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Case Report

Panniculitis at the Site of Subcutaneous Interferon Beta Injections in a Patient with Multiple Sclerosis

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Abstract

Interferon-β (INF-β) is associated with a high frequency of side effects, but severe local skin reactions are still rare. We report the case of complicated panniculitis induced by subcutaneous INF-β-1a injections in a 30-year-old woman, with a multiple sclerosis history. The patient developed, four years after the start of subcutaneous INF-β-1a treatment, painful erythematous ulcerated induration, which evolved into induration and fibrosis lesions. Through this case report, we would like to emphasize on the importance of preventive measures, to avoid such severe cutaneous adverse event, which may lead to lack of compliance and disease recrudescence.

Keywords: Panniculitis; Interferon Beta; Multiple Sclerosis

Introduction

Interferon-β (INF-β) is used for the treatment of inflammatory diseases, especially multiple sclerosis (MS). This last can decrease the frequency of exacerbation of MS by approximately 30% [1]. However, INF-β is associated with a high frequency of side effects, among which we cite local skin reactions to subcutaneous injection, such as pain, inflammation and induration at the injection site [2]. These local reactions can resolve spontaneously or with symptomatic treatment and are rarely severe.

Materials and Methods

We report the case of complicated panniculitis induced by subcutaneous INF-β-1a injections in a patient with MS.

This case was notified on December 2019 and was analyzed according to the French updated method for the causality assessment of adverse drug reactions [3].

Case Report and Discussion

A 30-year-old woman, with a MS history, was prescribed, since 2015, INF-β-1a, at the dose of 44 µg, three times a week. However, she did not always observe injection-side-rotation. One year later, she begun to develop, transient painful and inflammatory lesions at the injection sites, which used to regress spontaneously. In 2019, i.e. four years after the start of treatment, she developed painful erythematous induration, which ulcerated secondarily (Figure 1) and then evolved into induration and fibrosis lesions, so much that the treatment does not pass anymore into the skin.

Histological analysis confirmed the diagnosis of panniculitis. Investigations for common etiologies of panniculitis were excluded: no signs were found for lupus erythematous, scleroderma or dermatomyositis. Bacterial or other infectious agents were also excluded.

The patient was referred to the National Center of Pharmacovigilance. There, the case was assessed as I4(C1S3) according to the French updated method for the causality assessment of adverse drug reactions.

Figure 1: Cutaneous ulceration at the site of injection of INF-β.

The responsibility of INF-β-1a injections was retained in the genesis of the panniculitis because of: the suggestive location of the event (at the site of injections) and the negative investigations for other etiologies.

Local skin reactions after subcutaneous injections of INF-β-1a, in MS, are common and usually consisting of mild and localized erythema without induration, which resolve spontaneously [4]. Middle-aged-women are the most affected by this cutaneous side effect [5]. Severe skin reactions with INF-β-1a such as ulceration, necrosis and panniculitis are rare. In literature, few cases of panniculitis due to INF-β have been reported. Ball., *et al*. [6] reported five cases and Soria A., *et al*. [7] reported two cases of panniculitis induced by INF-β-1a in patients with MS.

The exact mechanism of panniculitis induced by INF-β-1ais still unknown [2]. Local inflammation can be explained by the immunological effect of IFN-β at the injection site. This effect can be partially due to transcriptional induction of chemokines (CXCL10 and CCL2), resulting in inflammatory cells extravasation [8,9]. Another theory has been put forward concerning the role of IL-2 in the genesis of panniculitis. In fact, lobular panniculitis was observed after subcutaneous administration of IL-2 [10]. Further studies are needed to confirm this theory.

Some factors have been associated with local skin reactions after INF-***β*** injections, such as, poor injection technique, inadequate skin cleansing and repeated administration at the same site [11]. Panniculitis can then be prevented by raising the patient's awareness of the importance of the rotation of injection sites, the manual palpation and the regular examination of all injection sites. Non-steroid anti-inflammatory gels and local corticosteroids can help patients and improve their compliance [5].

Once the side effect installed, we can switch to the intramuscular route [12]. Adequate training and automated injection devices may help to ensure a correct injection angle, so that to avoid cutaneous side effects with this route [13]. In fact, improperly administered intramuscular injection may also rarely be the source of skin adverse effects [14].

Conclusion

INF-***β*** in MS, has frequent side effects, which may lead to lack of compliance and rapid recrudescence of the disease. Through this case, we emphasize on the importance of preventive measures, to avoid this kind of complications and then to ensure good compliance.

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