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Case report

Stevens Johnson Syndrome in a patient undergoing gynaecological brachytherapy: An association or an incident?

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ABSTRACT

Background: Stevens Johnson Syndrome and Erythema Multiforme are hypersensitivity skin reactions generally arising in the context of multiple causes. Radiation therapy is considered to be one of these causes, although most reports are hindered by concomitant medications.

Aim: The aim of this paper was to present a case of Stevens Johnson Syndrome arising in a patient undergoing gynaecological brachytherapy with an unusual presentation.

Case: We describe a case of a 56-year-old woman with endometrial cancer undergoing adjuvant gynaecological radiotherapy. While undergoing a gynaecological brachytherapy boost, she developed bilateral conjunctivitis that progressed to oral mucositis and pruritic erythema with sloughing of the skin on her arms and legs but not the torso or irradiated fields (namely the vaginal mucosa).

Conclusion: This case illustrates the association of RT/SJS; however, it also raises the question of patients undergoing RT being more susceptible to SJS as opposed to a direct cause of the disease.

1. Background

Erythema Multiforme (EM) is a mild immune-mediated skin reaction characterised by targetoid lesions on the skin that may (EM major) or may not (EM minor) affect the mucosae. Stevens Johnson Syndrome (SJS) is a severe idiosyncratic reaction characterised by fever and mucocutaneous lesions leading to epidermal necrosis and sloughing. Both these nosologic entities are often associated with medications, although they might be triggered by other causes such as infections, vaccinations and foods.[1]

The association of radiation therapy (RT) and Erythema Multiforme or Stevens Johnson Syndrome has been described in the literature in several reports[2–13]; however, most of these describe cases of radiation therapy in association with medications, phenytoin being the most prevalent of these.[10–13] There is, however, a report of sparing SJS in irradiated fields in a patient undergoing radiotherapy.[14]

We experienced a case of SJS in a patient undergoing gynaecological brachytherapy and report it here.

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2. Case report

A 56-year-old Caucasian woman with a history of hypertension (medicated with irbesartan and hidroclorothiazide association) and osteoporosis (medicated with weekly alendronic acid) was diagnosed with an endometrial adenocarcinoma grade I stage IIB. She underwent hysterosalpingo-oophorectomy with lymphadenectomy. Eight weeks later, she received 50.4 Gy in 28 fractions of 1.8 Gy with a box technique using 15 MeV photons over 6 weeks with grade I genito-urinary toxicity, but without skin toxicity. Subsequently, she started a high dose-rate brachytherapy boost, with an intended full dose of 24 Gy in 4 weekly fractions of 6 Gy with a 30 mm wide vaginal cylinder.

A few days after the second fraction, a bilateral ocular hyperaemia with pruritus appeared. The patient was referred to an ophthalmologist, who prescribed ocular cloramphenicol. However, there was no improvement and these symptoms soon progressed to mild dysphagia. Except for the ocular antibiotic, no medication had been introduced during the post-surgery period. During pre-fraction observation an oral mucositis characterised by erosions and crusting as well as oedema of the lips and tongue were recognised. The vaginal mucosa was discretely hyperaemic and irregular, but there were no other observable lesions or vaginal discharge. She underwent the third fraction of brachytherapy; however, a few days later there was symptomatic progression with skin pain and erythroderma that progressed to targetoid patches of necrosis with epidermal detachment on her arms and legs, sparing the soles but not the palms. Thorax and scalp were also spared. She was referred to emergency and was admitted at the Dermatology Department.

Radiation therapy was discontinued on admission. Peripheral blood tests revealed a mild anaemia (haemoglobin – 11.8 g/dL) and a slight elevation in C reactive protein (1.3 mg/dL), but no leucocytosis or eosinophilia.

A biopsy of the lesions was performed and revealed a diagnosis consistent with Erythema Multiforme.

The patient was given wound and ocular care, as well as treatment with hydroxizine (25 mg/day) and oral prednisolone (20 mg once daily). During hospitalisation, the lesions became more intense, including the aforementioned pruritus, eventually progressing to vesicles and bullae with skin sloughing within days. However, they never spread out of the limb area, sparing the torso, the soles and the scalp. The mucosal lesions were also confined to the oral and ocular mucosae. The lesions gradually stabilized and regressed over two weeks.

The patient was discharged after 20 days. She undertook her last brachytherapy fraction on the day of her discharge, with no subsequent development of SJS or EM in a 3 month follow-up.

3. Discussion

This case illustrates the association between radiation therapy and EM/SJS that has been reported in several instances. However, as mentioned above, most reports of this association are hindered by the introduction of other medications.[2–13] Of these, the most prevalent are phenytoin[10–13] and amifostine,[5,6] but other medications have also been implicated, such as chemotherapy agents (gemcitabine,[3] temozolamide[4]) and other anticonvulsants (phenobarbital,[7] diphenylhydantoin[8]). There is also one published case of sparing SJS in irradiated fields of a patient undergoing phenobarbital and palliative radiation therapy for bone metastases.[14]

The peculiarity underlying this case rests with its presentation and evolution. Our patient was not submitted to new drug therapies while undergoing radiation. She maintained her hypertension (irbesartan and hydrochlorothiazide association) and osteoporosis (alendronate) usual medication, and despite one case report on SJS caused by hydrochlorothiazide in association with allopurinol[15] and a study implicating alendronate as a possible cause of EM,[16] she had taken these compounds for years without any reaction. However, she had also undergone external beam radiation therapy before brachytherapy without severe skin toxicity.

Furthermore, the skin reaction started in the ocular and oral mucosae before spreading to the limbs. The whole torso was spared including the irradiated areas, namely the pelvic area and vaginal mucosa, where a hyperaemia and irregularity can be attributed to grade I radiomucositis, although this might constitute a confounding factor leading to a bias in this case. This is, to our knowledge, the first such instance, since in most cases of SJS/RT association the onset of SJS is on the irradiated fields. Even though the pathological report issued a diagnosis of EM, this can be attributed to a biopsy of an incipient lesion, as the lesions progressed to sloughing of the skin.[17]

The lack of complications after the last fraction of brachytherapy raises the question of a lack of causality between radiation and the onset of this disease, since it can also be attributed to environmental factors. The patient was however still under corticosteroids and hidroxizine, which may have spared this complication, since radiation is known to produce oxidative reaction intermediates that are involved in hypersensitivity reactions.[18]

However, considering that RT is often seen as a cause of EM/SJS, the lack of data on these pathologies arising in patients not undergoing concomitant novel pharmacological therapies should raise the question of it being a factor leading to an increase in susceptibility as opposed to a direct cause of these syndromes.

4. Conclusion

We have described a case of Stevens Johnson Syndrome arising in a patient undergoing gynaecological brachytherapy with an unusual presentation. This case demonstrates that this syndrome may arise in patients undertaking radiation therapy but not undergoing concomitant medications; however, it also raises the question of a possible lack of causality between RT/EM.

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