Clinical Case Rounds in Child and Adolescent Psychiatry

Corticosteroid-Related Psychiatric Complications In the Treatment of Hodgkin's Lymphoma in an Adolescent

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Introduction

We present the case of an adolescent with Hodgkin's Lymphoma, who developed symptoms of psychosis and mania during his treatment. Psychiatric side-effects of corticosteroids in the adult population have long been recognized and documented. A wide range of mental status changes have been reported (Francois Sirois, 2003). However, case reports documenting psychosis or mania related to corticosteroid use in children are rare. Psychotic symptoms developing during the treatment of asthma have been described, sometimes with mood disorder symptoms (French et al, 2003, Couturier et al, 2001, and Dawson and Carter, 1998). Beshay and Pumariega (1998) presented the case of a boy treated for ulcerative colitis, who developed depressive and psychotic symptoms. There are also published cases of adolescents with Acute Lymphoblastic Leukemia developing psychotic symptoms during treatment with corticosteroids (Ducore et al, 1983, Kramer and Cottingham, 1999, Sutor et al, 1996).

Our case adds to the literature involving steroid-induced psychosis and mania in an adolescent with cancer.

Case Report

We report the case of a 14 year-old male diagnosed with Hodgkin's Lymphoma. His prior medical and psychiatric history was unremarkable. He was athletic, sociable, and on the honor role.

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Family history included a maternal grandparent with Bipolar Disorder, a parent who developed depressive symptoms following the patient's diagnosis of lymphoma, and a paternal grandparent who had alcohol-related difficulties.

His chemotherapy protocol included prednisone, with the last dose given during his fourth cycle of chemotherapy, in the month of admission for psychiatric symptoms. He had received chemotherapy for 15 days of each 30 day cycle. His prednisone dose in the month of admission was 75 mg a day. He was also on cyclophosphamide, vincristine, dapsone and procarbazine. He was on a dose of procarbazine of 100 mg/m^2/day during the month of admission and during the month preceding admission.

He presented to the Emergency Room two days before admission with grandiose delusions, but co-operative behavior. He was assessed by the oncology team that day and there were no new general medical issues or illicit substances detected. He was discharged from the Emergency Room. Two days later his parents brought him back. He displayed severe agitation, grandiose delusions, and pressured speech and required admission to the psychiatry unit.

He has multiple grandiose delusions. He believed that he was God, had created a computer program that could read minds, had billions of dollars, had cured ill people, could revive the dead, and could transport people with his mind. He had visual hallucinations, seeing flames on his hand that he believed were flames from hell.

Initially, he required physical restraints. Because of continued agitation and threats to harm other children, he was transferred to a secure adolescent psychiatry unit at another hospital. His severe agitation and belief that he had cured his cancer lead to a delay in the next

cycle of chemotherapy. The hope was that he could continue his chemotherapy within ten days. His olanzapine was switched to haloperidol. He settled significantly and was transferred back to his primary hospital a week later in order to resume chemotherapy. He developed significant extrapyramidal symptoms, requiring treatment with benztropine. He also developed blurred vision, likely secondary to his medications. His vision improved as these were tapered, and replaced with quetiapine.

Upon return to his primary hospital, his thought process was more organized, he was usually euthymic, and he had no hallucinations. He continued to express grandiose delusions about a computer business and money, but over time these faded. Thoughts about possessing special powers and curing illness lingered. He developed an appreciation of the need for quetiapine. Diagnostically, the possibility of a primary bipolar disorder was considered. The oncology team changed his chemotherapy protocol so that it no longer included steroids or procarbazine.

An MRI of his head, during his admission, showed mild global volume loss possibly related to steroids, no focal signal abnormality, and an incidental finding of a pineal gland cyst. He had a normal EEG.

He was discharged home after two months, with follow-up by Oncology and Psychiatry.

Discussion

Stiefel et al (1989) reviewed the characteristics of steroid related psychiatric symptoms in patients with cancer and other medical illnesses. Symptoms can occur early or after months of treatment, or can occur when steroids are tapered. Symptoms are usually reversible, but may persist. Higher dose appears to be the most important factor correlated with an increased risk of psychiatric side-effects. Duration of treatment has not shown the same relationship. There is little clarity as to whether a personal history of psychiatric illness is a risk factor. Patients with cancer often have medical complications and may be on other medications that increase the risk of psychiatric disturbances.

It remains unclear whether repeated exposure to corticosteroids increases the risk of psychiatric changes (Perantie and Brown, 2002). Our patient's earlier courses of steroid treatment did not precipitate significant psychiatric symptoms, but perhaps his repeated exposure did. He had a significant family history of mood disorders; this may play some role in the risk of developing psychiatric symptoms.

His treatment involved procarbazine, which has mild monoamine oxidase inhibiting properties. There have been two cases of mania in adults involving procarbazine (Carney et al, 1981, Krauthammer and Klerman, 1978). There is one case of procarbazine causing psychosis in a child (van Eys et al, 1987). Her psychotic symptoms did not appear until the dose was increased to 638 $mg/m^2/day$. Our patient's procarbazine dose was much lower, but it may have played a role in the development of his psychiatric symptoms, and may have acted in concert with the corticosteroids.

Conclusion

Knowledge regarding risk factors for psychiatric reactions to corticosteroids remains limited. Effects of concurrent medications will require planned studies to better elucidate the effects of individual agents. As others have proposed (Stiefel et al, 1989), it is important to study psychiatric disturbances related to corticosteroids, while controlling for type of illness, concurrent medications, and co-morbid medical conditions. Severe psychiatric reactions can contribute to a change in treatment that may not allow for an optimal outcome, in oncology and in other areas of medicine. Further research is needed to better understand the development of psychotic and mood symptoms in the treatment of cancers, and to develop prophylaxis strategies directed at these complications.

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Commentary on Corticosteroid-Related Psychiatric Complications In the Treatment of Hodgkin's Lymphoma in an Adolescent

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Mian et al. have presented an interesting case of a 14- year old male who developed manic symptoms during a course of steroids for Hodgkin's Lymphoma. This case is reminiscent of our case previously described in the literature of an adolescent female who became quite grandiose during a course of oral prednisone (Couturier et al., 2001). Both of these cases appear to represent steroid-induced mania. The authors correctly point out that repeated exposure to steroids, and a family history of bipolar disorder may be important factors to consider when treating young patients with steroids. These factors may increase the risk of mood and psychotic symptoms, although the literature is limited in this area. There remain many unanswered questions regarding steroid-induced psychiatric symptoms: 1) Are children and adolescents at greater risk than adults? 2) Should prophylaxis with a mood stabilizer be considered when treating someone at risk of mania or psychosis with steroids (e.g., someone with a personal history, family history, or multiple exposures)? 3) How long should patients with a steroid-induced mania or psychosis be treated following the episode if steroids have been withdrawn?

Given the paucity of evidence informing practice in this area, it is important to encourage publication of reports of single case descriptions and case series in order to improve our understanding of the link between therapeutic use of steroids and psychiatric symptoms.

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Omission:
The Editor and Section Editor of the Clinical Case Rounds in Child and Adolescent Psychiatry regret the omission to the Clinical Case Rounds presented in the November 2006 issue. The Commentary for the article entitled "Treatment Resistant Psychosis in an Adolescent with Scoliosis and a History of Early Feeding Difficulties" is included on the following page.