Facial ulceration in a renal transplant recipient

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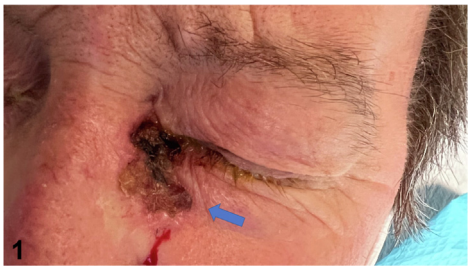

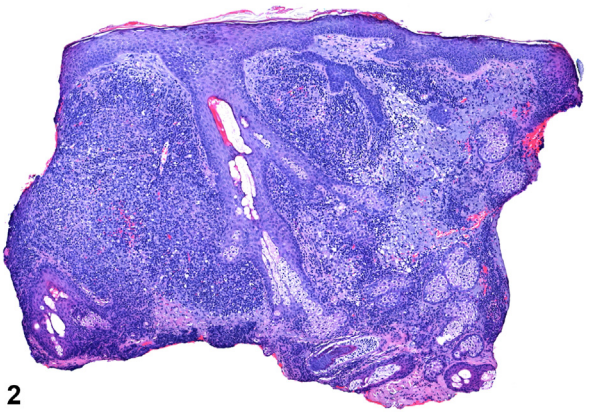

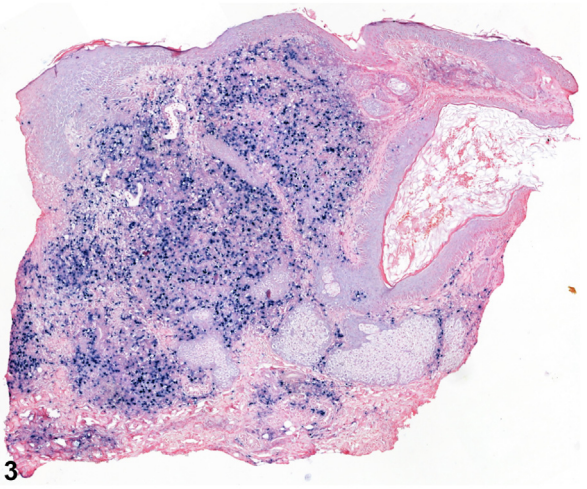

A 60-year-old man presented with a 3-week history of a painless, eroded, nodular, lesion of the left inner canthus (Fig 1). His medical history included binephrectomy and renal transplantation 15 years ago, as well as the surgical excision of a nodular basal cell carcinoma (nBCC) of the same left inner canthus 6 years earlier. The immunosuppressive medication consisted of methylprednisolone (8 mg/day), everolimus, and mycophenolate

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mofetil. A 3-mm punch biopsy stained with hematoxylin/eosin (H/E) revealed a dense dermal lymphoid infiltrate surrounding the pilosebaceous appendages and composed of lymphocytes without notable atypia, associated with numerous plasma cells (Fig 2).

Question 1: What is the most likely diagnosis?

A. Cutaneous leishmaniasis

B. Cutaneous post-transplant lymphoproliferative disorder (cPTLD)

C. Recurrent nBCC

D. Cutaneous cryptococcosis

E. Herpes simplex virus (HSV) infection

Answers:

A. Cutaneous leishmaniasis — Incorrect. Cutaneous leishmaniasis can present with facial ulceration, but our patient does not live in an endemic area and had no relevant travel history. H/E stain would reveal the amastigotes as round basophilic structures inside the macrophages.

B. cPTLD — Correct. PTLDs are a heterogenous group of systemic lymphoid proliferations that may occur during the post-transplantation immunosuppression.[1,2] PTLD is one of the most common and potentially life-threatening cause of malignancies after solid organ transplant.[1,2] The prognosis of PTLD is usually poor with survival rate between 30% to 70%.[2-4] Late onset PTLD, the involvement of internal organs, a central nervous system location, and a T cell lineage or thoracic organ transplantation are associated with a worse prognosis.[3] cPTLD is rather exceptional with approximately 5% of all PTLD cases affecting the skin. Clinically, cPTLD may present with papules, nodules, ulcerations, a maculopapular rash, or, as in our case, can imitate another dermatosis.[2]

C. Recurrent nBCC — Incorrect. Although clinically similar, the rapidity of onset makes nBCC a less likely diagnosis. Nevertheless, the previous surgical excision of an nBCC on the same site could have created an "immunocompromised cutaneous district", increasing the susceptibility to develop an immune-mediated skin disorder such as PTLD.[5]

D. Cutaneous cryptococcosis — Incorrect. Due to the immunosuppression, the patient is at higher risk to develop opportunistic infections. Cutaneous *Cryptococcus* spp. infection can present with polymorphic lesions and mostly occur on the head and neck, but H/E stain would show yeast-like organisms surrounded by a mucinous capsule.

E. HSV infection — Incorrect. HSV infection in the immunocompromised patient can have an atypical (ie, painless, ulcerative) presentation. Histology would show typical viral changes inside the keratinocytes (ie, cytoplasmic vacuolization, nuclei ballooning, and eosinophilic intranuclear inclusion).

Question 2: Which test would be the most appropriate for diagnosis?

A. Blood sample for Epstein-Barr virus (EBV) viral load

B. Positron emission tomography with computed tomography

C. Skin biopsy

D. Tzanck smear

E. Swab sample

Answers:

A. Blood sample for Epstein-Barr virus (EBV) viral load — Incorrect. EBV is a well-known driver of PTLD, leading to the proliferation and transformation of infected B-cells in the context of a declined T-cell immunosurveillance.[1-4] The EBV viral load in the peripheral blood can be measured for the screening and monitoring of PTLD, particularly in high risk patients, but it is not diagnostic as there is no cut-off value.[1,3] Furthermore, up to 20%-50% of PTLD are EBV-negative.[1-4] In these cases, the pathogenesis remains hypothetic.[1-4] To note, 4 weeks prior, our patient had evidence of a strongly positive peripheral blood polymerase chain reaction titer for EBV.

B. Positron emission tomography with computed tomography — Incorrect. These imaging techniques can be used for the initial staging and can help to monitor the response to treatment, but are not diagnostic.[3]

C. Skin biopsy — Correct. Histopathological examination with H/E stain is the gold standard of diagnosis for PTLD. Immunohistochemical stains, in situ hybridization and flow cytometry further help to determinate the subtype of PTLD.[3] The World Health Organization classification divides PTLD in 6 subtypes as follows: 3 non-destructive PTLDs, monomorphic PTLD, polymorphic PTLD, and classic Hodgkin's lymphoma-like PTLD.[1,2,4] In our

case, the final conclusion was a polymorphic EBV-positive cPTLD (Fig 3).

D. Tzanck smear – Incorrect. This test would be useful in the setting of HSV infection, cryptococcosis or leishmaniasis.

E. Swab sample – Incorrect. Culture of a swab sample is useful for the diagnosis of cryptococcosis. Polymerase chain reaction of a swab sample is used for the diagnosis of HSV or leishmaniasis.

Question 3: What would be the first-line treatment?

A. Surgical excision

B. Fluconazole 6 mg/kg once daily for 6-12 months.

C. Intravenous acyclovir 5 mg/kg/8 h for 7 days.

D. Reducing immunosuppressive medications.

E. Sodium stibogluconate, 20 mg/kg once daily for 20 days.

Answers:

A. Surgical excision – Incorrect. This would be first-line treatment for nBCC.

B. Fluconazole 6 mg/kg once daily for 6-12 months – Incorrect. This would be a valid treatment option for cutaneous cryptococcosis.

C. Intravenous acyclovir 5 mg/kg/8 h for 7 days – Incorrect. This would be the treatment of an HSV infection in an immunosuppressed patient.

D. Reducing immunosuppressive medications – Correct. The first-line treatment of PTLD is to reduce iatrogenic immunosuppression. Other treatment strategies include anti-B cell monoclonal antibodies such as rituximab, chemotherapy, adoptive immunotherapy, stem cell transplantation, surgery or radiation, or combination therapies.[1-4] cPTLD usually responds well to the reduction of immunosuppression.[2] In this case, the immunosuppressive regimen of the patient was decreased by discontinuation of mycophenolate mofetil in association with 4 cycles of rituximab 375 mg/m^2, resulting in a complete remission after 3 months.

E. Sodium stibogluconate, 20 mg/kg once daily for 20 days – Incorrect. This would be a therapeutic option for cutaneous leishmaniasis.

Abbreviations used:

ADPKD: autosomal dominant polycystic kidney disease
EBV: Epstein-Barr virus
H/E: hematoxylin/eosin
HHV8: human herpes virus 8
ISH: in situ hybridization
NBCC: nodular basal cell carcinoma
PTLD: post-transplant lymphoproliferative disorder
SOT: solid organ transplant
WHO: World Health Organization

Conflicts of interest
None disclosed.

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