A rare involvement in skin cancer: Merkel cell carcinoma with bone marrow infiltration in a kidney transplant recipient

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ABSTRACT

A 60-year-old man presented with a painless, rapidly growing, haemorrhagic pink nodule on the posterior of his thigh that had developed 1 month previously. He had a diagnosis of IgA nephropathy and had received a renal allograft 7 years before. An excisional biopsy was performed and the diagnosis of Merkel cell carcinoma (MCC) was made. No distant metastases was detected. 10 months after first presentation, due to the development of acute pancytopenia and concomitant FDG PET/CT findings compatible with disease progression, bone marrow biopsy was performed which revealed metastasis of MCC. Dermatologists and oncologists should be aware that MCC could potentially involve the bone marrow in organ transplant recipients. In the follow-up period, a complete blood count should be carried out; FDG PET/CT can be obtained to follow up the metabolic status of the disease and bone marrow biopsy should be performed if necessary.

KEYWORDS: Merkel, bone marrow, transplantation

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Introduction

Merkel cell carcinoma (MCC) is a rare but highly aggressive primary cutaneous neuroendocrine cancer with increasing incidence. MCC is strongly associated with immunosuppression and occurs more frequently in patients with organ transplantation, human immunodeficiency virus infection and haematological malignancies.[1] We present a case of MCC with bone marrow infiltration after renal transplantation, which illustrates the aggressive disease course seen in this patient group.

Case presentation

A 60-year-old man presented to our inpatient dermatology clinic with a painless, rapidly growing, haemorrhagic pink nodule on the posterior of his thigh that had developed 1 month previously. He had a diagnosis of IgA nephropathy and had received a renal allograft 7 years before. He developed chronic active antibody-mediated rejection treated with methylprednisolone, rituximab, intravenous immunoglobulin and plasmapheresis 6 years after renal transplantation. He was taking tacrolimus, mycophenolic acid and prednisolone for rejection currently.

Dermatological examination revealed a solitary, pinkish nodule with haemorrhagic crust on his right posterior upper thigh (Fig 1a, b). An excisional biopsy was performed and histopathological examination showed nest of medium size, monotonous mitosis containing hyperchromatic cells in a thin vascular stroma in the dermis on the ulcer background (Fig 1c, d). Immunohistochemistry showed positive staining

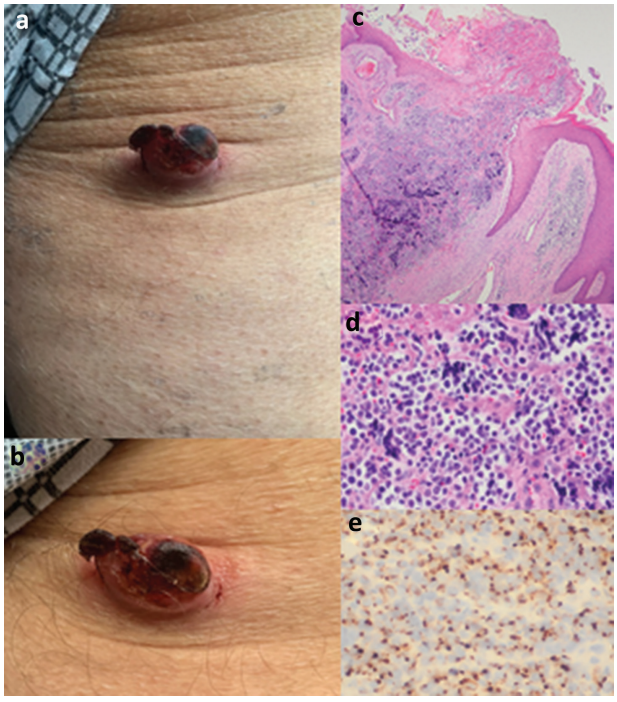

Fig 1. Initial presentation. (a, b) Appearance of the nodule. (c, d) Histopathological examination showed nest of medium size, monotonous mitosis containing hyperchromatic cells in a thin vascular stroma in the dermis on the ulcer background. (e) Immunohistochemistry showed positive staining for cytokeratin-20 in a perinuclear dot-like pattern.

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for cytokeratin-20 in a perinuclear dot-like pattern (Fig 1e), synaptophysin in a diffuse pattern and terminal deoxynucleotidyl transferase in a focal pattern. The tumour cells were negative for CD3, CD20 and thyroid transcription factor 1. These findings were consistent with MCC and confirmed the final diagnosis. (18)F-fluorodeoxyglucose (FDG) positron emission computed tomography (PET/CT) was performed following excision and did not reveal any distant metastases.

The patient received adjuvant radiation therapy to the tumour site postoperatively. 7 months later, control FDG PET/CT showed high FDG uptake in the abdominal-pelvic lymph nodes and right inguinal lymph nodes (Fig 2a–d). An additional focal FDG uptake in the left lobe of the liver was also present. Excisional biopsy from the right inguinal lymph node was consistent with metastasis of MCC. The patient received six cycles of chemotherapy with carboplatin and etoposide after he was found to have widespread nodal involvement for MCC. 3 months later, follow-up FDG PET/CT was obtained. In that PET study, FDG uptake in the abdominal-pelvic lymph nodes was higher than seen in the previous one and additional bone/bone marrow metastases were determined (Fig 2e–g). The results of the FDG PET/CT were compatible with disease progression. The focal FDG uptake in the liver was absent. Additionally, his laboratory work revealed severe pancytopenia with a white cell count of 1.7×10^3 uL, haemoglobin of 7.3 gr/dL and a platelet count of 51×10^3 uL. Due to the development of acute pancytopenia and concomitant FDG PET/CT findings, a decision was made to perform a bone marrow biopsy, which revealed hypercellular bone marrow with diffuse small, round infiltration of malignant cells consistent with metastasis of MCC (Fig 3). The patient, who was scheduled for nivolumab and denosumab treatments, died due to COVİD-19 infection within 2 weeks of the bone marrow biopsy.

Discussion

Solid organ transplantation increases the likelihood of MCC 4.95-fold among elderly adults and MCCs comprise approximately 1% of skin cancers seen in solid organ transplant recipients.[2,3] MCC also has a more aggressive course with increased morbidity

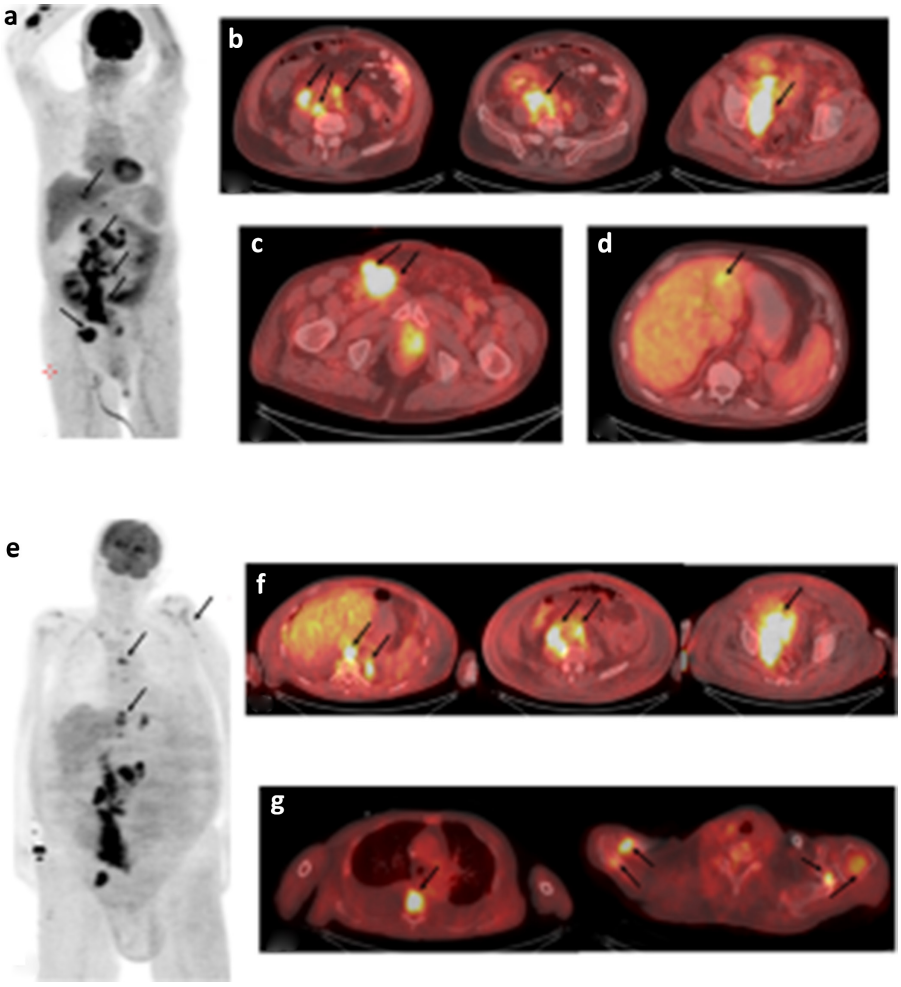

Fig 2. Follow-up following therapy. (a–d) Control FDG PET/CT carried out following adjuvant radiation therapy, 7 months after first presentation. High FDG uptake in the abdominal-pelvic lymph nodes and right inguinal lymph nodes was seen and there was additional focal FDG uptake in the left lobe of the liver. (Fig 2e–g). Follow-up FDG PET/CT following six cycles of chemotherapy with carboplatin and etoposide. FDG uptake in the abdominal-pelvic lymph nodes was now higher and additional bone/bone marrow metastases were determined.

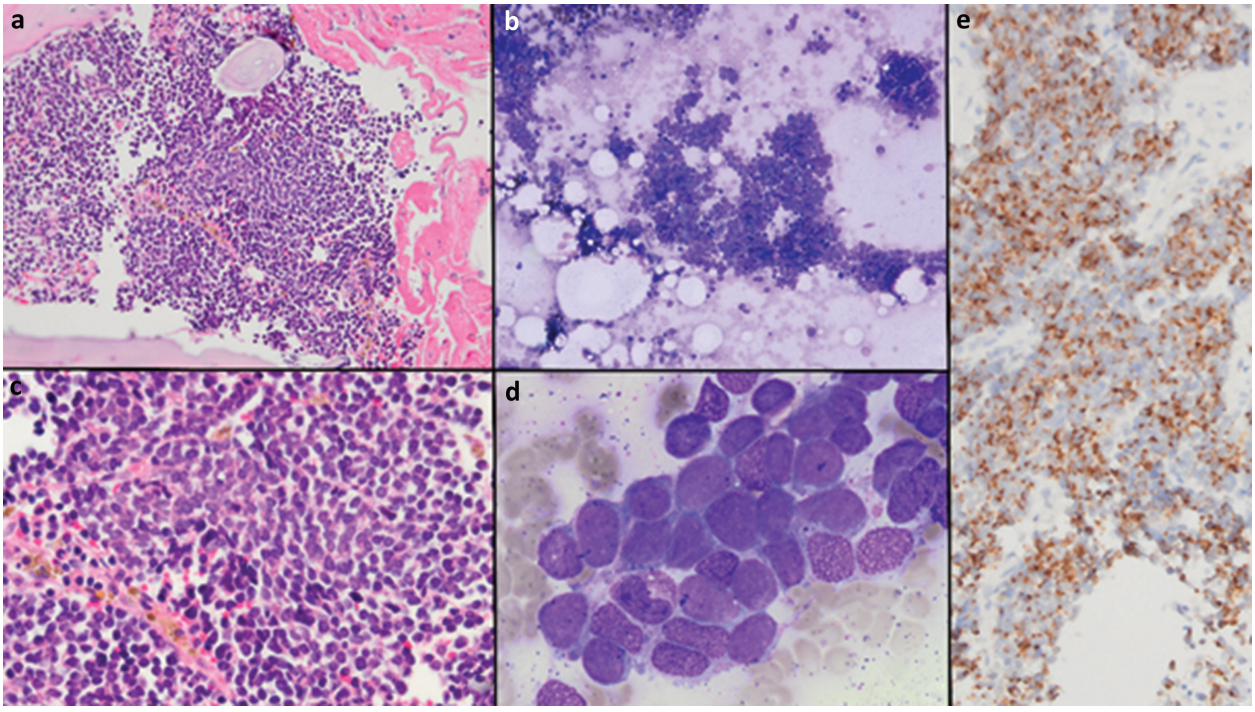

Fig 3. Bone marrow biopsy. (a) Low power magnification of H&E sections demonstrating a diffuse infiltrate that has completely wiped out normal bone marrow elements. (b) High power magnification of H&E sections shows small cells characterised by high nuclear/cytoplasmic ratio and blastic chromatin. (c) Bone marrow aspirate smear shows clusters of small round blue cells (May Grunwald Giemsa stain). (d) Close-up image of bone marrow aspirate smear demonstrating cohesive blastic cells (May Grunwald Giemsa stain). (e) Immunohistochemical stain demonstrating Cam5.2 (cytokeratin) positivity of the infiltrate.

and mortality in renal transplant recipients compared to the general population.[4,5] MCC has a strong tendency to local recurrence and nodal metastases; however, bone marrow involvement is very rare. It has been considered that there is a strong relationship between bone marrow involvement and immunosuppression. Bone marrow biopsy is currently not routinely performed for staging of MCC at the time of diagnosis. Bone marrow involvement in MCC may be under-reported and observed pancytopenia may be associated with therapy-induced immunosuppression.[1,6]

Conclusion

Dermatologists and oncologists should be aware that Merkel cell carcinoma could potentially involve the bone marrow in organ transplant recipients. In the follow-up period, a complete blood count should be carried out; FDG PET/CT can be obtained to follow up the metabolic status of the disease and bone marrow biopsy should be performed if necessary. ■

References

1 Khan A, Adil S, Estalilla OC, Jubelirer S. Bone marrow involvement with Merkel cell carcinoma. *BMJ Case Rep* 2020;13:e234234.
2 Lanoy E, Costagliola D, Engels EA. Skin cancers associated with HIV infection and solid-organ transplantation among elderly adults. *Int J Cancer* 2010;126:1724–31.
3 Penn I, First MR. Merkel's cell carcinoma in organ recipients: report of 41 cases. *Transplantation* 1999;68:1717–21.
4 Ponticelli C, Cucchiari D, Bencini P. Skin cancer in kidney transplant recipients. *J Nephrol* 2014;27:385–94.
5 Koljonen V, Sahi H, Böhling T, Mäkisalo H. Post-transplant Merkel cell carcinoma. *Acta Derm Venereol* 2016;96:442–7.
6 Kressin MK, Kim AS. Metastatic Merkel cell carcinoma in the bone marrow of a patient with plasma cell myeloma and therapy-related myelodysplastic syndrome. *Int J Clin Exp Pathol* 2012;5:1007–12.

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