 2 cytokine[9]. In this case we report a rare case of Sezary syndrome with involvement of central nervous system.

Case report

A 65 years old male presented with complaints of increasing breathlessness and cough with expectoration of 8 months duration. Patient also had numbness in bilateral hand and feet from last five months. On examination patient was conscious and oriented to time place and person.

The higher mental function, cranial nerve examination, motor examination was normal. There was 50% sensory loss for pain, touch and temperature in bilateral hand and below knee joint bilaterally. There was no history of diabetes mellitus. On further examination he had multiple papules and plaques over the body below neck involving trunk and lower limb [Figure-1and1b] along with generalized lymphadenopathy and generalized edema. His computed tomography brain was normal. Complete hemogram shows mild anemia (Hb-9gm/dl), TLC was increased (19000/µl), platelets show moderate thrombocytopenia (53000/µl). Peripheral smear examination revealed atypical lymphoid cells showing cerebriform nuclei, coarse chromatin, conspicuous to prominent nucleoli and scant basophilic cytoplasm(S/0-Sezary cells- 2300/µl)[figure-2].Outside FNA of inguinal lymph node revealed small to medium sized lymphoid cells with round to convoluted nuclei, coarse chromatin,prominent nucleoli and fragile cytoplasm admixed with reactive lymphoid population and the patient was advised for further workup to exclude lymphoproliferative disorder. Skin biopsy was performed from the lesion over trunk and after processing it, 4 µm sections were taken and stained with hematoxylin and eosin. On microscopy epidermis was unremarkable and the upper dermis revealed an intense band of lymphocytic infiltrate with mild focal epider Mo tropism. The atypical lymphocytes had hyperconvulated nuclei with coarse chromatin [Figure-3a and 3b] Immuno Histo chemistry was performed and revealed positivity for CD3 and CD45RO and negativity for CD26. [Figure 4a-4c].

Patient was managed with chemotherapy but after 3 months patient died due to sever chest infection. Although extracutaneous spread is not uncommon in advance stage of Sezary syndrome, Neurological complication is rare and result from leptomeningeal or central nervous system involvement.

Discussion

Polyneuropathy in a cancer patient may be related to chemotherapy and is rarely due to direct invasion of nerve[10,11]. Neuronal antigen expressed by the tumor

stimulation are immune response characterized by T cells, antibodies or both which attacks not only the tumor but also the neural tissue[12].Although these scenarios could be expected in lymphomas, nervous system involvement is not commonly reported in review of Sezary syndrome[13,14]. Sezary syndrome is an aggressive disease associated with poor prognosis and a median survival of two to three years.

It is clinically characterized by features of pruritis, early onset of erythroderma, lymphadenopathy and peripheral neuropathy.Other associated features include ectropion, fissuring and/or scaling of palm and soles, nail dystrophy, ankle edema and alopecia.

SSis indistinguishable from erythrodermia of eczematous origin, psoriasis and pharma coder Mia in early stages and can't be differentiated solely on clinical bases[15,16]. SS is characterized by a monoclonal proliferation of neoplastic T cells and an immunophenotype that is classically CD4+CD7-CD26- The malignant Tells in Sezary syndrome expresses the pan T cell markers CD2,CD3 and CD5 as well as CD45+RO+ and CD4+. SS can arise de novo or from preexisting lesions of the mycosis fungoides.

It is important to differentiate SS from erythroderma in MF progression as MF and its variants corresponds to more than 50% of cases of primary cutaneous T cell lymphomas. Patients with a previous history of MF who develop erythroderma are diagnosed as having an erythrodermic form of MF instead of SSin the WHO-EORTC classification. SS exhibits histological and immuno Histo chemical aspects that are indistinguishable from those observed in MF.

Trotter et al[17] have suggested that by including the patients with a circulating peripheral blood population of clonal T- cells only, the definition of SS can be further refined.Differential diagnosis between MF and SS can be further done by Immunostaining for MUM-1(Multiple myeloma oncogene), which might be positive in the SS and negative in MF. So, in this case the pathological features in skin, lymph node and peripheral blood with minimal invasion of bone marrow, suggested that the origin of the lymphoma was in peripheral T - lymphocytes.

Our patient had axonal peripheral neuropathy without central nervous system involvement. Neuropathic symptoms started prior to the chemotherapeutic drug induced peripheral neuropathy. These findings support the idea that the neuropathy was associated with Sezary syndrome.

Conclusion

This case emphasizes the importance of keeping polyneuropathy in mind which dealing with patient with Sezary syndrome, although it is difficult to treat and suggest the possible role of neurotropism of malignant cells.

Figures

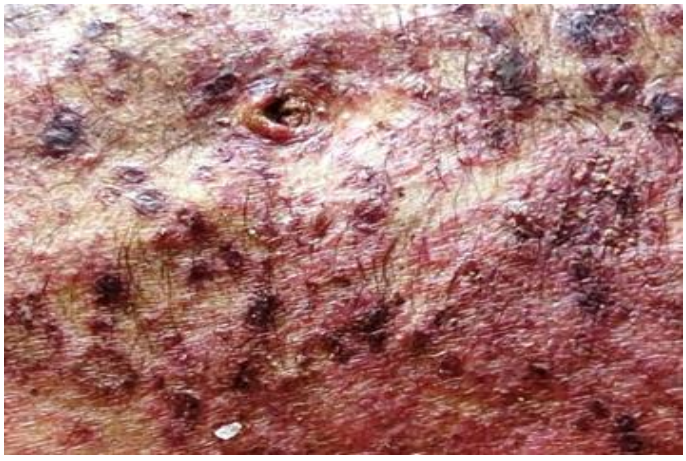

Figure 1a: shows multiple papules and plaques over the trunk.

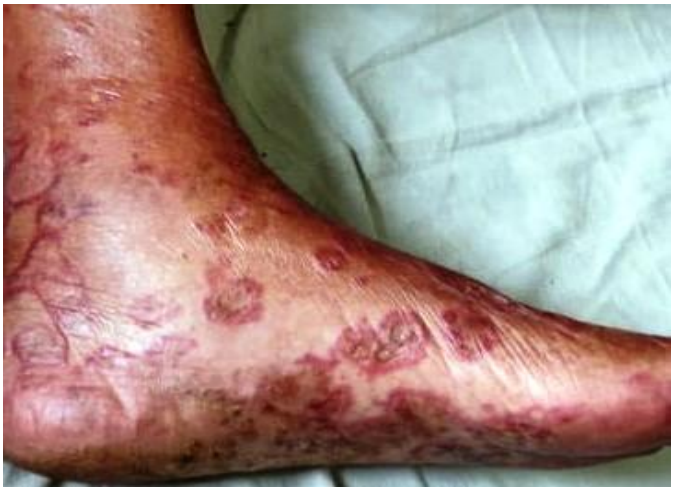

Figure 1b: Shows multiple scaly plaques on lower limb.

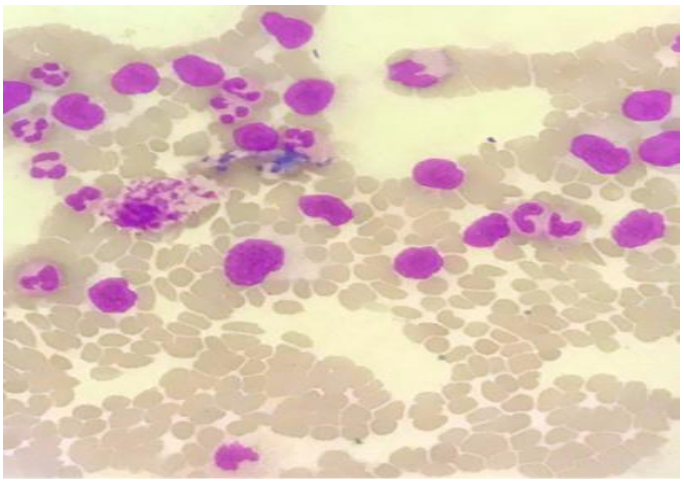

Figure 2: Peripheral blood smear showing lymphoid cells having cerebriform nuclei and scant basophilic cytoplasm (S/0- Sezary cells). (Leishman; X400)

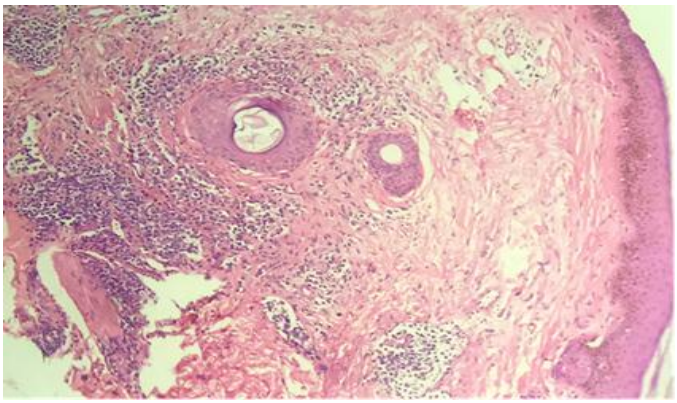

Figure 3a: Microphotograph showing upper dermis revealed an intense band of atypical lymphocytic infiltrate with mild focal epider Mo tropism (H&E:X100).

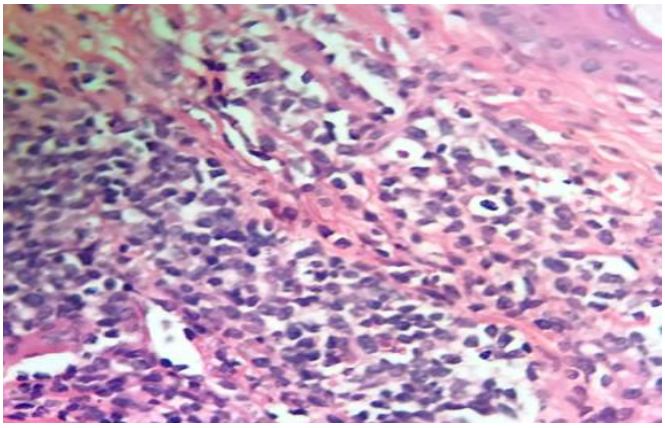

Figure 3b: Photomicrograph showing atypical lymphocytes having hyperconvulated nuclei with coarse chromatin (H&E; X400).

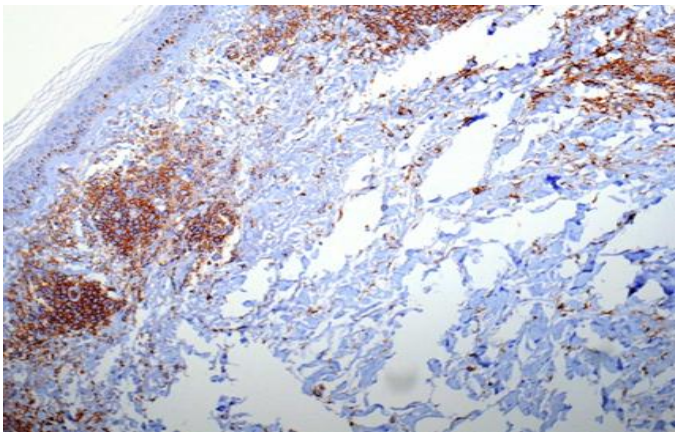

Figure 4 a: Immunohistochemistry with CD3 showing diffuse positivity in the atypical lymphoid cells. (CD3, 100X).

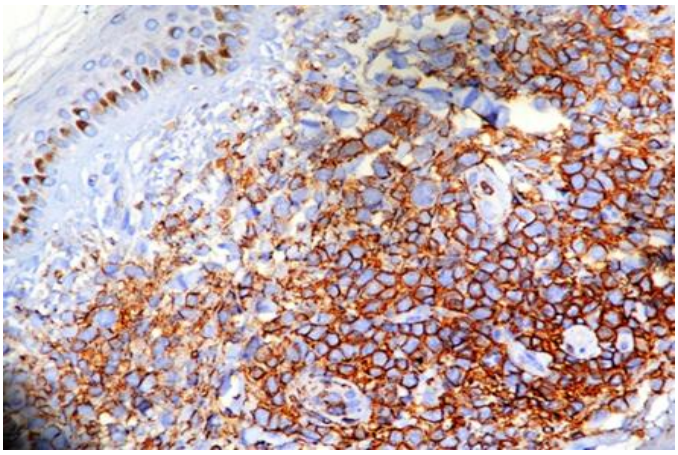

Figure 4 b: Immunohistochemistry with $CD45RO^{+}$ showing diffuse positivity in the atypical lymphoid cells. (CD45RO+, 400X).

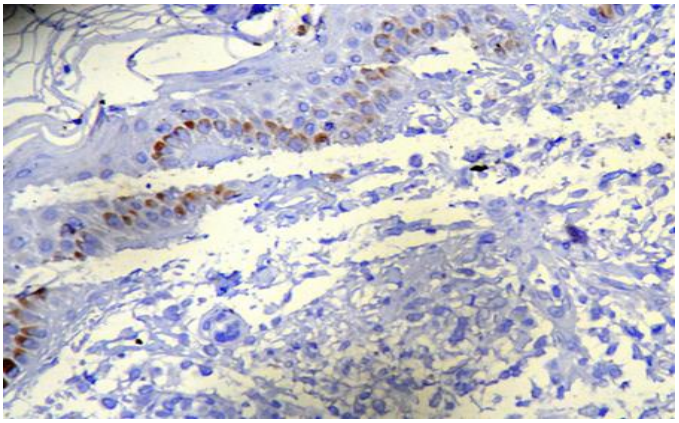

Figure 4 c: Immunohistochemistry with CD 26 showing diffuse negativity in the atypical lymphoid cells. (CD 26, 400X).

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