Netherlands
The Journal of Medicine

A skin lesion that catches the eye

L. Louter*, I.P.G. Botden, R.F.J. Schop

Department of Internal Medicine, IJsselland Hospital, Capelle aan den IJssel, the Netherlands,
*corresponding author: tel.: +31 (0)10-2585193, fax : +31 (0)15-2603598,
e-mail: leonoralouter@gmail.com

ABSTRACT

Primary cutaneous gamma-delta T-cell lymphoma (PCGD-TCL) is rare and only represents 1% of all cutaneous T-cell lymphomas. To our knowledge, only 40 cases have been described. It often presents with generalised skin lesions, preferentially affecting the extremities. There is a well-documented association with haemophagocytic syndrome. Treatment is difficult since PCGD-TCL is often resistant to chemotherapy and radiotherapy. Most case reports describe an aggressive clinical course with an estimated mean survival of 15 months.

We present a 72-year-old female patient with stage IV primary cutaneous gamma-delta T-cell lymphoma. Our patient presented with fever, night sweats and multiple skin lesions (*figure 1*). Computed axial tomography of chest and abdomen revealed multiple solid nodular lesions in both kidneys. During admission a subconjunctival lesion appeared and progressed rapidly (*figure 2*).

Histopathological examination of skin biopsy revealed infiltration of atypical lymphocytes with hyperchromatic irregular nuclei. Immunophenotyping pattern of skin biopsy was compatible with PCGD-TLC. Clonal gamma-delta T-cells were also detected by immunohistochemical analysis of peripheral blood and bone marrow. Polymerase chain reaction amplification revealed clonal rearrangement of the T-cell receptor gamma chain gene. These findings together were consistent with stage IV primary cutaneous gamma-delta T-cell lymphoma. The rapid progression of the subconjunctival extra-nodal manifestation is characteristic for the aggressive course of this lymphoma. Our patient was treated with two cycles of CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone). However, her clinical condition deteriorated rapidly. She declined further therapy and died within three months of initial presentation.

KEYWORDS

Haemophagocytic syndrome, primary cutaneous gamma-delta T-cell lymphoma, subconjunctival lesion

CASE REPORT

A 72-year-old female patient presented with fever, night sweats and multiple skin lesions. Her history included paroxysmal atrial fibrillation, hypertension and a stroke. At physical examination there were no enlarged lymph nodes. Multiple erythematous cutaneous nodules were present on the upper extremities and abdomen (*figure 1*). A skin biopsy was performed.

Laboratory results showed: haemoglobin 7.2 mmol/l, leucocytes 1.3 x 10^9/l with a lymphocytopenia of 0.4 x 10^9/l, thrombocytes 99 x 10^9/l, lactate dehydrogenase 857 IU/l and haptoglobin <0.1 g/l.

Viral serology was negative for human immunodeficiency virus, Epstein-Barr virus, Cytomegalovirus, and hepatitis A, B and C. Autoimmune serology was also negative. Computed axial tomography of the chest and abdomen revealed multiple solid nodular lesions in both kidneys. During her admission a subconjunctival lesion appeared and progressed rapidly within three days (*figure 2*).

DIAGNOSIS

Histopathological examination of the skin biopsy revealed an infiltration of atypical lymphocytes with hyperchromatic irregular nuclei. Immunophenotyping by immunohistochemical analysis characterised the infiltrate as CD2+, CD3+, CD4-, CD5-, CD7-, CD8-, CD20-, CD30- and CD56-. Polymerase chain reaction amplification revealed clonal rearrangement of the T-cell receptor gamma chain gene. Clonal gamma-delta T-cells were also detected by

immunohistochemical analysis of peripheral blood and bone marrow. These findings together were consistent with stage IV primary cutaneous gamma-delta T-cell lymphoma (PCGD-TCL) accompanied by multiple extra nodal manifestations.

Figure 1. *Multiple erythematous cutaneous nodules on the upper extremities*

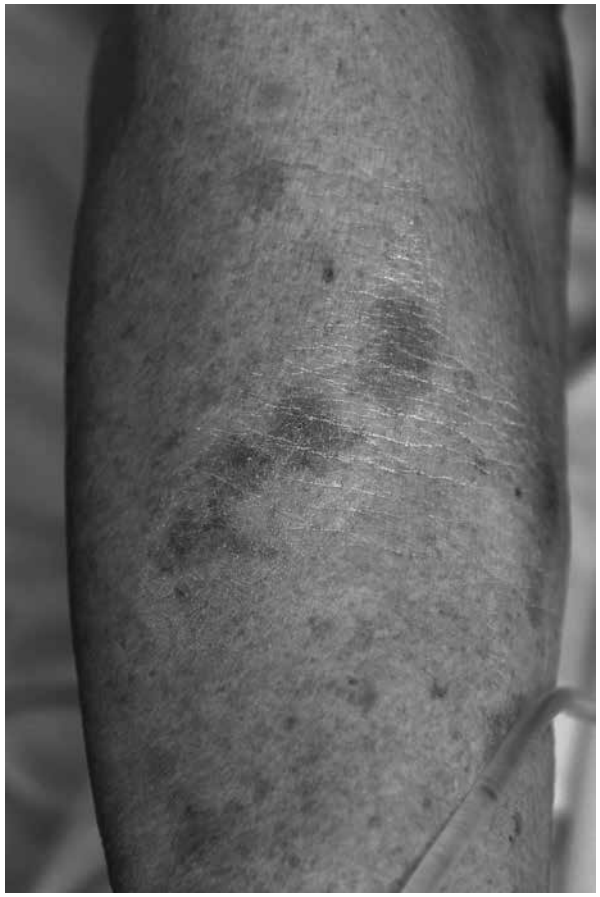
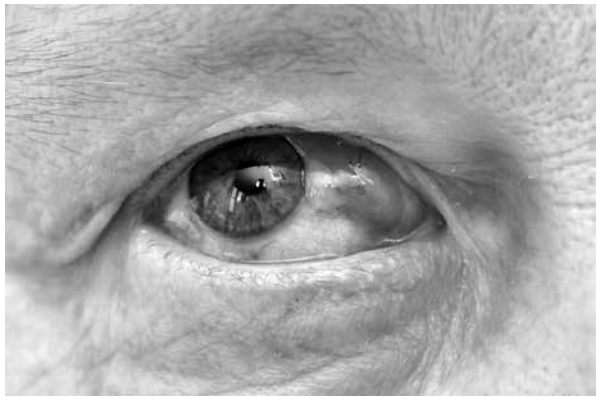


Figure 2. *Subconjunctival lesion*



T-cell lymphomas represent less than 15% of all non-Hodgkin lymphomas. PCGD-TCL has been included in the WHO classification of myeloid and lymphoid neoplasms since 2008 and has been estimated to represent 1% of all cutaneous T- cell lymphomas. To our knowledge, only 40 cases have been described.[1]

PCGD-TCL is composed of a clonal proliferation of mature, activated gamma-delta T-cells with a cytotoxic phenotype. It often presents with generalised skin lesions, preferentially affecting the extremities. Dissemination to mucosa and other extra-nodal sites is frequently observed, but involvement of lymph nodes, spleen or bone marrow is uncommon. There is a well-documented association with haemophagocytic syndrome, also known as haemophagocytic lymphohistiocytosis.[2]

The diagnosis in our patient was compatible with the characteristic immunophenotype of PCGD-TLC, although CD56 was negative.[3] There was clonal rearrangement of the T-cell receptor gamma chain gene. This is seen in approximately 70% of all cases.[4] Treatment is difficult, as PCGD-TCL is often resistant to chemotherapy and radiotherapy. There are no clinical trials targeting PCGD-TCL. Systemic multiagent chemotherapy CHOP has previously been used. In young patients allogeneic haematopoietic stem cell transplantation should be considered.[1] Most case reports describe an aggressive clinical course with an estimated mean survival of 15 months.[1,2,4]

Our patient was treated with two cycles of CHOP and experienced multiple septic episodes. Although the subconjunctival and skin lesions improved, her clinical condition deteriorated rapidly. She declined further therapy and died within three months of initial presentation.

ACKNOWLEDGEMENT

The authors thank Dr. R.F. Hoedemaeker, Department of Pathology, Pathan, Rotterdam

REFERENCES

1. Koch R, Jaffe ES, Mensing C, Zeis M, Schmitz N, Sander CA. Cutaneous gamma/delta T-cell lymphoma. J Dtsch Dermatolol Ges. 2009;7:1065-7.
2. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. Blood. 2005;5:3768-85.
3. Toro JR, Beaty M, Sorbara L, et al. T-cell lymphoma of the skin: a clinical, microscopic, and molecular study. Arch Dermatol. 2000;136:1024-32.
4. Aguilera P, Mascaró JM Jr, Martinez A, et al. Cutaneous gamma/delta T cell lymphoma: a histopathologic mimicker of lupus erythematosus profundus (lupus panniculitis). J Am Acad Dermatol. 2007;56:643-7.