CD30+/ALK-: PRIMARY CUTANEOUS LYMPHOMA PRESENTING AS BENIGN SOLITARY ULCER

Karpagam Janardhan¹, Mahsheena KM², L.P. Thangavelu³, Hana Abdul Kareem⁴.

¹Professor, General Pathology, Sri Ramakrishna Dental College & Pathologist, HISTOLAB, Coimbatore. Tamil Nadu State, India.
²PG resident, MD Pathology, Dept. of Pathology, Karuna Medical College, Palakkad, Kerala. India.
³Chairman / Surgeon, Ashwin Hospital, Coimbatore, India.
⁴PG resident, MD Pathology, Dept. of Pathology, Karuna Medical College, Palakkad, Kerala. India.

ABSTRACT
Primary cutaneous anaplastic large cell lymphoma is a rare anaplastic CD30+ positive large T-cell lymphoma which originates as well as confined to the skin, characterized by reddish or brownish, solitary or loco regional nodules and tumors with a tendency to ulcerate. Here we report a case of CD30(+),ALK(-),PCALCL in a 40yr old male presenting with a solitary slow growing ulceroproliferative lesion of 6 months duration. PCALCL usually have a favourable prognosis with a disease-related survival rate of around 90%.

INTRODUCTION
CD30(+) cutaneous lymphoproliferative disorders (CLPDs) involves the spectrum of disorders such as lymphomatoid papulosis, borderline cases and primary cutaneous anaplastic large cell lymphoma [PCALCL]. They are the second most common group of cutaneous lymphomas with a diffuse, non-epidermotropic infiltrate composed of anaplastic large lymphoid cells that are CD30(+),CD4(+), EMA(-), ALK(+), CD15(-) and TIA1(+/-) [1].

CASE REPORT:
40 year old male presented with an ulceroproliferative growth on his left cubital fossa that gradually increased in size for a period of 6months and measuring 8x8cm with rolled out margins. Incision biopsy was done 3 months back and reported as severe active inflammatory lesion. Other systems were normal. There is no history of diabetes or hypertension.

MRI of left forearm showed an ill-defined intensely enhancing skin based soft tissue lesion measuring approximately 6x1.8x4.5cm on the anterior aspect of proximal forearm extending upto elbow. Lesion is infiltrating into the subcutaneous fat with no definable fat plane between the lesion and underlying flexor group muscles.-likely infiltration of epimysium [Fig 1 A & B].

Excision biopsy was done and sent for HPE.

Intraoperative findings:
Ulceroproliferative growth measuring 8x8cm on the anterior aspect of left forearm with raised edges was seen. Excision biopsy with skin grafting of the involved area was performed. Fig 2 [A&B] and sent for HPE.

GROSS EXAMINATION:
Received an oval piece of skin with subcutis measuring 10.5x9x1.5cm. The skin surface showed an...
irregular friable ulceroproliferative growth measuring 8x5.5x1.3cm that was 1cm and 1.5cm from two lateral margins and 0.5cm from the inferior margin. Cut section of the tumour was pale to dark brown and grossly limited to subcutis and 0.2cm from the base [Fig 3A & B].

**MICROSCOPIC EXAMINATION:**

Showed epidermis with ulceration and irregular acanthosis [Fig 4] Dermis showed an infiltrating lesion involving the subcutis and composed of large sheets of anaplastic cells with round, oval, indented nuclei with prominent nucleoli and copious cytoplasm [Fig 5A & B]. Few cells resembling RS-like cells were noted [Fig 6A & B]. Plenty of mitotic figures seen along with inflammatory infiltrate composed of small lymphocytes, eosinophils, neutrophils and histiocytes [Fig 7A, B, C]. The surgical margins were free of tumour.

Differentials considered were Non-Hodgkin’s lymphoma, malignant melanoma and poorly differentiated carcinoma. Tissue was taken up for IHC and IHC report was: CD4-positive, CD30-positive, LCA-positive, ALK-1-negative, PAX-5-negative, CD20–negative, Melan-A-negative, S-100-negative, HMB-45-negative [Fig 8A, B, C, D, E].

Final diagnosis was Primary cutaneous CD30-positive ALK-negative Anaplastic Large-cell lymphoma.

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<tr>
<th>Figure 1A &amp; B shows an ill defined intensely enhancing skin based soft tissue lesion on anterior aspect of proximal forearm extending unto elbow. Lesion is infiltrating into subcutaneous fat with no definable fat plane between the lesion and underlying flexor group muscles.</th>
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<th>Figure 2 [A&amp;B] shows an ulceroproliferative lesion with raised edges and skin grafted after excision of the whole lesion.</th>
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<th>Figure 3A Shows a pale to black ulceroproliferative growth with rolled out edges and B-shows growth extending upto subcutis.</th>
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Figure 4 Shows epidermis shows irregular acanthosis with adjacent area of ulceration

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<th>Figure 5</th>
<th>A: Large sheets of anaplastic cells. Figure 5 B – Shows individual cells with round/oval, indented nuclei (hallmark or buttock cells), prominent nucleoli and copious cytoplasm.</th>
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<td><img src="image" alt="Fig5A 10X" /></td>
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Figure 6 Shows cells resembling RS-like cells

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<th>Figure 6</th>
<th>A: Shows cells resembling RS-like cells</th>
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Figure 7A- shows plenty of abnormal mitosis

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<th>Figure 7B</th>
<th>B- showing inflammatory infiltrate composed of lymphocytes, eosinophils, neutrophils and histiocytes.</th>
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<td>Fig7A 40x</td>
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<td>B 40x</td>
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DISCUSSION

Primary cutaneous anaplastic large cell lymphoma contributes about 30% of cases of cutaneous T-cell lymphoma and is the second most commonest group which includes ALCL and lymphomatoid papulosis which usually present at a median age 60yrs and commonest sites of occurrence being trunk, extremities and buttocks (WHO, 2000). They usually have a male preponderance and present as solitary or localised red to violacous papules, nodules or tumours and often ulcerate but usually have a favourable prognosis (David Weedon, 2000).

In our case, the 40 yr old patient had a solitary ulceroc proliferative growth. The incidence of PCALCL contributes about 1.7% of peripheral T-Cell NHL (Diamantidis et al., 2009). Histologically they show a diffuse infiltrating lesion composed of a large sized T-lymphocytes with characteristic anaplastic cells having round, oval or irregular nuclei with eosinophilic nucleoli and abundant cytoplasm and often with no epidermotropism (Kempf et al., 2011). Upto 44 percent of patients is reported to have a spontaneous complete or partial regression (Vergier et al., 1988). PCALCL has a favourable prognosis with 5yr survival rates between 76% to 96%, in contrast to its nodular part (Benner and Willemze, 2009). Lymphomatoid papulosis and systemic ALCL with cutaneous manifestation are the two most differential diagnosis (Kadin, 2009). 39% show frequent cutaneous recurrence and about 13% show cutaneous
dissemination to regional lymph nodes (Bekkenk et al., 2000). Our patient did not have any extra cutaneous manifestations. Patient refused to undergo bone marrow biopsy. As the peripheral smear was normal, it was unlikely to have a marrow involvement. He was advised chemotherapy and radiotherapy but he was willing for only radiotherapy. Hence he received 6 cycles of radiotherapy and lesions healed well with no recurrence. Patient with localised lesion are treated with radiation therapy, removal of lesion and/or low dose methotrexate.

Multiagent chemotherapy are preferred especially in multi focal PCALCL. CHOP which is the most common type of multiagent chemotherapy used in Malignant Lymphomas, are no longer recommended as first line therapy for multi focal or relapsing PCALCL limited to the skin. Low dose methotrexate (5-25 mg/week), which is generally not a myelosupressive agent, is the first line therapy for multi focal PCALCL (Chou et al., 1996). Anecdotal reports have shown the use of systemic retinoids, including Bexarotene, IFN-Alpha, and thalidomide as effective treatment for multi focal PCALCL which are not responsive to other therapies. With this kind of immune modulatory therapy, maintenance therapy over months to years seems to be necessary (French et al., 2000; Lee et al., 2009).

CONCLUSION
We presented our case for bringing into attention of how an isolated slow growing ulceroproliferative lesion is important in a setting of completely otherwise normal person with no symptoms of a lymphoproliferative lesion.

ACKNOWLEDGEMENTS: NONE

CONFLICT OF INTEREST:
The authors declare that they have no conflict of interest.

STATEMENT OF HUMAN AND ANIMAL RIGHTS
All procedures performed in human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

REFERENCES