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CORRESPONDENCE

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A case of ruptured Baker's cyst induced by nivolumab and ipilimumab

Emerging evidences have demonstrated the great efficacy of immune checkpoint inhibitors (ICIs) for various malignancies through enhancing antitumor immune responses. On the contrary, ICIs can cause immune-related adverse effects (irAEs) affecting various organ systems. Here, we report the rare case of ruptured Baker's cyst induced by ICIs.

A 50-year-old Japanese woman referred to our department with a 3-month history of the vulvar enlarging nodule. She had no history of musculoskeletal diseases. Clinical examination revealed a 12×16 mm-sized black nodule on the right vulva (Figure 1A) and ipsilateral swollen inguinal lymph nodes. The tumor was resected with a 10-mm margin, and the sentinel lymph node biopsy (SLNB) was performed. The resection specimen showed massive invasion of round to oval tumor cells with melanin in the dermis (Figure 1B). The tumor thickness was 2.9 mm, and the SLNB was negative. Positron emission tomography-computed tomography (CT) found

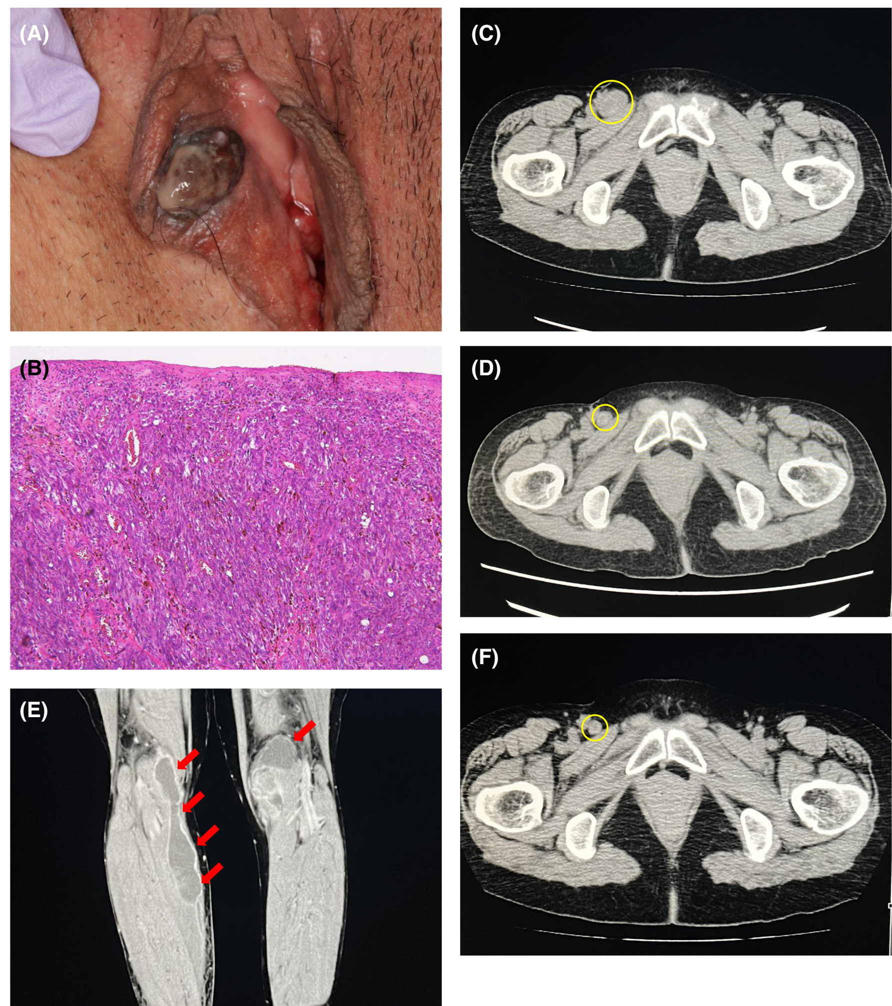

FIGURE 1 (A) Clinical presentation at first visit showing a black nodule on the right vulva. (B) Histological image of the nodule showing massive invasion of round to oval tumor cells with melanin (hematoxylin–eosin staining, ×200). (C) Computed tomography image 20 months later after resection. The yellow circle indicates the swollen inguinal lymph node. (D) Computed tomography image after two courses of the combination of nivolumab and ipilimumab. The yellow circle indicates the swollen inguinal lymph node, which decreased in size. (E) Contrast-enhanced computed tomography image when knee symptoms appeared. Low-density areas with a light edge (red arrow) are present in both knees and the right one extends inferiorly along the gastrocnemius muscle (15.2 cm in long diameter). Laboratory tests showed mild leukocytosis (12,500/μl) and increased c-reactive protein level (4.86 mg/dl) at this time. (F) Computed tomography image 20 months after the administration of first immune checkpoint inhibitor therapy. The yellow circle indicates the inguinal lymph node, which decreased further in size.

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no evidence of distant metastasis. The diagnosis of malignant melanoma pT3bN0M0, stage IIB, was made. After surgery, she was followed up without additional treatment. Twenty months later, the metastasis appeared in right inguinal and external iliac lymph nodes (Figure 1C). The combination of nivolumab and ipilimumab every 3 weeks was started. After two courses, enteritis developed and she received oral prednisone 60 mg daily with the cessation of the chemotherapy, although lymph node metastases decreased in size (Figure 1D). During tapering prednisone, she developed pancreatitis, which was relieved by fasting and supplementation. Prednisone was tapered to 5 mg daily 2 months later and the administration of nivolumab alone was resumed. However, 2 days after the single nivolumab use, bilateral knee pain and right knee swelling appeared. Contrast-enhanced CT revealed that low-density areas with a light edge were present in both knees and that the right one extended inferiorly along the gastrocnemius muscle (Figure 1E). Rheumatoid factor and anticyclic citrullinated peptide antibody were negative. She was diagnosed as ruptured Baker's cyst induced by ICIs. The dose of prednisone was increased to 20 mg daily and salazopyrin was added, resulting in the gradual improvement. Although nivolumab was stopped, metastatic lesions have kept the decrease in size for more than 20 months (Figure 1F).

Most musculoskeletal irAEs are mild arthralgia, whereas a minority of patients develop inflammatory arthritis (IA) with more pronounced pain.[1,2] In this report, we presented the seronegative IA case presenting as ruptured Baker's cyst during the ICI treatment. Baker's cysts rarely manifest alone and are usually associated with other articular inflammatory conditions.[3] The history of more than one irAE like our case is associated with a more persistent course of arthritis.[4] Mild persistent inflammation without subjective symptoms might exist after first ICI therapy in our case. There has been one report of ruptured Baker's cyst during the nivolumab treatment.[1] Consistent with the above hypothesis, the patient developed occasional self-remitting bilateral knee joint pain preceded by several other irAEs prior to the onset of ruptured Baker's cyst. It is important to pay attention to potential musculoskeletal irAEs in ICI-treated patients with multiple irAEs.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS STATEMENT

Approval of the research protocol: No human participant was involved in this study.

Informed Consent: Informed consent was obtained from the patient.

Registry and the Registration No.: N/A.

Animal Studies: N/A.

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REFERENCES

1. Thapa B, Ali A, Nair R, Vashisht R, Calabrese C. A case of severe seronegative inflammatory arthritis due to nivolumab and review of the literature. Case Rep Rheumatol. 2019;2019:1326734.
2. Melissaropoulos K, Klavdianou K, Filippopoulou A, Kalofonou F, Kalofonos H, Daoussis D. Rheumatic manifestations in patients treated with immune checkpoint inhibitors. Int J Mol Sci. 2020;21:3389.
3. Herman AM, Marzo JM. Popliteal cysts: a current review. Orthopedics. 2014;37:e678–84.
4. Braaten TJ, Brahmer JR, Forde PM, Le D, Lipson EJ, Naidoo J, et al. Immune checkpoint inhibitor-induced inflammatory arthritis persists after immunotherapy cessation. Ann Rheum Dis. 2020;79:332–8.