Title: Hand-foot syndrome associated with use of sorafenib in a patient with papillary thyroid cancer: a case report

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ABSTRACT

Background: Hand-foot syndrome (HFS), also known as palmar-plantar Erythrodysesthesia (PPE), acral erythema or Burgdorf reaction, is a dermatologic toxic reaction to certain chemotherapies, including sorafenib. A high incidence of adverse events is already described in dermatological clinical trials of this drug, but its use in medical practice, common in the patient with metastatic thyroid carcinoma has not yet been reported. Sorafenib (BAY 43-9006) is an orally administered multi-level kinase inhibitor, approved for treatment of solid tumors such as renal cell carcinoma, hepatocellular carcinoma and recently for metastatic thyroid carcinoma.

Case presentation: We report a case of a 29 year old Latin woman diagnosed with papillary thyroid carcinoma, who was initially given a total thyroidectomy, central and bilateral neck lymph node removal followed by a radioiodine therapy. Subsequent evaluation indicated locoregional progressive disease and metastatic involvement in both lungs. Following this, the patient was prescribed 200 mg of sorafenib administered every 12 hours, but after four days, she presented with a skin reaction compatible with hand-foot syndrome. After discontinuation of the therapy, this reaction ceased.

Conclusion: Sorafenib as a new therapeutic option for patients with advanced radioactive iodine (RAI)-refractory disease, it is important that clinicians are fully aware of the potential adverse effects. All patients on Sorafenib therapy should be educated to recognize the first symptoms to obtaining the maximal benefit from this anti-neoplastic rescue therapy.

2. Please restructure your manuscript so that all figures and tables are placed
after the references section
A. The manuscript was adjusted
Reviewer: Matteo Santoni
Minor Essential Revisions:
Q: In this Case report, the authors well underline the importance of a prompt management of adverse events in patients treated with targeted agents. HFS represents one of the most common toxicities associated with the use of this drugs, and this case well shows the impact that HFS may have on patient quality of life and compliance to therapy.
I suggest just to add to the conclusion two important focuses. At first, the possibility to restart this therapy at lower doses after the recovery of major toxicities. Moreover, the fact that the appearance of adverse events in the early phases of the treatment with anti-VEGFR TKIs is often associated with good response rate.
A: The manuscript was adjusted
“The most frequently used therapies are topical emollients, pain medications and reduction from the full dose or discontinuation of the Sorafenib therapy followed by resumption of treatment at 50% of the full dose often associated with good response rate” and the Consensus panel recommendations was adjusted.
Reviewer: Giuseppe Procopio
Major
1) hand foot skin reaction is a well done adverse events related to sorafenib exposure, in renal and hepatocellular carcinoma.
No news was added from this experience
A: The manuscript was adjusted
Adverse events with the use of Sorafenib for treatment of renal carcinoma [12] occur in up to 73% of patients as case of fatigue, rash / desquamation (up to 66% of patients), hand-foot skin reaction (up to 62% of patients) and diarrhea (up to 58% of patients). Similar prevalence is observed in treatment of hepatocellular carcinoma [13].
2) The conclusions are too long. Some informations on the mechanism of action should be in preference moved in the background section. The conclusion should be simplifie and rewritten in terms of bullet point
A: The manuscript was adjusted and was simplify
Sorafenib (BAY 43-9006) is the first approved systemic therapy in the management of differentiated thyroid cancer. The use of Sorafenib, is however associated with a relatively high incidence of adverse events already described in dermatological clinical trials of this drug, but its use in medical practice, common in the patient with metastatic thyroid carcinoma has not yet been reported and this is one of the first post marketing reports.
Hand-foot syndrome (HFS) is a relatively frequent dermatologic toxic reaction to
certain chemotherapies for cancer. Its pathogenesis is not well defined, it is usually mild, but can progress to a severe condition that limits function and affects quality of life. The most frequently used therapies are topical emollients, pain medications and reduction from the full dose or discontinuation of the Sorafenib therapy followed by resumption of treatment at 50% of the full dose often associated with good response rate.

Given the incidence of thyroid carcinoma, and the importance of Sorafenib as a new therapeutic option for patients with advanced radioactive iodine (RAI)-refractory disease, it is important that clinicians including endocrinologists, medical oncologists who manage these therapies are fully aware of the potential adverse effects. All patients on Sorafenib therapy should be educated to recognize the first symptoms, to manage initial prevention and consider dose reduction or discontinue the therapy to improve the patient’s quality of life by minimizing the impact of adverse events while obtaining the maximal benefit from this anti-neoplastic rescue therapy.

Minor

1) In general the adverse events should be classified, in agreement to the NCI-CTC grade. Please report the toxicity grade of this event

A: Given these clinical findings the dermatological reaction was classified as Grade 3 and the Sorafenib treatment was discontinued.

A: “The National Cancer Institute (NCI) grading systems for dermatologic toxicities (NCI Common Terminology Criteria [CTC] v2.0 and CTC for Adverse Events [CTCAE] v3.0 (see Table 1 [16]).”

2) Key words please add Tyrosin kinase inhibitor and targeted therapies

A: KEYWORDS:

Hand-foot syndrome, Palmo-plantar Erythrodysesthesia, Sorafenib, Thyroid Cancer, Tyrosin kinase inhibitor, Targeted therapies.

With best wishes,

Carlos Alberto Velandia

On behalf of Authors group