Bullous pemphigoid triggered by radiotherapy for breast cancer

Pemphigoïde bulleuse déclenchée par une radiothérapie pour un cancer du sein

Bullous pemphigoid (BP) is the most common autoimmune subepidermal blistering disease of the skin and mucous membranes. It is characterized by autoantibodies against structural proteins of the dermal–epidermal junction and responsible for itch, localized or generalized bullous lesions followed by skin erosions. It is usually an idiopathic condition affecting mainly the elderly [1]. However, various exogenous factors have been implicated in the pathogenesis of the disease, such as medications, trauma, surgery, UV phototherapy [2] or percutaneous ionizing radiation (radiotherapy, RT) [3,4]. We report on a case of BP that was triggered within a month after RT for breast cancer.

Observation

A 68-year Finnish woman was referred for the management of a recent blistering disease. Her medical history was notable for a ductal adenocarcinoma of the right breast diagnosed in November 2015. The tumor was strictly localized to the right breast with no lymph node or metastatic dissemination. It was 10 mm, staged grade II, expressed estrogen receptor (100%), but was progesterone receptor and HER-2 negative. After tumor resection, she received postoperatively a percutaneous RT of 40.05 Gy in 2.67 fractions for three weeks from the end of December to the end of January. The hypofractionated regimen corresponded to 45 Gy in 2 Gy fractions with an α/β value of 3.5 Gy. Aromatase inhibitor (letrozol) was rapidly stopped because of side effects (fatigue, fever, heart rhythm issue). After RT, she developed an itchy rash mainly localized to the right breast before extending to the whole body that resolved with oral anti-histamines. Within less than a month after RT, itchy vesicles and blisters appeared on the right breast and led to larger hemorrhagic blisters and erosions (figure 1A). She then presented 2-3 weeks later similar lesions mainly on the extremities with a gloves and socks disposition (hands, wrists and soles, figure 1B). More discrete itchy papules were located on the thighs and elbows. The mucosae were intact. Histopathological analysis showed a subepidermal blister with an inflammatory infiltrate of lymphocytes, macrophages and eosinophils. Direct immunofluorescence microscopy showed linear deposits of C3, IgG, and some IgA along the dermal–epidermal junction. ELISA B180 NC16A antibodies (Abs) were positive at 100 U/mL (N < 9). Desmoglein 3 Abs were found at a low level of 13 (ELISA, N < 7). Hypereosinophilia was elevated at 980/mm³. Oral prednisolon at the dose of 40 mg/day (0.6 mg/kg/d) in association with superpotent corticosteroid ointment (clobetasol propionate) on the affected areas allowed a control of the disease. At one month of follow-up and at a prednisolone dosage of 20 mg daily, BP was in complete remission with no symptoms, or new blisters. The patients presented only fully healed non-infiltrated reddish lesions (figure 2). We plan to taper gradually the prednisolone dosage of 5 mg every 2 weeks over the next 2 months.

Figure 1

A. Well demarcated erythema with post-bullous erosions and crusts of the right breast previously treated with radiotherapy. B. Round and polycyclic post-bullous erosions of the hands and forearms
During RT rechallenge [8]. Hormonal therapy has been some-
induced by radiation. Another hypothesis is that the patient
irradiated area may be explained by the local modifications
with unmasking antigens. The localization of the disease to the
formation of auto-Abs by the alteration of the basal membrane
expected that the tissue damages induced by the RT induce the
of side effects. The mechanisms remain unclear, but it is sus-
tected that the tissue damages induced by the RT induce the
formation of auto-Abs by the alteration of the basal membrane
with unmasking antigens. The localization of the disease to the
irradiated area may be explained by the local modifications
induced by radiation. Another hypothesis is that the patient
would be predisposed to develop BP (with pre-existing low
levels of Abs) and the RT would enhance the deposition of
Abs in damaged skin [4]. The diagnosis is based on histopatho-
logical examination and direct immunofluorescence. The man-
agement is similar to idiopathic BP and seems to achieve most
of the time proper control [4]. Therapeutic options include
application of local corticosteroid ointments, oral corticosteroids
and immunosuppressive treatments according to the extension of
these disease [1].

BP can occur early or lately after RT. This side effect should be
known by oncologists and radiotherapists to allow its rapid
identification and proper management.

Disclosure of interest: the authors declare that they have no competing
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Favorable outcome after one month of oral prednisolon

Discussion

We report here a new case of BP that has occurred rapidly after
completion of RT for breast cancer. This is a rare adverse event
[3,4]. A review published in 2007 collected 27 reports from
1982 to 2007 [3]. A Pubmed search was performed in May
2016 using the keywords “bullous pemphigoid AND radiother-
apy” and led us to estimate now the number of reported cases
to approximately 40 cases, knowing that additional cases could
go unnoticed if simply mentioned in series of patients with BP
[5] or just not reported.

RT associated BP affects mainly women with breast carcinomas
[3,4]. Nevertheless, it has been reported also in male patients,
and with other cancers (vulva, lung, esophagus) [3,4]. Nguyen
et al. found that BP occurred in 70% of the cases after RT
completion and in 30% during RT [4]. The reviews are conflicting
regarding whether BP occurs mainly within the first year [4] or
after the first year of RT [3]. According to Mul et al. [3], cases
within the first month after RT are uncommon. The median total
dose of radiation is around 50 Gy. Clinically, BP is usually local-
ized and restricted to the site of RT, but it can extend outside the
irradiated areas and even become generalized, or sometimes be
generalized immediately [3,4]. Rarely, the lesions are only
outside the radiation area [3,4]. Furthermore, cases of exacer-
bation of pre-existing BP during RT have been reported [6,7] or
during RT rechallenge [8]. Hormonal therapy has been some-
times involved, but in our case, it was stopped rapidly because
of side effects. The mechanisms remain unclear, but it is sus-
pected that the tissue damages induced by the RT induce the
formation of auto-Abs by the alteration of the basal membrane
with unmasking antigens. The localization of the disease to the
irradiated area may be explained by the local modifications
induced by radiation. Another hypothesis is that the patient

Figure 2

Favorable outcome after one month of oral prednisolon