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Haemorragic and Ulcerative Mucositis in a Patient Treated With Sunitinib for Metastatic Ileocaecal Gastrointestinal Tumour: A Case Report

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***Abstract*— Gastrointestinal stromal tumours (GIST) are the most common subtype of soft tissue sarcoma. First-line treatment of advanced and metastatic forms is based on Imatinib; for patients who are refractory to or intolerant of Imatinib, treatment with Sunitinib has demonstrated efficacy with an acceptable safety profile. We report the exceptional occurrence of grade 4 mucositis in a patient treated with sunitinib for metastatic GIST.**

The case

We present the case of a 66-year-old female Moroccan patient treated for gastrointestinal stromal tumour metastatic to the liver. She was started on sunitinib after progression on imatinib, during the 3rd course of sunitinib the patient presented with haemorrhagic and ulcerative mucositis, requiring the discontinuation of this treatment and hospitalisation for urgent therapeutic management. The evolution was characterised by a resolution of symptoms after 15 days of treatment, the case was discussed in the medical staff and it was decided to stop sunitinib definitively in our patient.

Conclusion

Sunitinib is a multi-targeted tyrosine kinase inhibitor indicated for advanced GIST after progression or intolerance to imatinib. Side effects associated with imatinib rarely exceed grade 2, the toxicity experienced by our patient was an unusual event.

Index terms— Metastatic GIST, Sunitinib, toxicity, mucositis

I. INTRODUCTION

Gastrointestinal stromal tumours (GIST) are considered to be the most common subtype of soft tissue sarcoma and the most common mesenchymal tumour of the gastrointestinal tract [1-2-3]. GISTs are equally distributed between men and women, with an average age of 60 [2].

These are tumours derived from Cajal cells that can develop anywhere in the digestive tract, but mainly in the stomach and small intestine in half and one third of patients respectively [2]. At the molecular level, around 80% of GISTs carry the c-KIT mutation [1-4], followed by the PDGRF-α mutation in 10% of cases, with other rarer mutations [5-6].

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In the past, these tumours were considered to be refractory to treatments such as chemotherapy and radiotherapy [2]; until the approval of imatinib, a selective anti C-kit and anti-PDGFRA (Platelet-Derived Growth Factor Receptor) tyrosine kinase inhibitor for the treatment of advanced GIST [7-8], this treatment is considered revolutionary.

In patients resistant to or intolerant of Imatinib, treatment with Sunitinib was initially effective as follows: 50 mg per day for 4 weeks out of 6 [9]. Subsequently, a continuous regimen of 37.5 mg per day was also shown to be effective and well tolerated [10].

We present the rare occurrence of grade 4 mucositis in a patient treated with sunitinib for metastatic GIST.

II. THE CASE:

This is a 66-year-old female Moroccan patient, with no previous medical history, diagnosed 4 years ago with GIST metastatic to the liver, initially treated with Imatinib 400 mg, then progressed 2 years later and switched to Imatinib 800 mg. the patient remained stable and then progressed one year later. The decision of our medical oncology staff was to start the patient on Sunitinib at a dose of 50 mg per day for 04 weeks out of 06. We then switched to the continuous regimen 37.5 mg per day because of grade 3 hepatic cytolysis after the first course.

In the 3rd cycle, the patient presented to the intercourse with grade 4 ulcerative and haemorrhagic mucositis (**Figure 1**).

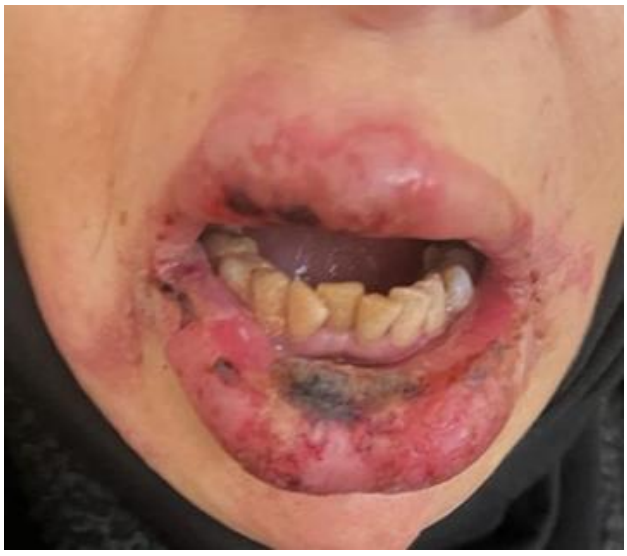

Figure 1

The patient was admitted urgently to our medical oncology department, receiving local care, mouthwash with bicarbonated serum, and intravenous treatment with fluconazole after a check of the liver function, we also initiated parenteral nutrition, given the impossibility of the oral route.

The evolution was favourable, with resumption of oral feeding 4 days later and complete healing after 2 weeks of treatment. Sunitinib was definitively stopped in our patient.

III. DISCUSSION:

Sunitinib is a multi-target tyrosine kinase inhibitor, anti VEGFRs (Vascular Endothelial Growth Factor Receptors), anti-KIT, anti PDGFR (α and β) [11], this orally administered small molecule is indicated in gastrointestinal stromal tumours with intolerance or resistance to imatinib [9].

The most frequent side effects are fatigue and asthenia, hypothyroidism, skin toxicities, haematological toxicities, and oral toxicities which generally do not exceed grade 2, including mucositis [11], a percentage of 1 to 3% of grade 3 mucositis have been reported with sunitinib [12-13].

Sunitinib has been reported to cause oral toxicities in up to 32% of patients treated for solid tumours, with an RR of 1.8 for stomatitis of any grade [14-15], which is a significant percentage and should encourage practitioners to prevent, detect and treat these events. These toxicities usually appear during the first 2 weeks of treatment, leading to dose reductions in 26% [16].

Treatment with sunitinib can cause hypersensitivity of the oral mucosa, dysgeusia, ulcerations and even cheilitis [16-11-17], it should be noted that dysgeusia can affect almost half of the patients treated with sunitinib [12-18-19].

Mucositis secondary to sunitinib is generally functional, unlike chemotherapy-related mucositis which is often more severe with destruction and ulceration of the oral mucosa which may extend to the rest of the digestive tract. Although mucositis is fairly common in patients treated with sunitinib [12-20], there is only one case of severe necrotic and ulcerative oral involvement associated with sunitinib reported in the literature [11-21].

The oral toxicities associated with sunitinib may be due to the involvement of VEGF (Vascular Endothelial Growth Factor) in the maintenance of salivary function and the integrity of the oral mucosa [22]. Inhibition of VEGF is thought to cause dry mouth, which may contribute to these toxicities [14].

Data suggest a relationship between the frequency and intensity of side effects associated with sunitinib and genetic polymorphism: genes encoding metabolic enzymes, trans membrane transporters and therapeutic targets. Female gender, age and small body surface area are thought to contribute to severe side effects [11-23].

IV. CONCLUSION:

Oral toxicities associated with sunitinib, even of moderate severity, are very annoying for patients. They are often associated with difficulty in eating and dysgeusia, which can lead to anorexia and therefore weight loss and malnutrition, and sometimes to cosmetic damage, as in our patient; hence the need for prevention and screening at every consultation. Fortunately, the side-effects of sunitinib generally do not exceed grade 2, and the toxicity experienced by our patient is a very rare event.

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Competing interests

The authors declare they have no competing interest

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