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LETTER

Four cases of hemorrhagic herpes zoster associated with dabigatran therapy

Dear Editor,

In 2015, we reported three patients in therapy with clopidogrel who developed hemorrhagic herpes zoster (HHZ).[1] In the last months, we observed four patients with HHZ who were in therapy with dabigatran, an oral anticoagulant. This drug acts by inhibiting free and fibrin-bound thrombin.[2] It was initially approved to prevent embolisms in patients with non-valvular atrial fibrillation.[2] Dabigatran showed to be effective and well tolerated: esophagitis, gastrointestinal hemorrhages, myocardial infarction, hepatitis, nephritis and allergic reactions are rare side effects.[2] Furthermore, coagulation monitoring is unnecessary.[2] To our knowledge, only one case[3] of HHZ associated with dabigatran therapy was reported in the literature.

The patients were four Caucasian females aged 73, 69, 85, and 69 years, respectively, in therapy with dabigatran (150–220 mg/day) for 3–8 weeks. Two patients were subjected to recent hip or knee arthroplasty; two patients were affected by peripheral arterial disease. In two patients, HZ was lumbosacral (Figure 1A); in one patient it was thoracobrachial (Figure 1B) and in one patient it was cervicobrachial (Figure 1C). Diagnosis of HZ was based on clinical picture (painful erythematous, vesicular and purpuric lesions along a dermatome) and cytological examinations (presence of multinucleated giant cells with ballooning degeneration; presence of multiple nuclei, with different shape and size). Laboratory examinations showed increase in erythrocyte sedimentation rate in all patients, leukocytosis in two patients, monocytosis and mild thrombocytopenia in one patient each. Positive anti-varicella zoster virus IgG and IgM were detected in two patients. Complete remission without complications was observed in all patients with valacyclovir (3 g/day for 7 days). In all patients, dabigatran was not stopped. Follow up (≤9 months) was negative.

HHZ is a very rare variety of HZ. In a group of 107 patients with HZ, HHZ was diagnosed in three cases.[4] HHZ usually occurs in immunocompromised patients because of chronic polyarthritis,[5] colon carcinoma,[6] Evans syndrome,[6] diabetes,[7] kidney transplant,[8] idiopathic thrombocytopenic purpura,[9] rheumatoid arthritis.[10,11] In addition, several patients were in therapy with systemic corticosteroids[5,8,9,11] or methotrexate.[10] An additional association of HHZ is with HIV infection[12,13]: in a group of 527 HIV-positive males with HZ, the hemorrhagic variety was recorded in 20 of them (3.8%).[11,12]

In summary, we reported four cases of HHZ in patients in therapy with dabigatran. No other possible causes of HHZ (diabetes, autoimmune diseases, malignant tumors, transplants, AIDS, Coronavirus Disease-19, previous or concomitant therapy with corticosteroids or immunosuppressive drugs) were established in these patients. Two of them had mild thrombocytopenia before the appearance of HHZ. In another patient, mild thrombocytopenia (113.000 platelets/mm^3) was observed when he was admitted to hospital. It was hypothesized that thrombocytopenia makes these patients more susceptible to the appearance of HHZ.[3] However, in these patients, we cannot consider HHZ as a true side effect of dabigatran: the latter may be considered as an uncommon risk factor for the development of purpuric-hemorrhagic lesions in patients with HZ.

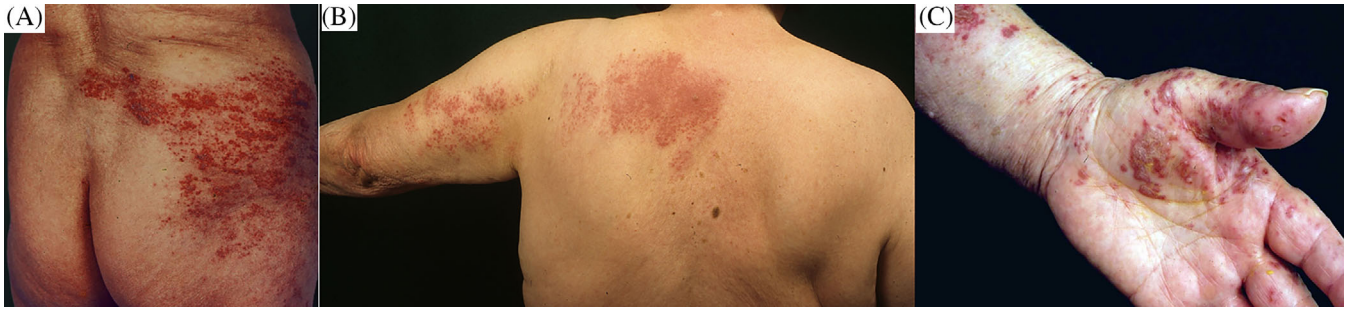

FIGURE 1 (A) Lumbosacral HHZ. (B) Thoracobrachial HHZ. (C) Cervicobrachial HHZ

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Informed consent to publish photographs has been obtained by the patients.

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