Case of bullous pemphigoid in a 28-year-old woman affected by tuberous sclerosis complex

Dear Editor,

A 28-year-old woman accompanied by her mother was referred to our department for evaluation of an erythematous pruritic plaque of the left leg. A diagnosis of tuberous sclerosis complex (TSC) was made at the age of 2 years. Molecular analysis revealed a sporadic mutation in the *TSC-2* gene, which is localized on the short arm of chromosome 16 (16p13) and encode for tuberin. Although no epileptic attack had been observed since the age of 15 years, the patient continued with prophylactic anticonvulsant therapy with vigabatrin. In our patient, the TSC is associated with autism with a severe grade of intellectual disability. Her medical reports described the presence of cortical dysplasias, retinal hamartomas, dental enamel pits and intraoral pits. In October 2006, at the age of 19 years, after bilateral nephrectomy due to polycystic kidneys related to TSC, the patient received a renal graft transplant from a deceased donor. After kidney transplantation she took mycophenolate mofetil without side-effects or transplant rejection. The mother reported that the erythematous plaque of the left leg was mildly itchy and appeared 6 months before the visit. Physical examination revealed a tense bulla on the erythematous plaque of the left leg (Fig. 1a) and the presence of

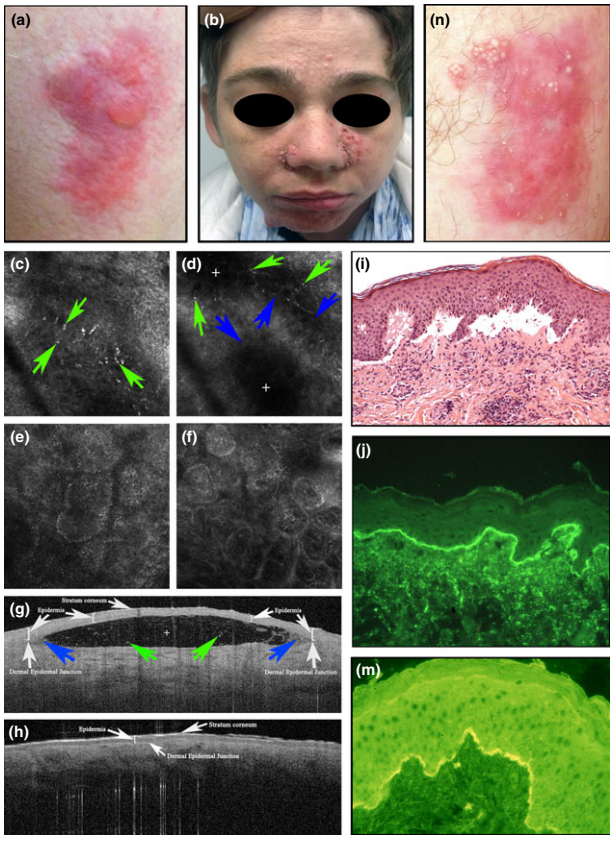

Figure 1. The patient had a tense bulla on an erythematous pruritic plaque of the (a) left leg and (b) facial angiofibromas. (c) Reflectance confocal microscopy (RCM) performed on the tense bulla of the left leg revealed substantially normal superficial layers of the epidermis and the presence of a mild spongiosis that appeared as a darker area, compared with the surrounding epithelium with increased intercellular spaces, in which were present bright and pinpoint structures corresponding to inflammatory cells (green arrows). (d) RCM showed at the level of the dermoepidermal junction (DEJ) the presence of a dark, ovoid to round, well-demarcated area filled by some bright and pinpoint structures, which correspond on histology to the subepidermal bulla (+) with some inflammatory cells inside (green arrows). Furthermore, RCM revealed the presence of mildly refractive homogeneous material inside of this dark area that appeared like grayish material corresponding to fibrin deposition (blue arrows). (e,f) Instead, RCM executed on the healthy skin surface adjacent to the erythematous plaque showed normal layered architecture of the skin. (g) Optical coherence tomography (OCT) performed on the tense bulla of the left leg revealed the presence of subepidermal bulla (+) that appeared like dark, ovoid to round, well-demarcated lobule at the level of the DEJ. Furthermore, some inflammatory cells (green arrows), which looked like grey pinpoint structures, infiltrated the cleft and this may be reflected as more grayish appearance of the bulla in the OCT image. Moreover, OCT showed the presence of fibrin deposit (blue arrows) inside the subepidermal cleft that appeared like grayish homogeneous material. (h) Instead, OCT executed on the healthy skin surface adjacent to the erythematous plaque showed the normal layered architecture of the skin. (g,h) The stratum corneum, epidermis and DEJ are marked by white arrows. (i) Histopathological findings of the skin biopsy revealed at the level of the DEJ a subepidermal bulla with some inflammatory cells and fibrin deposition inside, an infiltrate of inflammatory cells with many eosinophils in the upper dermis and a mild spongiosis with variable amount of inflammatory cells between epidermal keratinocytes (hematoxylin–eosin, original magnification ×10). (j) Direct immunofluorescence showed immunoglobulin (Ig)G and C3 deposit to the DEJ, while IgM and IgA were negative. (m) Indirect immunofluorescence revealed antibodies directed to the DEJ with a titer of 1:40. (n) After 4 months of topical corticosteroid therapy, we observed the presence of milia and post-inflammatory pigmentation.

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facial angiofibromas (Fig. 1b) related to TSC, while did not reveal other skin or mucosal lesions. The mother reported that a few days before the visit she noticed for the first time the appearance of a blister. Clinical examination along with reflectance confocal microscopy (RCM) (Vivascope 3000®; Caliber I.D., Rochester, NY, USA) and optical coherence tomography (OCT) (VivoSight®; Michelson Diagnostics, Maidstone, UK) performed on the tense bulla of the left leg suggested a diagnosis of bullous pemphigoid (BP) (Fig. 1c,d,g).[1,2] Instead, RCM and OCT executed on the healthy skin surface adjacent to the erythematous plaque showed normal layered architecture of the skin (Fig. 1e,f,h). Then, we executed indirect immunofluorescence and two biopsies, one for histopathological examination and one for direct immunofluorescence. Histopathological examination confirmed our diagnostic suspicion (Fig. 1i). Direct immunofluorescence showed immunoglobulin (Ig)G and C3 deposit to the dermoepidermal junction (DEJ) (Fig. 1l). Indirect immunofluorescence revealed antibodies directed to the DEJ with a titer of 1:40 (Fig. 1m). Moreover, we performed enzyme-linked immunoassay (ELISA) test: anti-BP180 IgG 106.89 U/mL and anti-BP230 IgG 1.20 U/mL. Based on all these findings, a diagnosis of BP was made. The patient subsequently underwent only topical corticosteroid therapy with clobetasol propionate 0.05% cream that was tapered over 4 months: every day in the first month, every other day in the second month, twice a week in the third month and once a week in the fourth month. After the end of the therapy, we observed the presence of milia and post-inflammatory pigmentation (Fig. 1n). In 2 years of follow up, there was no evidence of relapse or any additional lesion on other sites. In the published work, to the best of our knowledge, the association between BP and TSC is not reported.[3–5] We did not find a correlation between BP and TSC, and we think that the occurrence of both diseases in a single individual is only accidental and extremely rare.

Written informed consent was obtained from the patient's legal guardian(s) (including the patient's mother) for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Chemotherapy-induced inflammation of seborrheic keratoses due to pemetrexed treatment

Dear Editor,

Inflammation of seborrheic keratoses (ISK) is a rare adverse cutaneous reaction to chemotherapy. It is characterized by the inflammation of existing seborrheic keratosis (SK) after the administration of chemotherapy.[1] Here, we report two cases of ISK induced by pemetrexed. This is the first report about pemetrexed-induced ISK.

Case 1 involved a 75-year-old Japanese woman with lung cancer who developed numerous pruritic rashes 7 days after the injection of pemetrexed. A physical examination revealed inflammatory erythema, which was confined to multiple small brown papules on her neck and upper chest (Fig. 1a,b). A histopathological examination detected numerous infiltrates of lymphocytes and eosinophils in the upper dermis around SK (Fig. 1c,d). The number of infiltrated $CD4^+$ and $CD8^+$ cells were approximately the same (data not shown). The SK at other sites were not inflamed. The erythema around the SK subsided 7 days after difluprednate ointment treatment (Fig. 1e,f). The

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