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First Illustrated Case Series of Indolent Primary Cutaneous Gamma Delta T-Cell Lymphoma

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INTRODUCTION

Primary cutaneous gamma delta T-cell lymphomas (PCGDTCL) are rare, representing less than 1% of all cutaneous lymphomas. The etiology is uncertain but involves chronic antigen stimulation and immunosuppression. PCGDTCL are a defined entity of the EORTC WHO classification of 2018 with various clinical presentations, most often manifesting as nodules or infiltrated plaques. The prognosis is generally poor and macrophage activation syndrome may occur. Treatment is mostly aggressive yet resistance to multiple chemotherapy or radiation therapy is common leading to frequent relapses. However, cases with an indolent evolution have been rarely reported in the literature since 2005, that have been successfully treated with systemic corticosteroids, methotrexate, bexarotene or phototherapy. We provide a retrospective series of five new indolent cases.

OBSERVATION

We report five cases of patients with heterogeneous clinical presentations diagnosed as PCGDTCL with indolent course: an 81-year-old man who presented with infiltrated plaques of the face & left thigh (case 1), and four women aged 27, 70, 35 and 66, who presented respectively with localized subcutaneous nodular lesions of the lower limbs (case 2 and 4),urticarial lesions of the trunk (case 3) as well as nodular and necrotic lesions on the lower limbs (case 5). Despite a confirmed diagnosis of PCGDTCL, the clinical course was indolent, and the patients achieved partial to complete response to treatment with various treatments such as bexarotene or methotrexate & systemic corticosteroids, with follow up ranging up to 6 years. However, 66-year-old patient (case 5) progressed with diffuse and aggressive disease after a 3-year follow-up. Clonal T-cell receptor gamma chain gene rearrangement analysis was performed using PCR and was detected in all our patients, which had not been determined in previous biopsies. Nodal & visceral involvement was excluded by various imaging modalities mainly CT scans,, as well as bone marrow puncture performed in patients 3 & 5.

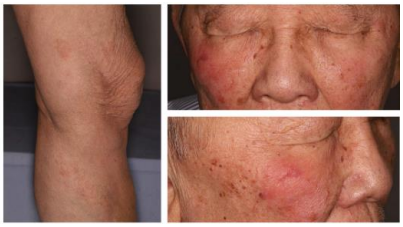
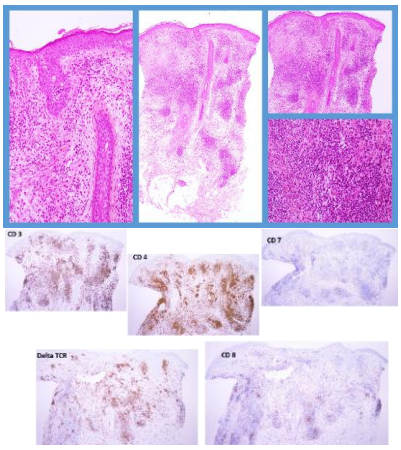


Figure 1: multiple infiltrated plaques in an 81-year-old male (patient 1)



Immunohistochemical markers of patient #1 showing CD3+, CD4+, CD8+, TIA-1, TCR delta

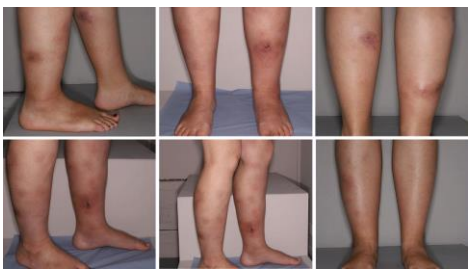


Figure 2: multiple subcutaneous nodules in a young female (patient 2)

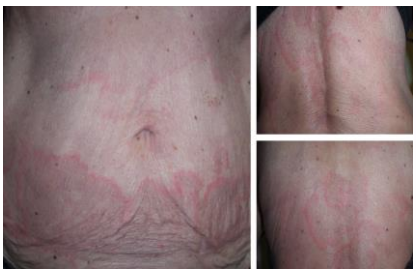


Figure 3: urticarian plaques on the abdomen & back of patient 3

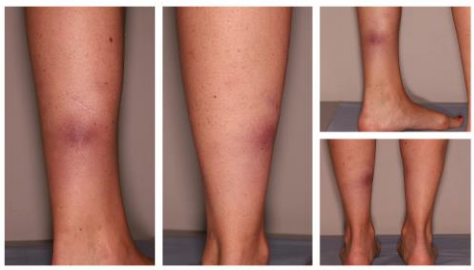


Figure 4: multiple subcutaneous nodules localized in the inferior limbs in a young female (patient 4)

DISCUSSION

Our five cases highlight the importance of knowing the possibility of an indolent form of PCGDTCL, and the possibility to achieve a clinical remission with immunomodulatory treatments. This would prevent the unnecessary use of heavy treatments such as chemotherapy. A few case reports of equally indolent forms have already been described in the literature with various presentations of localized or diffuse lesions, as well as variable courses of progression. A few remained indolent while others
became aggressive several years later. Conventional treatments such as phototherapy, radiotherapy or systemic corticosteroids proved to be efficient with most of such cases. However, some patients received multiple lines of treatment including polychemotherapy achieving partial to complete responses. They remain in remission several years post-treatment until 15 years of follow-up. Nevertheless, it is prudent to maintain close surveillance to early detect any secondarily aggressive development.

Case Demographics	Lesion at Diagnosis	Areas Affected	Ulceration	Histology & Immunohistochemistry	Diagnosis	Treatment	Response	Follow-up Period
81-year-old male 22/10/1940 (Patient #1)	Erythematous infiltrated plaque	Cheeks & Thighs	No	CD3+, CD4+, CD8+, TIA-1, TCR gamma	September 2020	Plaquenil before diagnostic confirmation then Bexarotene but due to hypertriglyceridemia switch to Methotrexate	Partial clinical response at 11-months	11 months
27-year-old female 22/06/1994 (Patient #2)	Subcutaneous nodules without associated fistulation or ulceration	Lower Limbs	Yes (after two months of initial presentation)	CD2+, CD3+, CD56+, granzyme +, CD4-, CD8-, TCR gamma	May 2019	6 cures of CHOP in 2016 then Plaquenil 400mg per day (due to suspicion of lupus panniculitis) before final switch to Methotrexate	Complete remission at 12 months	28 months
70-year-old female 18/07/1951 (Patient #3)	Urticarial-like lesions	Abdomen & Back	No	CD3+, CD4-, CD8-, CD5-, CD7-, TCR gamma	March 2016	6 cycles of CHOP at PTCL-NOS then Methotrexate 10mg PO	Complete remission at 27 months	67 months
35-year-old female 21/10/1986 (Patient #4)	12 inflammatory subcutaneous nodules with cupuliforme scars	Lower limbs	No	CD3+, CD4+, CD5+, CD7+, CD8+, granzyme +, TCR gamma	July 2017	General corticotherapy then Methotrexate 15mg PO once a week switched to Bexarotene due to 4 episodes of new lesions appearing despite healing of old lesions	Partial remission (Appearance of new lesions)	50 months
66-year-old female 10/05/1944 (Patient #5)	Multiple subcutaneous nodules with necrosis & inflammatory polyarthralgia	Lower Limbs	Yes	CD3+, CD4+, CD8-, TCR gamma	Summer 2005	6 cycles of CHOP followed by autogenic stem-cell transplantation	Partial remission but death due to respiratory distress attributed to an aspergillosis pulmonary infection	30/03/2010 29/04/2010 Passed away on the 03/05/2010

Table 1: Clinical, histological, & immunohistochemical manifestations as well as treatment, response & follow-up of our 5 patients

Références :

1. Kreuter, A., Koushk-Jalali, B., Mitrakos, G., Oellig, F., Assaf, C., Cerroni, L., & Tigges, C. (2020). Bendamustine Monotherapy for Primary Cutaneous Gamma-Delta T-Cell Lymphoma. JAMA dermatology, 156(10), 1029-1030.
2. Vergez, F., Largeaud, L., Oberic, L., & Rieu, J. B. (2019). Do not jump to hasty conclusions: all gamma delta T-cells neoplasms are not aggressive!. *Blood research*, *54*(4), 243-243.
3. Warnnissorn, N., Suthiwartnarueput, W., Chakkavittumrong, P., & Limvorapitak, W. (2019). Primary cutaneous gamma delta T-cell lymphoma with complete remission after CHOP therapy: The first case report from Thailand with literature review. *Thammasat Medical Journal*, *19*(2), 427-432.
4. Junkins-Hopkins, J. M. (2019). Indolent gamma delta positive indolent cutaneous T-cell lymphoma: two cases and review of the literature. *European Journal of Cancer*, *119*, S21.
5. Ali, L., Young, M. R., Bayerl, M. G., Helm, K. F., & Clarke, L. E. (2015). Gamma-delta T-cell lymphoma arising in a long-standing cutaneous plaque. *Journal of cutaneous pathology*, *42*(12), 987-991.
6. Hosler, G. A., Liégeois, N., Anhalt, G. J., & Moresi, J. M. (2008). Transformation of cutaneous gamma/delta T-cell lymphoma following 15 years of indolent behavior. *Journal of cutaneous pathology*, *35*(11), 1063-1067.
7. von Dücker, L., Fleischer, M., Stutz, N., Thieme, M., Witte, M., Zillikens, D., ... & Terheyden, P. (2020). Primary cutaneous gamma-delta T-cell lymphoma with long-term indolent clinical course initially mimicking lupus erythematosus profundus. *Frontiers in oncology*, *10*, 133.
8. Vin, H., Talpur, R., Tetzlaff, M. T., & Duvic, M. (2014). T-cell receptor-γ in gamma-delta phenotype cutaneous T-cell lymphoma can be accompanied by atypical expression of CD30, CD4, or TCRβF1 and an indolent clinical course. *Clinical Lymphoma, Myeloma and Leukemia*, *14*(6), e195-e200.
9. Willemze, R., Cerroni, L., Kempf, W., Berti, E., Facchetti, F., Swerdlow, S. H., & Jaffe, E. S. (2019). The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas. *Blood, The Journal of the American Society of Hematology*, *133*(16), 1703-1714.