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Correspondence

A case of cytomegalovirus-induced skin erosions mimicking bullous pemphigoid relapse

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Dear Editor:

We report a case of bullous pemphigoid (BP) that presented with skin ulcers induced by cytomegalovirus (CMV) infection and mimicked BP relapse.

An 87-year-old male was admitted to our hospital for multiple blisters on the whole body for a week (Day 0) (Figure 1a). A skin biopsy specimen from the trunk showed a subepidermal blister (Figure 1b). His CLEIA titer for anti-BP180 antibody was 298.3 U/ml (normal range: <9). We made diagnosed BP, and the bullous pemphigoid disease area index (BPDAI) was 67. We treated him with prednisolone at 50 mg/day on Day 4 after admission, and the lesions largely resolved. On Day 23, nine erosions which did not accompany blisters appeared not on the anogenital area, but on the buttocks (Figure 1c), and we detected cytomegalovirus antigenemia in three CMV-positive cells per two slides by the C10/11 method with immunohistochemical staining by BML Inc. (Tokyo, Japan). We diagnosed a mild local relapse of BP. Anti-BP180 antibody was 632.9 U/ml on Day 8 and 278.5 U/ml on Day 22. We tapered the prednisolone to 45 mg/day on Day 22 and administered intravenous immunoglobulin (IVIG) 0.4 g/kg/day for five days. Then, we tapered the prednisolone by 5 mg/day per week. CMV-positive cells increased to 18 cells on Day 27. We started ganciclovir as a maintenance dose. Although the patient had no organ symptoms, including pancytopenia, lung lesions and eye lesions, CMV-positive cells increased to 174 cells per two slides on Day 34. Thus, we increased the ganciclovir at the initial treatment dose. On Day 40, he presented hematemesis and melena, and he died of bleeding from gastric ulcers despite of vonoprazan administered to prevent gastric ulcers associated with stress and high-dose steroid treatment. The erosions remained until his death. A skin biopsy specimen from the trunk on Day 34 showed infiltrating cells with intranuclear inclusion bodies that stained positive for anti-CMV antibody but did not present eosinophilic infiltration in the dermis (Figure 1d, e), and after his death, we

diagnosed the erosions as having emerged from CMV infection. The clinical course is summarized in Figure 1f.

Various opportunistic infections including CMV often occur as a result of immunosuppressive treatments for autoimmune bullous diseases [1], [2]. CMV can affect almost all organs and cause tissue-invasive diseases. CMV infection occasionally shows cutaneous manifestations in immunocompromised patients and causes various skin lesions, such as petechiae, nodules and ulcers [3]. Most of the lesions affected by CMV are erosions and ulcers localized mainly to the anogenital area [4]. The lesions of BP are located on sites expressed to mechanical stress. When BP patients present erosions and ulcers, we should consider not only herpes simplex and herpes zoster infection, but also CMV infection. We assumed that the present CMV erosions occurred via hematogenous spread to the buttocks. Asano-Mori et al. reported that high-grade CMV antigenemia as >50 positive cells per two slides is associated with a significantly elevated risk of CMV disease [5]. We considered the patient's reappearing erosions to be BP relapse, even though the index of anti-BP180 antibody had decreased. However, from the absence of blisters and eosinophilic infiltration, we concluded that the BP had not relapsed. We did not recognize the erosions as CMV skin lesions because the numbers of CMV positive cells were low. CMV antigenemia and real-time PCR for CMV in the blood are useful for monitoring CMV infection. Ganciclovir administration at a maintenance dose is recommended when more than 20 CMV-positive cells are detected in patients with CMV non-syndromic infection. Ganciclovir administration at the initial treatment dose is recommended for patients with symptoms of CMV infection [6]. We assumed the cause of death to be CMV gastric ulcers in our case. We should have selected not ganciclovir preemptive therapy, but a treatment for developed CMV disease, even though there were fewer than 50 CMV positive cells. We consider that, when antigenemia progresses despite steroid reduction and IVIG, a strong therapy should be initiated promptly. The present case further suggests that not only should checking for

CMV antigenemia be considered, but so should taking a skin biopsy to precisely diagnose reappearing erosions in BP patients with CMV antigenemia, even if the CMV antigenemia grade is low.

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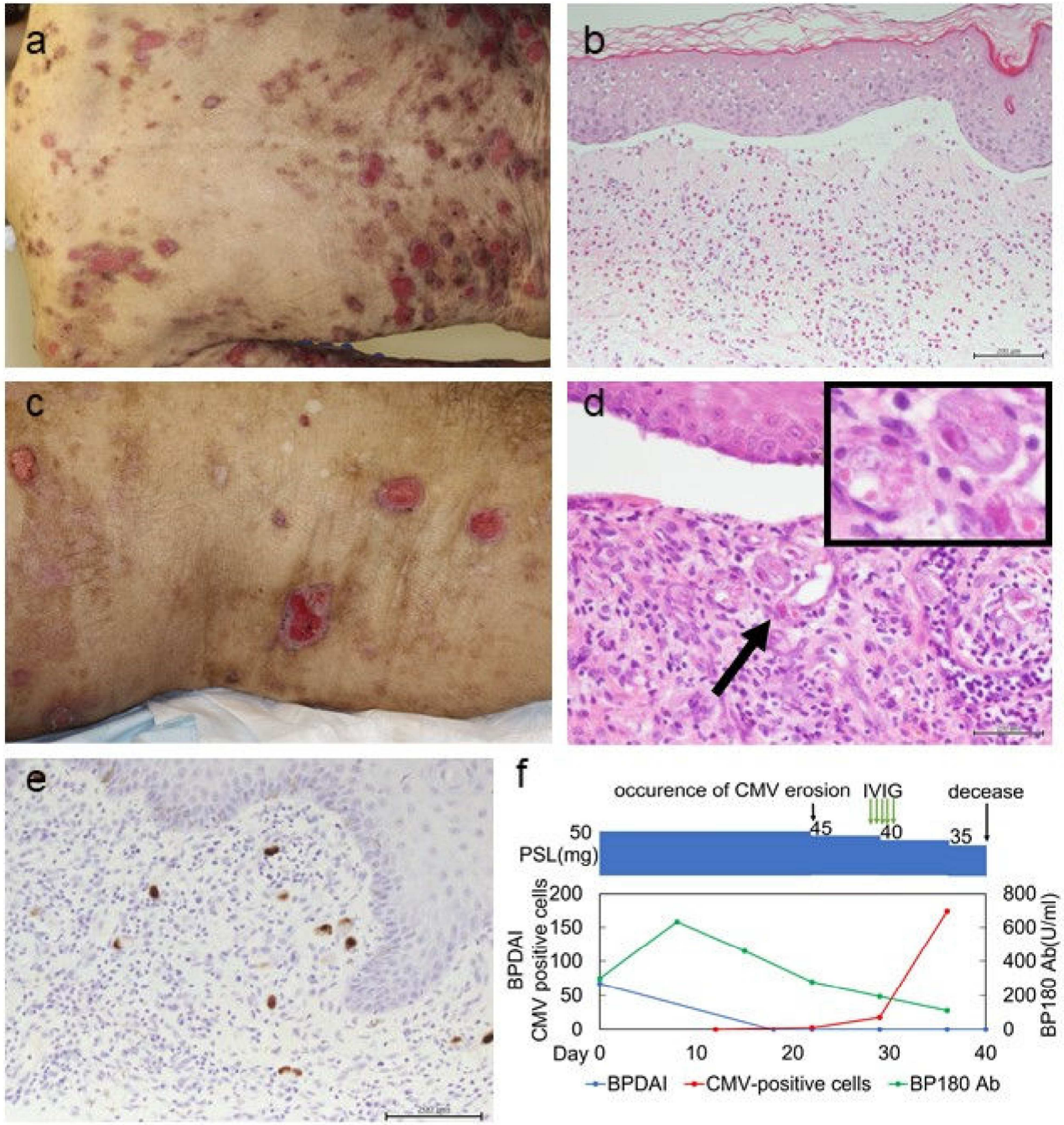
Figure legends

Figure 1. Clinical and histopathological features of the present case, and the clinical course.

(a) The patient shows blisters and erosions on the whole body. (b) A skin biopsy specimen from a blister on the trunk at BP onset shows a subepidermal blister (hematoxylin-eosin [HE], original magnification x200). (c) The patient has erosions on the buttocks on Day 23. (d) A skin biopsy specimen from an erosion on the buttocks on Day 23 shows the infiltration of cells with inclusion bodies (arrows) in the dermis. The inset shows an enlarged view of the inclusion bodies (HE, original magnification x400). (e) Some infiltrating cells in the dermis have inclusion bodies positively stained with anti-CMV antibody (anti-CMV antibody stain, original magnification x200). (f) The clinical course in the present case. We started prednisolone at 50 mg/day on Day 4. IVIG and the prednisolone dosage are indicated by green arrows and blue boxes, respectively. The Bullous Pemphigoid Disease Area Index (BPDAI) and the numbers of peripheral blood CMV positive cells per two slides are indicated by the blue and the red line, respectively, on the left Y-axis. Anti-BP180 antibody (BP180 Ab) titers are indicated by the green line on the right Y-axis.


a
b
c
d
e
f
occurence of CMV erosion
IVIG
decease
50
PSL(mg)
45
40
35
BPDAI
CMV positive cells
200
150
100
50
0
800
600
400
200
0
BP180 Ab(U/ml)
Day 0
10
20
30
40
BPDAI
CMV-positive cells
BP180 Ab