

Failure to wean due to steroid psychosis

Fahmi Y. Khan, MD.

Since their introduction as therapeutic agents, corticosteroids have been associated with psychiatric symptoms ranging from mood disturbances to (florid) psychosis. By the time there have been reported psychotic reactions in patients receiving steroids or after sudden withdrawal of long time corticosteroids therapy. In this report a 40-year-old male patient known to have bronchial asthma since childhood, presented to the Accident and Emergency Department with marked shortness of breath. His medical history was otherwise unremarkable. Ventolin (β_2 agonist) and Atrovent (anticholinergic) was delivered via nebulizers and methylprednisolone was given at a dose of 60 mg intravenously (IV), every 6 hours. The patient's condition deteriorated over the next hours and he was subsequently electively ventilated via cuffed endotracheal tube and transferred to the medical intensive care unit (MICU).

In the MICU, the patient was put on mechanical ventilator and was given the following drugs: methylprednisolone 60 mg, every 6 hours IV, nebulized Ventolin and Atrovent; midazolam and remifentanyl IV. No muscle relaxants were used. On the following days, the patient became stable and he was prepared for weaning by tapering the dose of sedatives (midazolam and remifentanyl). Remifentanyl was stopped initially, while the patient remain calm, then midazolam was tapered gradually. As soon as the dose of midazolam decreased below the therapeutic level, the patient showed interrupted appearance of excitation and aggressiveness and fought with the ventilator, thus weaning was postponed. Investigations, including electrolytes, arterial blood gas, liver function test, chest x-ray and renal function tests were normal. Attempts to wean the patient continued but failed, as the patient became aggressive without sedatives, which makes the weaning process more difficult. Weaning failure were suspected due to steroid psychosis, methyl- prednisolon was withdrawn and haloperidol was administered, while the patient was kept on midazolam and bronchodilators. Psychotic symptoms, consisting of interrupted appearance of excitation and aggressiveness were gradually eliminated and completely disappeared at approximately 7 days after onset. On the following days, the patient behavior became reasonable, haloperidol and midazolam were stopped and weaning succeeded.

Glucocorticoid therapy causes psychiatric side effects in many patients. The frequency of occurrence varies from study to study. Although psychiatric side effects occur most commonly in women and middle-aged patients, no clinical features have been identified to predict which patients are at risk.¹ Patients with a family history of depression or alcoholism are at increased risk for affective diseases when given glucocorticoids.²

In one prospective but uncontrolled study of 50 patients for example, large doses of glucocorticoids, given for various ophthalmologic indications, induced hypomanic symptoms in approximately 30% and depressive symptoms in about 10% by the end of one week.³ A second report found that patients treated with prednisone doses of 5-40 mg/day for at least one year had a partial loss of explicit memory, elderly patients were more susceptible to memory impairment with less protracted treatment.⁴ The systemic side effect of steroids such as diabetes, glaucoma, osteoporosis, are well known to physicians. The most prominent psychiatric side effects of this drug consist of emotional liability, anxiety, distractibility, interrupted appearance of excitation and aggressiveness, pressured speech, sensory flooding, insomnia, depression, perplexity, agitation, auditory and visual hallucinations, intermittent memory impairment, mutism, disturbance of body image, delusions, apathy and hypomania. The mechanism by which glucocorticoids produce psychiatric symptoms is probably multifactorial, including both direct and indirect effects on the brain.⁵

Our patient who had no previous history of psychiatric problems, developed psychotic symptoms, consisting of interrupted appearance of excitation and aggressiveness 2 days after steroid initiation. When steroid was stopped the psychotic symptoms, were gradually eliminated and completely disappeared approximately 7 days after onset. The time and course of events suggested that steroid was the cause of the psychotic symptoms, which cause weaning to fail in this patient, since no other causes could explain the psychotic reaction. Dose reduction or discontinuation of the systemic corticosteroid is associated with improvement in psychiatric symptoms in many studies. Lithium has been used successfully to both manage and prevent glucocorticoid-associated affective disorders.⁶ Other reports suggest valporic acid, neuroleptics such as haloperidol, can also be useful to treat these symptoms. Of particular note, was the fact that tricyclic antidepressants produced an exacerbation or worsening of the clinical state in all patients to whom they were administered.⁷ Thus, steroid psychosis should be considered in the differential

diagnosis, in patients under steroid therapy, who do not wean from mechanical ventilation after 48-72 hours of the resolution of the underlying disease process.

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From the Department of Medicine, Hamad General Hospital, Doha, Qatar. Address correspondence and reprint requests to Dr. Fahmi Y. Khan, Senior Specialist, Department of Medicine, Hamad General Hospital, Doha, Qatar. Tel. +974 4879228/5275989. Fax. +974 4392273. E-mail: fakhnqal@yahoo.co.uk

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Paclitaxel in relapsed high risk anthracycline treated breast cancer patients

Manal M. Elhabbash, MBBC, MD,
Abukris A. Alwindi, FRCP.

Breast cancer is the most common malignancy afflicting women, and second most common cause of cancer death in women. Considerable progress has been made in the treatment of breast cancer, and mortality is decreasing in developed countries. Despite this, the majority of breast cancer patients will develop metastases and eventually die of the disease. Response to chemotherapy, while frequent, is usually short-lived and the median survival for patients treated with chemotherapy for metastatic disease ranges between 18-24 months.¹ The introduction of new agents has improved prognosis in chemotherapy, pretreated patients.¹ In

1994, paclitaxel was approved for the treatment of metastatic (or advanced) breast cancer (MBC) following failure with standard anthracycline-based on chemotherapy, or in patients who had relapsed after initial chemotherapy.

In this study, we report our experience with paclitaxel in our patients who relapsed following anthracycline chemotherapy, and who are mostly premenopausal women, as opposed to other studies that included mostly postmenopausal women. The aim of this study is to assess response rate, mean duration of response, median time to progression, and survival rate in MBC patients who received paclitaxel. This retrospective study was performed at Tripoli Medical Center, Tripoli, Libya. Women with a histologically confirmed diagnosis of breast carcinoma and evidence of metastatic disease who were on regular follow up and relapsed after adjuvant treatment, were included in our study. All patients included have an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2. All patients received paclitaxel as single agent in a dose of 175 mg/m² IV infusion over 3 hours every 3 weeks. Premedication with dexamethasone and antihistamine was given prior to the paclitaxel dose. Median of 6 cycles was administered per patients (1-9 cycles). Imaging procedures included chest, abdomen, CT scan and bone isotope scans. These were repeated to assess objective response every 3 treatment cycles. Forty-two patients were included in this study in the period between June 1997-June 2004. The age of the patients ranged from 28-67 years with a median age of 45 years at diagnosis. Premenopausal women represented 61.9% and postmenopausal women represented 38.1%, 58.14% had stage II disease, 25.6% had stage III, 14% had stage IV, and 2.3% were unknown, 86% were node positive, 11.6% were negative and unknown in 2.4%. Histological diagnosis was as follows: invasive duct carcinoma in 81.4%, 11.6% lobular carcinoma, 4.7% medullary carcinoma and inflammatory type in 2.3%. Estrogen and progesterone receptors were studied in 43% of patients where their receptors were positive in 44.4% and 55.6% were negative. Regarding type of surgery, modified radical mastectomy was carried out in 81.4% and lumpectomy and axillary clearance was carried out in 11.6%, and only biopsy was done in 9.3%. In those who had positive lymph nodes, the median number of involved node >4 (5-8 lymph node). Radiotherapy as loco regional treatment as 50 gray over 25 fraction was given to 73%, in those who have more than 3 positive lymph node, locally advanced disease or those who had breast conserving surgery. Tamoxifen tab. 20 mg/day was given to all patients who have estrogen positive or where the receptor status was unknown. Chemotherapy as CAF Cyclophosphamide,