Geriatric Manic Delirium With No Previous History of Mania

To the Editor: Manic delirium is a life-threatening psychiatric condition that is usually reported in younger female patients, and almost unequivocally in those with a previous diagnosis of bipolar disorder.(1) We describe the unusual case of a neurologically and psychiatrically intact older woman with no previous history, who suffered a sudden onset of affect instability, delusions, excitement, grandiosity, and insomnia characteristic of mania. The concomitant episodes of disorientation, confusion, and altered consciousness typical of delirium were also present. We depict the naturalistic, complex, and prolonged course of this syndrome with a close temporal association to the palliative cycle of carboplatin and Paclitaxel (CarboTaxol) chemotherapy.

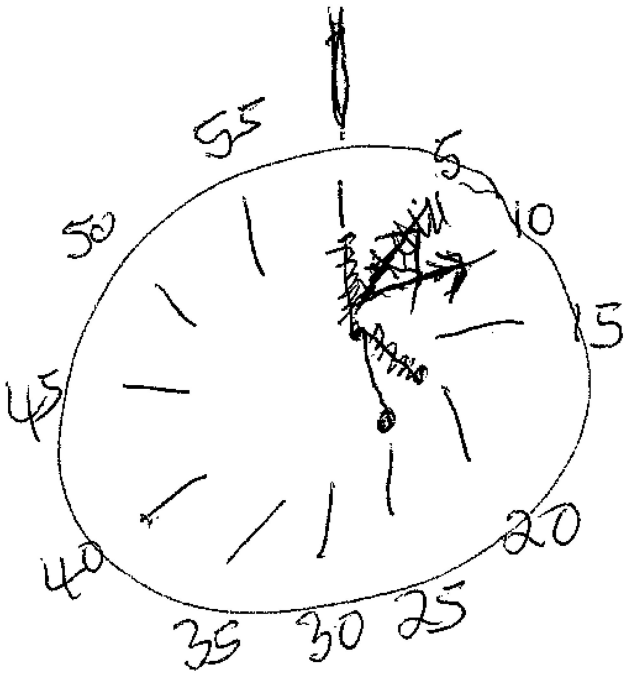
Case Report

"Ms A," a respected and revered teacher in her 70s, had two successive admissions to a teaching hospital, after episodes of confusion and atypical behavior at home. She had no past history or family history of neuropsychiatric illness (e.g., bipolar disorder) and had a decade-long history of suffering with various cancers. While treated with tamoxifen for her breast cancer a few years earlier, she developed tubular cancer, and more recently was diagnosed with malignant mixed Mullerian adenosarcoma (MMMT; Stage 1C) for which she was treated with carboplatin and Paclitaxel chemotherapy (CarboTaxol regimen), followed by pelvic radiotherapy and brachytherapy. According to her husband and children, the neuropsychiatric symptoms leading to the admissions started abruptly, within 2 weeks of her second cycle of palliative chemotherapy with CarboTaxol. One evening, her husband found her trying to switch on the TV with the mobile phone. She appeared agitated when challenged about her behavior and insisted that "through her genial invention (sic)," she managed to re-wire their mobile so that it could be "multifunctional."

Similar outbursts of affective instability, pressured logorrhoea, tangential thinking, delusions, and irrational, grandiose, disinhibited and, at times, argumentative behavior were accompanied with progressive disturbance in her sleep cycle, personal hygiene, and eating during the next few weeks. The latter led to a dramatic drop in her BMI. Incidents of inappropriate toileting, disrobing, and extended naked periods were also reported. She gradually completely deferred from activities of daily living, and her husband had to take over most of the household duties. Her first admission followed the further abrupt decline in her mental state, with prominent confusion, "flight of ideas," and loss of selectivity of mental processes. In the hospital, no unequivocal etiology of her delirium was found, and, after some improvement in her cognition, she was discharged home. Her family insisted that she continued acting out of character when at home, with prominent mixed affective instability, lingering predominantly in the hypomania/manic spectrum. Her premorbid prim demeanor, with ascetic and anankastic traits, was overwhelmingly replaced with flippant, jovial, inappropriate elements. She was reported to have contacted her young grandsons at school requesting them to do shopping errands for her. She also sent strange, "jargonistic" mobile phone messages. For example: "So xiting!!!. . .Ta for efforts. Must have gone away. Please forget about her." (sic) More circumscribed microepisodes of psychosis and altered consciousness were also recounted. The second admission, during which our liaison psychiatric team was involved, followed similar escalation, some 6 weeks after the very first presentation. When in the hospital, she showed psychomotor agitation. She pulled out her intravenous cannula and started hitting, biting, and kicking the nursing staff while also trying to throw things out of the window. She was not responding to questions and kept rhythmically repeating "I blow my nose on M11, noo, nee, noo" (sic). Lorazepam 1 mg iv was given, with some success in calming her down. Mild hyponatremia was diagnosed and subsequently corrected. She was also empirically treated with antibiotics. CT and MRI scans of her head showed only normal involutional changes, with some small-vessel ischemia and no features to suggest parenchymal metastatic deposits. During examinations in ensuing days, she proved bemused, albeit an amicable and willing participant, with heightened affect. The nursing staff pointed to continuing fluctuating states, with prominent nocturnal excitement and grandiose, confabulatory, delusional, and hallucinatory elements present. Her speech

was not dysphasic, but she showed marked logorrhea, with constant switches between topics. "Yes, these cards are from my friend." (sic) Then, turning to the "get-well" cards on her night desk, she would continue addressing them: "Nice dress. This nurse reminded me, you need to collect my grandson from school. Today the party is later. It is soon Christmas, it will be fun." (sic) Her behavioral lack of spontaneity was in marked contrast to her disinhibited speech, and she usually stayed in bed without any drive to initiate goal-directed actions. Overall, she showed very limited insight into her presentation. No suicidal ideation was ever present or reported. The diagnosis of manic delirium was made, and she was initiated on quetiapine 50 mg nocte, which, within 48 hours, reduced her affective and psychotic symptomatology and ameliorated her sleep architecture. Also, valproate 500 mg MR OD (Epilim Chrono) was started. Apart from this medication, she was only taking omeprazole, Movicol, senna, and Buscopan tablets. Her cognitive profile, a few weeks into admission, was relatively preserved, with frontal presentation; for example, resolution of conflicting tasks was somewhat impaired. She scored 29/30 on the Mini-Mental State Exam (MMSE) and 80/100 on Addenbrookes Cognitive Examination (ACE-R), losing points on working memory, fluency, language, and visuospatial abilities (Figure 1). The multidisciplinary team decision was made to postpone the subsequent cycles of the chemotherapy. One month later, on medication, no further psychotic symptomatology was noted, and the disinhibition, dysexecutive, affective, and cognitive elements of her mental state were all reported improved and stable.

FIGURE 1. From Addenbrooke's Cognitive Examination (ACE-R) Test



The patient was asked to draw a clock-face with numbers and the hands at 10 minutes past 5 o'clock: one of the tasks used to test visuospatial ability.

Discussion

Bell gave a detailed account of manic delirium as early as 1849 and described it as a psychiatric emergency.(2) It is a severe psychiatric syndrome, which, despite its recognizable features and pathognomic fusion of both mania and delirium elements, is not always accurately recognized and effectively treated.(1,3,4) The accepted gold standard treatment for this condition in many countries is ECT, or, if that is not available, high-dose benzodiazepines.(1,3) Typical antipsychotics and anticholinergic drugs are thought to be contraindicated, whereas quetiapine, clozapine, lithium, and valproate are used as a second-line treatment.(1) Carbotaxol (Paclitaxel and carboplatin) chemotherapy combination can be given for a number of conditions (e.g., ovarian cancer), and this is the only chemotherapy treatment recommended by The National Institute for Clinical Excellence (NICE) as initial therapy.(5) The combination is also recommended in recurrent (or resistant) ovarian cancer, and, so far, there have been no reported psychiatric complications of its use. To our knowledge, this is the first report to show the possible association of the abrupt onset of manic delirium in a geriatric patient and carbotaxol chemotherapy regimen for the malignant mixed Mullerian adenosarcoma.

There are several other unique aspects to this case. Its undulatory naturalistic crescendo course provides the informative retrospective insight. Here, intravenous benzodiazepines, and later, oral quetiapine and valproate were found to act effectively and rapidly to decrease the symptoms of manic delirium. It is possible that their effect appears magnified by the natural regression of this somewhat

milder subtype of the syndrome. Furthermore, unlike the majority of reported and analyzed cases in the literature, our patient was an older woman with no salient personal or family psychiatric history. Interestingly, she had been treated with tamoxifen for her breast cancer in the past. Tamoxifen is an antiestrogen with protein kinase C (PKC) inhibitory properties at high doses.(6) It has been found to be very successful in reducing manic symptoms in double-blind trials, which is believed to be reflection of its effects on PKC.(6–8) Manji and his colleagues (1999) were the first to recognize the importance of PKC signaling to the pathophysiology and treatment of mania, and this relevance is now also being extended to the possible treatment of schizophrenia.(9,10) It is tempting to postulate here that previous treatment by tamoxifen caused an imbalance in the PKC signaling in our patient in the longer term, and consequently increased the intrinsic neuronal networks susceptibility to the manic and psychotic phenotype.

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