CASE REPORT

Two faces of gamma–delta mycosis fungoides: before and after renal transplantation

Knut Erich Prillinger,¹ Franz Trautinger,¹ Melitta Kitzwögerer,² Johanna Eder¹

¹Department of Dermatology and Venereology, Karl Landsteiner University of Health Sciences, Sankt Pölten, Austria

²Department of Clinical Pathology, University Hospital St Pölten, Karl Landsteiner University, St Pölten, Austria

Correspondence to

Dr Knut Erich Prillinger, knut.prillinger@stpoelten.lknoe.at

Accepted 10 February 2017

SUMMARY

We describe a patient with a 30-year history of mycosis fungoides (MF) and renal transplantation performed 3 years before he presented with an ulcerated tumour in the lumbosacral area. Biopsy revealed a lymphatic infiltrate of medium-sized, pleomorphic T cells expressing the gamma–delta T-cell receptor. Radiological staging and bone marrow biopsy revealed no extracutaneous involvement. Despite reduction in systemic immunosuppressants, total skin electron beam radiotherapy and systemic chemotherapy, the disease followed a highly aggressive course and the patient died 31 years after initial diagnosis of MF. Pre-existing MF is not listed as a contraindication for solid organ transplantation. With an ever-increasing number of organ recipients, the number of MF patients undergoing solid organ transplantation will be likely to increase. Systematic collection and analysis of such cases is thus warranted to lead to a better understanding to what kind MF gets influenced by solid organ transplantation and ongoing immunosuppression.

BACKGROUND

Mycosis fungoides (MF) represents the most common subtype of cutaneous T-cell lymphoma (CTCL) in patients who had non-transplants. Gamma–delta MF is an uncommon variant characterised by the expression of the gamma–delta T-cell receptor (TCR). The majority of post-transplant lymphoproliferative disorders (PTLD) are B-cell-derived non-Hodgkin's lymphomas (NHL). This case demonstrates that on solid organ transplantation MF, though indolent for the preceding decades, can change its face to an aggressive condition. It emphasises the need for screening for pre-existing skin conditions prior to organ transplantation and better understanding the group of gamma–delta TCR+ lymphoproliferative disorders.

CASE PRESENTATION

We report on a patient with a 30-year history of MF. His medical history was remarkable for renal transplantation 3 years before due to chronic kidney disease of unknown origin. Since then, he has received immunosuppressive therapy with ciclosporin, mycophenolate and corticosteroids. The earlier diagnosis of MF that has been made in the early 1980s of the past century was based on clinical presentation and histological findings of an epidermotropic infiltrate of atypical lymphocytes. Since then, the disease had characteristically taken an indolent course with limited patches and plaques and the occasional need for

8-methoxypsoralen and ultraviolet-A photochemotherapy (PUVA) followed by remission and relapse but without disease progression.

At first presentation at our ward, physical examination revealed a reddish-brown tumour in the lumbosacral area with central ulceration and disseminated erythematous plaques on the trunk. There was no lymphadenopathy and the patient was in good general condition.

INVESTIGATIONS

Biopsy specimens taken from various sites and time-points uniformly showed a dense, superficial and deep nodular infiltrate (figure 1A) of medium/large-sized pleomorphic lymphocytes (figure 1B) with partial epidermotropism (figure 1C). Immunohistochemistry analysis revealed a CD3+, CD5+, CD7+ and a CD56–, CD30–, CD4–, CD8– and β F1– phenotype with strong expression of the TCR-gamma, TIA-1, perforin and granzyme B. Staining with Ki-67 demonstrated a high proliferation index (around 70%). In situ hybridisation for Epstein-Barr virus was negative. Laboratory findings including complete blood count, renal and liver function tests, lactate dehydrogenase, serum electrophoresis and immune-electrophoresis were only remarkable for normocytic anaemia (Hb 11.6 g/L) and elevated serum creatinine (1.86 mg/dL). Immunophenotyping of the blood was unremarkable.

Reassessment of the initial skin biopsy specimens and comparison with the current pathological findings revealed a similar phenotype with cytotoxic, TCR-gamma+ atypical lymphocytes with large cell transformation.

Results of further staging investigations, including bone marrow biopsy, lymph node ultrasound scan, chest X-ray and CT of the neck, chest and abdomen, were unremarkable. We diagnosed a primary cutaneous tumour-stage gamma–delta MF with cytotoxic phenotype.

OUTCOME AND FOLLOW-UP

Immunosuppressive therapy with ciclosporin was changed to sirolimus and localised radiotherapy was applied to the large lumbosacral lesion. Owing to progression with generalised skin lesions (figure 2A) after an initial good local response, therapy was extended to total skin electron beam radiation (TSEB). Owing to signs of renal failure requiring haemodialysis, TSEB had to be interrupted but could be continued up to a total dose of 36 Gy after recovery of renal function resulting in partial remission (figure 2B). On further progression and the

CrossMark

To cite: Prillinger KE, Trautinger F, Kitzwögerer M, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-216990

Figure 1 (A) H&E $\times 4$: showing a dense superficial and deep nodular infiltrate, (B) H&E $\times 20$: showing a medium-sized to large-sized, pleomorphic, lymphoid infiltrate and (C) H&E $\times 10$: showing lymphoid epidermotropism.

appearance of a suspicious pulmonary mass not accessible to biopsy, systemic chemotherapy with bendamustine was initiated. While the patient received three treatment cycles in monthly intervals, the disease was rapidly progressive with widespread ulceronecrotic plaques and nodules affecting the whole body surface including the genital mucosa (figure 2C). The patient died 31 years after initial diagnosis and 3 years after renal transplantation.

DISCUSSION

CTCL are a heterogeneous group of extranodal NHL characterised by their primary manifestation on the skin. MF represents the most common type of CTCL affecting mainly

middle-aged people with a slight male predominance.¹ To what extent immunosuppression and the consecutively impaired tumour surveillance play a role in disease pathogenesis and progression is unclear. In the WHO-EORTC Classification for Cutaneous Lymphomas and the 2008 WHO classification of lymphoid neoplasms, MF and its variants are characterised by a distinct correlation of clinicopathological features.² Among these variants, cases of MF expressing the gamma-delta TCR are documented. The literature indicates that these phenotypic variations do not affect the clinical course in early-stage MF.³ The loss of pan T-cell antigen markers and expression of CD30 and cytotoxic proteins (granzyme B, T-cell intracellular antigen-1 (TIA-1) and perforin) occurs in a minority of MF patients. Large cell transformation defined by the presence of more than 25% of large cells on histological findings is reported predominantly in tumour-stage lesions and is associated with poor prognosis.⁴

An important differential diagnosis of gamma-delta MF is the group of primary cutaneous gamma-delta T-cell lymphomas (CGD-TCL), a provisional entity in the WHO-EORTC classification of cutaneous lymphomas. They are exceedingly rare accounting for <1% of CTCL and are characterised by poor prognosis. In some cases, discrimination of advanced gamma-delta MF and CGD-TCL is not possible, as they can share clinical and histological patterns. To what extent gamma-delta TCR expression influences clinical behaviour in CTCL is poorly understood.

The development of lymphomas after solid organ transplantation is a well-known problem of transplantation medicine, first described by Penn *et al*⁵ in the late 1960s when organ transplantation entered clinical medicine. Based on characteristics different to other lymphoproliferative disorders (eg, more aggressive behaviour, poor response to traditional therapies, often extranodal involvement with preference to the central nervous system), PTLN are recognised as a separate group in the 2008 WHO classification of haematopoietic and lymphoid tissues.⁶ Among patients with solid organ transplantation, renal transplant recipients have the lowest risk (1.4%) and lung transplant recipients the highest risk (4.5%) for the development of PTLN.⁷ The duration and intensity of immunosuppressive therapy, particularly during the first year after organ transplantation, are supposed to be more important risk factors for PTLN than the specific drug used.⁸ Although PTLN can initially appear in the skin, the development of MF seems not to be affected by solid organ transplantation. Clarke *et al*⁹ reported about a similar incidence of MF in transplant recipients and the normal population.

To the best of our knowledge, there is no literature about the influence of solid organ transplantation on the course of pre-existing MF. With a total rate of solid organ transplantation of 90 procedures/million/year in Austria and an estimated incidence of MF of 0.4/100 000/year, the likelihood of a patient with MF to receive a transplant is presumably low.¹⁰ However, the chronicity and incurability of the disease together with an increasing lifespan and increasing transplantation rates make it likely that an increasing number of patients with MF will become eligible for and undergo organ transplantation. Based on the experience with the clinical course in our patient screening for skin disease and recognition of early MF (and of course also other PCL although they are much less likely to occur), evaluation of individual risk, appropriate interdisciplinary consultation and counselling prior to transplantation, and thorough observation and documentation if transplantation is performed should be mandatory.

Figure 2 Clinical presentation: (A) before total skin electron beam therapy (TSEBT), (B) partial remission during TSEBT with intermittent haemodialysis and (C) progression during chemotherapy with bendamustine.

It can of course not be excluded that the progressive course described here in an unusual variant of MF is unrelated to renal transplantation and iatrogenic immunosuppression. Similar aggressive transformations can occur in MF without apparent cause and medical intervention even after prolonged indolent course.

Only with collecting and evaluating additional cases, knowledge about the contribution of the specific immunophenotype and other potential risk factors (including age, gender, immunosuppressive drugs and others) will accumulate and allow for more specific interventions to avoid cutaneous lymphoma-related fatalities in patients after transplantation with functioning allogeneic organs.

Learning points

- Mycosis fungoides (MF) represents the most common subtype of primary cutaneous lymphomas in patients who had non-transplants and may take an aggressive course on immunosuppressive medication.
- Gamma-delta MF is an uncommon variant with uncertain biological behaviour requiring particular care during follow-up to recognise progression early.
- Most post-transplant lymphoproliferative disorders are of B-cell origin with a different disease course and prognosis compared with non-Hodgkin's lymphomas in patients who had non-transplants.

Contributors KEP wrote the manuscript and had the initial idea of writing the article. FT made the diagnosis, cared for the patient and wrote the manuscript. MK did the histopathology and thus contributed significantly to reaching the final diagnosis. JE cared for the patient and wrote the manuscript.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Willemze R, Jaffe ES, Burg G, *et al.* WHO-EORTC classification for cutaneous lymphomas. *Blood* 2005;105:3768–85.
- 2 Olsen E, Vonderheid E, Pimpinelli N, *et al.* Revisions to the staging and classification of mycosis fungoides and Sezary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC). *Blood* 2007;10:1713–22.
- 3 Massone C, Crisman G, Kerl H, *et al.* The prognosis of early mycosis fungoides is not influenced by phenotype and T-cell clonality. *Br J Dermatol* 2008;159:881–6.
- 4 Herrmann JL, Hughey LC. Recognizing large-cell transformation of mycosis fungoides. *J Am Acad Dermatol* 2012;67:665–72.
- 5 Penn I, Hammond W, Bretschneider L, *et al.* Malignant lymphomas in transplantation patients. *Transplant Proc* 1969;1:106–12.
- 6 Ravat FE, Spittle MF, Russell-Jones R. Primary cutaneous T-cell lymphoma occurring after organ transplantation. *J Am Acad Dermatol*. 2006;54:668–75.
- 7 Leblond V, Sutton L, Dorent R, *et al.* Lymphoproliferative disorders after organ transplantation: a report of 24 cases observed in a single center. *J Clin Oncol* 1995;13:961–8.
- 8 Opelz G, Henderson R. Incidence of non-Hodgkin lymphoma in kidney and heart transplant recipients. *Lancet* 1993;342:1514–16.
- 9 Clarke CA, Morton LM, Lynch C, *et al.* Risk of lymphoma subtypes after solid organ transplantation in the United States. *Br J Cancer* 2013;109:280–8.
- 10 <http://www.goeg.at>. Transplantat Jahresbericht. 2014.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow