Brain & Development 29 (2007) 666–669

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Case report

Hypomanic mood in a child patient treated with interferon-α 2a: Case report

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Received 18 June 2006; received in revised form 23 March 2007; accepted 26 March 2007

Abstract

We report on a male child born in Rumania, adopted by an Italian family, and who at 10 years of age was submitted to interferon-α 2a therapy for chronic hepatitis B. About 30 days after the beginning of the treatment he developed hypomanic mood and psychogenic seizures. Psychological evaluation showed hyperactivity, distractibility, excessive talkativeness, grandiosity and racing thoughts. Temperamental traits were characterized by an elevated emotionality. The patient was successfully administered risperidone and cognitive-behavioral therapy; six months of treatment with interferon led to positive outcome of hepatitis B. Since affective symptoms may occur in children treated with IFN, a careful evaluation of psychiatric disturbances and adequate intervention are needed.

Keywords: Hepatitis; Interferon; Child; Hypomanic mood

1. Introduction

Adverse reactions associated with the interferon therapy (IFN) are common in adult patients and usually occur about 1–3 months after the beginning of treatment. They involve an influenza-like reaction with fever, hypo or hypertension, tachycardia, gastrointestinal disorders, weakness, myalgia, nausea, headache, or late hematologic, infectious, autoimmune, and systemic side effects [1–3].

Neuropsychiatric complications associated with IFN therapy have also been reported in adults, including cognitive dysfunction and mood change of varying severity [4]. These problems are the most common causes of treatment discontinuation. The toxicity mechanism of IFN is not yet understood, including whether toxicity is dose-dependent with variations of the daily dose, the mode of administration, and medical history [5]. No significant neuro-psychiatric adverse effects have been reported in the pediatric age [6,7]. We report on a child patient who manifested hypomanic mood during IFN therapy.

2. Case report

The male child, who born in Rumania and adopted by an Italian family, had no history of violence, neglect, physical, sexual abuse, or significant traumas before adoption; no dysfunctional relationship was present in the adoptive family. The child was 10-years-old and had not yet reached the prepubertal stage of development.

He was affected by chronic hepatitis B, with seropositive results for HBsAg and HBeAg, detectable serum levels of HBV DNA, high levels of alanine aminotransferase and chronic active hepatitis histologically.

He was given interferon-α 2a therapy, administered by subcutaneous injections, three times per week, with each dose containing 3 MIU (Million International Units).

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doi:10.1016/j.braindev.2007.03.010

About 30 days after the beginning of therapy, his parents noticed that the child manifested a change of mood characterized by marked irritability and psychomotor agitation, accompanied by an excessive involvement in activities with a high risk for painful consequences. For evaluation of these reasons, the boy was referred to the Division of Child Neurology and Psychiatry of Catania University Hospital.

He presented episodes of staring, loss of consciousness, closed eyes, thrashing and chaotic jerky movements of the limbs, trunk and head. The crises recurred at intervals during the week, each episode lasting approximately 10–20 min. Post-critical arousal was slow and followed by headache and irritability. Neurological examination, laboratory analysis, ophthalmologic examination, electrocardiogram, interictal EEG, and magnetic resonance imaging (MRI) were all normal; ictal video-EEG did not reveal any electric abnormality. In considering IFN-induced depression, it is important to rule out the possibility that other physiological causes (general medical conditions) may be the source of the depression and to determine whether such disorder requires isolated treatment [8]. IFN can affect the hematological system and produce thyroid gland dysfunction, causing symptoms that appear similar to major depression or other mood disorder or contribute to the precipitation of psychiatric symptoms. IFN, particularly IFN-α, is known to induce thyroid dysfunction in more than 10% of treated patients [9]. However, in our patient, no manifestation of endocrine disorders, such as thyroid gland or collagen disorder, were present.

Psychological assessment was performed with the following instruments:

(1) Behavior and mental evaluation; (2) Wechsler Intelligence Scale for Children-Revised (WISC-R), to measure the intelligence quotient [10]; (3) Parent Child Behavior Checklist (CBCL), to examine internalizing and externalizing features [11]; (4) Multidimensional Anxiety Scale for Children (MASC), to investigate the anxiety [12]; (5) Emotionality–Activity–Sociability–Shyness Scale (EAS), to evaluate the following temperamental traits: Emotionality (tendency to become easily upset), Activity (tendency to be restless), Sociability (tendency to prefer the presence of other over solitude) and Shyness (uneasiness in novel or unfamiliar social situations) [13]. Parental consent was obtained.

3. Results

(1) Behavior and mental evaluation: the child displayed hyperactivity, distractibility, excessive talkativeness, irritability and decreased need of sleep; he also showed a tendency to engage in dangerous activities. Mental status examination revealed inflated self-esteem, increase rhythm of speech and racing thoughts. During the day, he was more talkative, his attention was too easily drawn to unimportant or irrelevant external stimuli, he wanted to be the center of attention and showed an excessive involvement in pleasurable activities that have a high potential for painful consequences. These episodes were associated with an unequivocal change in functioning at school and at home with his parents.

(2) WISC-R: the IQ was within the normality (total score: 80).

(3) CBCL: he displayed a pathological score in the CBCL total (*T*-score: 82) and in the following subscales: somatic complaints, attention problems, and aggressive behavior (*T*-scores: 85, 80 and 88, respectively);

(4) MASC: he had a score in the pathological range in MASC total (*T*-score: 76) and in social anxiety and separation panic subscales (*T*-scores: 74 and 80 respectively);

(5) EAS: indicated an elevated emotionality (raw score: 2.90).

4. Course

During his stay in the child neuropsychiatry division, the patient manifested persistent hypomanic mood, as well as episodes of staring, loss of consciousness, thrashing and chaotic jerky movements of the limbs, as described previously, which recurred sometimes during the day and at bed-time. Post-critical arousal was often characterized by aggressive and violent behavior. The patient was treated with a neuroleptic mood stabilizer (risperidone: dose of 1 mg daily) and cognitive-behavioral treatment. The goals of therapy were the modulation of temperamental extremes and improvement of coping strategies.

Interferon α-2a therapy was continued for six months: acceptable safety profile and efficacy were indicated by normalization of alanine aminotransferase and absence of HBV DNA and HbeAg. The risperidone combined with cognitive-behavioral therapy led to progressive withdrawal of hypomanic traits and psychogenic seizures. At six months, follow-up confirmed an improvement of psychiatric symptoms: the child displayed a reduction of hyperactivity and talkativeness; he paid more attention to normal activities, and he was more able to engage in conversation with the physician. He also showed a reduction of dangerous activities and increased regulation of sleep. His scores on both the CBCL and MASC were reduced.

In particular, the CBCL total score decreased from 82 to 62, and T-scores of somatic complaints, attention problems, and aggressive behavior subscales decreased from 85 to 70 (98th percentile), from 80 to 68 (<98th percentile) and from 88 to 74 (>98th percentile), respec-

tively. The total score on the MASC showed a reduction from 76 to 60, and *T*-scores on the MASC social anxiety and separation panic subscales decreased from 74 to 62 and from 80 to 68, respectively. EAS scores did not change.

5. Discussion

IFN is an effective therapy in patients with chronic hepatitis. In adult patients, neuropsychiatric complications have been reported frequently: they include confusion, impaired concentration, depression, irritability, insomnia, anxiety, behavior disturbances, psychosis, severe subcortico-frontal impairment, choreic movements and others. The toxicity mechanism of IFN is not yet understood, including whether the toxicity is dependent on variations in daily dose, mode of administration, and medical history [4].

Throughout IFN therapy, however, adverse neurologic effects rarely have been reported in children. Two subjects experienced seizures that required neither anticonvulsant therapy nor discontinuation of interferon treatment [14], and spastic diplegia as a complication of interferon-α 2a treatment for hemangiomas of infancy was reversible [15].

A considerable amount of evidence suggests that monoamine dysfunction, including especially decreased 5-HT levels, contributes to the etiology of IFN-induced psychiatric disorder. Additional reasons for psychiatric disturbances induced by IFN include hypothalamic–pituitary–adrenocortical (HPA) axis activation; proinflammatory cytokine activation such as interleukin(IL)-1[β], inteleukin (IL)-6, and tumor necrosis factor (TNF)-[α]; decreased peptidase levels; increased intercellular adhesion molecule-1, and increased nitric oxide levels [16–18].

Our 10-year-old patient had a treatment regimen of 3 MIU/day of interferon-α 2a , three times a week, by subcutaneous injection because of chronic HBV.

One month after the beginning of the interferon therapy, an affective episode with elevated mood and psychogenic crises (probably induced by external triggers) occurred that gave further evidence of emotional dysfunction [19]. The patient was submitted successfully to therapy with an atypical antipsychotic drug (risperidone) and cognitive-behavioral intervention.

For management of side effects with mood stabilizers in patients with chronic hepatitis, possible liver toxicity must be taken into account (valproic acid and carbamazepine). Risperidone was chosen rather than lithium because the boy had difficulties in swallowing pills and refused any non-liquid medical preparation. Therefore, risperidone (which is available as a syrup) was administered. After six months, a reduction of psychiatric symptoms was evident; there was an apparent complete recovery from the HBV. In adult patients, mania induced by the interferon therapy may be pharmacologically treated by mood stabilizers such as lithium, valproic acid and carbamazepine, as well atypical antipsychotics, such as risperidone, aripiprazole and quetiapine [20–22].

Our experience confirmed that IFN is an effective and tolerable therapy in children with chronic hepatitis B virus infection, although hypomanic mood could arise throughout IFN therapy, pharmacological and cognitive-behavioral treatment may allow completion of the full course of IFN therapy.

To our knowledge, this is the first report of hypomanic mood in a pediatric patient on interferon therapy successfully that has been treated by risperidone and cognitive-behavioral therapy. Further contributions, however, are needed to investigate both the frequency and the management of adverse psychiatric effects in children who are being treated with IFN.

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