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A Case report on Hand -foot- syndrome due to Capecitabine Adverse drug reaction.

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ABSTRACT:
Capecitabine is a prodrug of 5-Fluorouracil and is commonly used to treat breast, colon and gastric cancer. The drug is also known to cause Hand and Foot Syndrome (HFS). Which can be life threatening for some patients. The comorbidities such as old Age, Hypertension and Asthma could increase the risk of HFS in the patient and it is necessary to look for any signs and symptoms of HFS in such patients. This is a case report of a 65-year-old woman who is diagnosed with colorectal cancer and prescribed with Oxaliplatin and Capecitabine as primary treatment for the same. She has experienced HFS during treatment which has been described in detail in this case report. Discussion of various possible cause of HFS, changes in lab parameters and further progression of disease into Steven-Jonsen Syndrome is also discussed.

Introduction

Capecitabine is a fluoropyrimidine, a systemic prodrug of 5-Fluorouracil (5-FU), with the advantage of oral administration used to treat various type of cancer. Capecitabine can induce hand and foot syndrome (HFS), also known as palmar-plantar erythrodysesthesia, is a common and limiting adverse reaction to capecitabine, a chemotherapeutic drug used in patients with breast, colon, and gastric cancer.[1] HFS is characterized by erythema, edema, dysesthesia, and can progress to blistering and ulceration.[1] The incidence of HFS in patients treated with capecitabine ranges from 22% to 77%.[1,2] HFS causes significant functional and quality impairments in patients, leading to the need for prompt recognition and discontinuation of capecitabine with supportive treatment.[3] A pharmacogenetic study has also been conducted to understand the occurrence and grades of HFS, shedding light on the associations of genetic variations with the toxicity.[2] Genetic studies have revealed that patient with reduced expression of CDH4 gene that is responsible for synthesis of R-cadherin. The protein is necessary for the maintenance of

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normal skin structure.[4] While another study findings shows that renin-angiotensin system inhibitors, increased body surface area and patient with decreased albumin levels are at greater risk of developing HFS.[5] Additionally, a systematic review of case reports has been carried out to provide insights into the self-identification and management of HFS, emphasizing the effect of structured teaching programs on patients receiving capecitabine-based treatment.[6]

Case Presentation

A 65 yrs. old lady, Mrs. R, presented to our OPD in March 2018 with complaints of increased frequency of stools since the last 5 months associated with passing of blood with stools. She also had complaints of fatigue and significant weight loss. She was on regular treatment for essential hypertension and Bronchial Asthma. She had undergone Tubectomy surgery thirty years back.

Clinical examination showed mild pallor. Per rectal examination showed an ulcerative growth in the posterior half of the rectum commencing about 3 cm from the anal verge and extending to about 8 cm from the anal verge. Biopsy from the rectal lesion was reported as Poorly differentiated adenocarcinoma. PET CT scan study showed FDG avid circumferential thickening of the lower rectum and upper anal canal. FDG avid left supraclavicular, abdominal and pelvic lymphadenopathy is in keeping with nodal metastases.

In view of this being a stage IV carcinoma rectum, palliative intent of treatment was explained and Mrs. R was initiated on palliative Chemotherapy with Oxaliplatin and Capecitabine. K-ras mutational study was deferred as there was financial constraints for initiating Bevazucimab.

The dose of Oxaliplatin administered was 120 mg (85 mg/m2) and that of Capecitabine planned was 1500 mg twice daily (1250 mg/m2 given twice daily for 14 days). The first cycle of Chemotherapy was given on 18th April 2018.

Mrs. R was admitted on the 12th day post chemotherapy (was on Capecitabine 12th day) with complaints of loose stools and mucositis. Clinically, there was mild hyperpigmentation of the soles and palms of both lower and upper limbs. As there was clinical suggestion of an early Hand–foot syndrome induced by Capecitabine and presence of mucositis, Capecitabine was discontinued.

On the day of admission (29/4/2018), Blood investigations showed anaemia (Hb 8.7 g/dL) and Total WBC counts of 8100/mm^3 and platelet count of 3.4 lac/mm^3. The serum creatinine and liver function tests reports were in the normal range.

Mrs. R was initiated on Intravenous Hydration, Antibiotics (Piperacillin + Tazobactam / Metronidazole) and anti-fungal therapy.

The subsequent week showed worsening of the symptoms and by the 6th day of admission, she developed deepening of the hyperpigmentation over the soles and palms with fluid filled blebs over the soles of the feet. Oral mucositis had worsened, with the patient able to take in only a liquid diet. The skin over the entire body had become hyper pigmented and stretched and shiny.

On 4/5/2108, the blood counts showed neutropenia (TC 1600/ mm^3 and ANC of 480/ mm^3). The Intravenous antibiotics were changed to Inj. Meropenem and Teicoplanin and Mrs. R was shifted to an Isolation room and reverse barrier nursing instituted.

On 6/5/2018, Total counts had fallen to 900/mm^3 with platelet count of 15,000/ mm^3.

On 9/5/2018, the total counts had further fallen to 400/mm^3. The clinical picture of mucositis, skin hyperpigmentation and hand –foot syndrome had further worsened, that the patient was not able to move out of the bed. The skin over the perineum and peri-anal region had ulcerated. Dermatology consult opined that this could be a Steven–Johnsons syndrome and oral steroids were initiated with topical steroid creams. Loose stools persisted during this period.

10/5/2018, Mrs. R had a sudden episode of loss of consciousness for which CPR was instituted, but she could not be revived and Death was declared.

Discussion

The age of Mrs. R could be a predisposing factor in the early onset of HFS. Studies have suggested that there is a correlation with age and risk of HFS in the patient but no specific study has been conducted for geriatric patient.[1] In another study it has been seen that there is an increased incidence of HFS in patient with increased age.[7] The patient

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experienced diarrhea post therapy. The diarrhea is one of the common adverse effects of the therapy as suggested by the study.[7] The patient was a known case of hypertension and was on antihypertensive medication. In the studies it has been shown that there is a significant relationship between increased risk of HFS and Hypertension in patient receiving Capecitabine.[8,9] Patient being asthmatic could be another predisposing factor for HFS, but there were no relevant study proving the same has been found. The co-administration of Capecitabine and Oxaliplatin could have increased risk of HFS in the patient as the studies have demonstrated a positive relationship between HFS and co-administration of both drugs.[7,10,11] The patient was presented with mucositis and studies have also reported high incidence of mucositis with Capecitabine.[12-14] The lab reports of Mrs. R have shown Neutropenia. The studies have shown incidence of neutropenia in patient receiving Capecitabine.[15,16] The patient was suspected for Steven-Johnson Syndrome for which treatment was initiated. Several case reports have been documented Steven-Johnson syndrome induced due to Capecitabine.[17-19] The further investigation for Steven-Johnson syndrome could not be concluded as patient died the next day of suspected Steven-Johnson Syndrome & adverse drug reaction assessment could have given insight of the event.

Conclusion

Multiple comorbid conditions could have aggregated and resulted into HFS to this patient as she was old, receiving treatment for hypertension and asthma and after prescribing with capecitabine developed HFS. Further investigations are needed for such events that could also progress to Steven-Johnson Syndrome.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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