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Case Report

Bleomycin induced flagellate erythema in a patient with thalamic mixed germ cell tumour: Report of a rare adverse effect

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KEYWORDS

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Abstract Bleomycin induced flagellate dermatitis is an uncommon and unique adverse effect. With the declining use of bleomycin, this complication is becoming increasingly infrequent in day-to-day clinical practice. We herein describe a case of a 13 year old male patient with left thalamic mixed germ cell tumour treated by multimodality approach, who developed flagellate erythema after two cycles of combination chemotherapy with bleomycin, etoposide and cisplatin (BEP). This brief report highlights the importance of awareness and timely identification and management of this dermatological toxicity in patients undergoing bleomycin based combination chemotherapy.

Introduction

Bleomycin is an antibiotic antitumour agent first developed in Japan by Umezawa in 1966 [1]. Cytotoxic effect results from generation of activated oxygen-free radicals, which cause single and double-stranded DNA break and subsequent cell death. Presently bleomycin is commonly used as a part of combination regimens for management of Hodgkin's and non-Hodgkin's lymphoma, germ cell tumour, squamous cell carcinoma of head and neck, gynaecological system and skin. It is also used as a sclerosing agent for pleurodesis in recurrent malignant pleural effusion [2].

Bleomycin induced toxicities are more prominent in lungs and skin due to a low concentration of the metabolizing enzyme-bleomycin hydrolase in these organs [2,3]. The spectrum of bleomycin induced dermatological toxicity includes Raynaud's phenomenon, hyperkeratosis, nail bed changes, peeling of skin on palmar and planter surface, digital gangrene and pigmentary alterations [2,4,5]. Flagellate erythema is a rare but unique toxicity of bleomycin with a reported incidence of 8–20% in medical literature [2,4,5]. Flagellate erythema was first reported as an adverse effect of bleomycin in 1970 by Moulin et al. [6]. However, with the decreasing use of bleomycin, this unique reaction has become infrequent in common clinical practice [2,4].

Clinical case

A 13 year old male patient presented with headache and bilateral dimness of vision for the last 6 months. He did not have any pre-existing dermatological disorder or allergic condition.

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Contrast enhanced magnetic resonance imaging (MRI) of brain showed a $3.5 \times 3.5 \times 4$ cm heterogeneously enhancing solid-cystic mass involving left thalamus (Fig. 1). He was evaluated in the department of Neurosurgery and underwent gross total excision of tumour. Post-operative histopathology revealed mixed germ cell tumour with components of germinoma and teratoma. Immunohistochemistry was positive for placental alkaline phosphatase (PLAP) and CD117. Cerebrospinal fluid (CSF) cytology showed no evidence of malignant cells. Serum tumour markers were within normal limit. MRI of whole spine showed suspicious drop metastasis. He underwent craniospinal irradiation 36 Gray/20 fractions/4 weeks followed by boost of 10 Gray/5 fractions/1 week. Subsequently he was planned for 3 cycles of chemotherapy with bleomycin (15 units/m^2 IV day 1), etoposide (100 mg/m^2 IV day 1–5) and cisplatin (20 mg/m^2 IV day 1–5) (paediatric BEP regimen) every 3 weeks. However he developed progressive, erythematous, painless, non-pruritic, linear lesions in trunk and upper extremities after the second cycle of chemotherapy (Fig. 2). There was no mucosal involvement or systemic upset. The lesions resembled flagellate erythema and bleomycin was considered the putative agent. Bleomycin was omitted and the regimen was changed to combination of etoposide and cisplatin (EP). Oral antihistaminics (Cetirizine-5 mg once daily) and topical corticosteroid (Betamethasone local application twice daily for 2 weeks) to affected areas of skin were started expeditiously. Though the rash stabilized, unfortunately after the third cycle of chemotherapy, he developed complicated febrile neutropenia and died of septic shock in spite of aggressive supportive management with fluids, intravenous antibiotics and granulocyte colony stimulating factor.

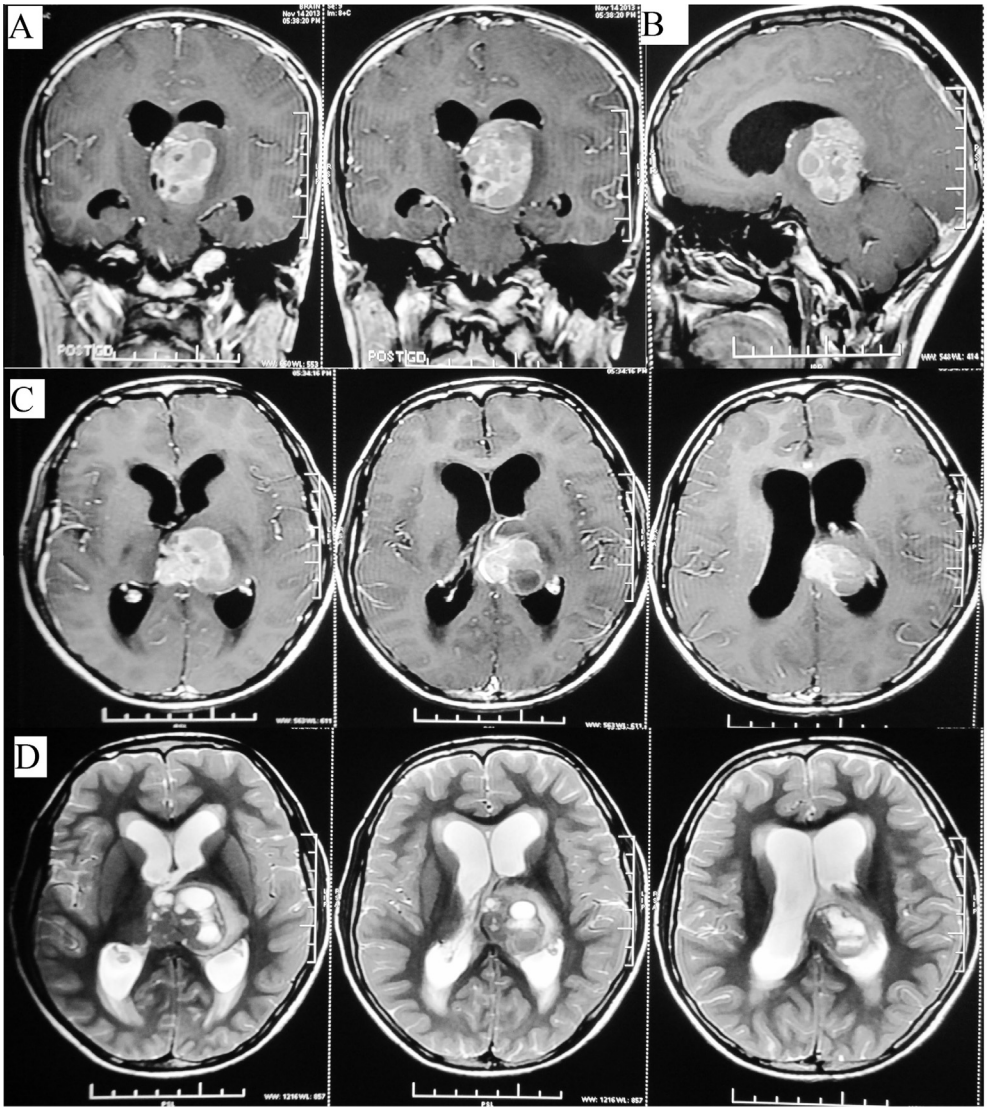

Figure 1 T1 weighted post gadolinium (A) coronal, (B) sagittal and (C) axial MR images of brain show a well-defined, heterogeneously enhancing, solid-cystic lesion in left thalamus, crossing across the mid-line and causing mass effect and dilatation of lateral ventricles. On T2 weighted axial MR images (D), the lesion is heterogeneous with solid and cystic components being iso-intense and hyperintense to grey matter respectively.