

SUICIDE ATTEMPT OF A PATIENT RECEIVING INTERFERON ALPHA THERAPY FOR CHRONIC MYELOID LEUKEMIA

KRONİK MYELOİD LÖSEMİ NEDENİYLE ALFA İNTERFERON TEDAVİSİ GÖREN BİR HASTANIN İNTİHAR GİRİŞİMİ

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SUMMARY: This is a presentation of a 38-year-old male patient who had a low-velocity gunshot wound because of a suicide attempt. The suicide attempt occurred after two months of antidepressive drug therapy for a Major Depressive Disorder episode that emerged during alpha-interferon therapy because of his chronic myeloid leukemia illness. A comminuted mandibular body fracture was reconstructed by iliac bone graft. Antipsychotic and anxiolytic drug therapies were added, and the dose of the antidepressant drug was increased after the suicide attempt. Symptoms deceased after this medical treatment protocol. Our colleagues should be aware of the possible psychiatric side effects of interferon and the consider psychiatric and medical management of such patients, as well as reconstruction.

Key Words: Interferon, Psychiatric Side Effects.

INTRODUCTION

Self-inflicted gunshot wounds to the face during suicide attempts constitute a certain amount of maxillofacial firearm injuries (1, 2). Some of the mental disorders develop as a side effect of drugs such as antiepileptics (3) or corticosteroids (4), which are used for the treatment of organic diseases. Interferon has been used as an antiviral antineoplastic agent, and numerous psychiatric complications, including depression and suicidal behavior, have been attributed to interferon therapy (5-12).

Several lines of evidence suggest interferon-alpha (IFN- α) may mediate neurotoxicity via the

ÖZET: Kronik myeloid lösemi nedeni ile alfa-interferon tedavisi sürdürülürken major depresif bozukluk tanısı ile antidepressif tedavi önerilen ve iki ay sonra intihar girişimi sonucu yüzünden düşük hızlı ateşli silah yaralanması (ASY) geçiren 38 yaşında bir erkek hasta sunulmaktadır. Çok parçalı mandibula frakturü iliak kemik grefti ile onarılmıştır. İntihar girişimi sonrası psikiyatrik tedaviye antipsikotik, anksiyolitik ilaçlar eklenmiş, antidepressif ilacın dozu yükseltilmiştir. Hasta bu tedaviye iyi cevap vermiştir. Meslektaşlarımız interferonun olası psikiyatrik yan etkilerinden haberdar olmalı ve bu tür hastalarda rekonstrüksiyon yanında psikiyatrik ve tıbbi tedaviyi de gözönünde bulundurmalıdır.

Anahtar Kelimeler: İnterferon, Psikiyatrik Yan Etkiler.

neuroendocrine, neurotransmitter, cytokine and free radical pathways (13, 14). IFN- α does not cross the blood-brain barrier, so its effects likely derive from indirect actions on the central nervous system. Proposed etiologies include direct stimulation or inhibition of the hypothalamic-pituitary axis, interferon-induced changes in thyroid function, indirect effects of IFN- α on the opioid receptor system, interferon-mediated alterations in neurotransmitter levels, and toxic effects of secondary cytokines (e.g., interleukin-1) (15,16).

Psychiatric management of the suicide attempter and decision-making about the fate of interferon therapy after suicidal behavior require

special emphasis, as does reconstructive management.

PATIENT REPORT

A 38-year-old man was presented with a close-range gunshot wound to the face. The patient had shot himself with his pistol in an attempt to commit suicide. The entrance wound of the bullet was on the right submandibular region, and the exit wound was on the right infrazygomatic area. Radiographic and CT studies revealed a comminuted fracture of the right mandibular body and a small anterior maxillary sinus wall defect. The patient was immediately taken to the operating theater, and general anesthesia was given via nasotracheal intubation. All the devitalized soft tissue and bony fragments were conservatively debrided. The marginal mandibular branch of the facial nerve was severely lacerated. A bony defect, 4 cm in length, developed on the mandibular body; bony segments were stabilized using a reconstruction plate. The bony defect of the anterior maxillary sinus wall was 5 mm and was left untouched. The orbital floor and infraorbital nerve was intact. Intraoral mucosal and external skin lacerations were closed primarily. The postoperative period was uneventful. Three months later, the mandibular defect was restored with a monocortical iliac bone graft harvested from the left side. Excellent occlusion was achieved, and the mandibular opening was 36 mm one year later. However functional loss of the marginal mandibular branch was persistent.

Medical and Psychiatric History of the Patient

The patient had been diagnosed with chronic myeloid leukemia (CML) one year before the suicide attempt and received interferon alpha-2a (9 million unit/day, daily) and cytarabine (10 mg/day, 10 days per month) for 6 months. Then the interferon therapy was switched to interferon alpha-2b (10 million unit/day, 6 days per week) for another 6 months in combination with cytarabine. Two months before the suicide attempt, he was referred to the psychiatry clinic with complaints including insomnia, boredom, demoralization, sensitivity, intolerability and depression. During the psychiatric interview, his appearance was anxious; he was conscious, and his orientation and perception functions were

complete. He had good insight about his illness. He was in a depressed and anxious mood. He had feelings of worthlessness, sensitivity and inappropriate guilt and partial psychomotor agitation. He was diagnosed with Major Depressive Disorder, single episode through DSM IV criteria (17), and given citalopram 20 mg/day pharmacotherapy.

At the first month follow-up the patient was in remission and was recommended to continue the same pharmacotherapy. He had been in remission since the interferon therapy had been instituted. The patient had no history of a pre-existing psychiatric disorder or complaints before the diagnosis of CML. He had a favorable family environment with his spouse and two children. No blood relative had any psychiatric history.

During the 5-day hospitalization period in the plastic surgery department, interferon therapy was discontinued and intensive psychiatric treatment was established with the diagnosis of a severe depressive disorder with psychotic features. Then the patient was transferred to a psychiatry clinic for further psychiatric therapy, and interferon alpha-2b therapy was re-instituted after an oncology consultation. He was exhausted and depressed and had low insight about his illness. He had feelings of worthlessness, sensitivity and inappropriate guilt, which were delusional on this occasion. There was retardation in his psychomotor activity. He was diagnosed with Major Depressive Disorder, recurrent through DSM IV criteria (17). Antipsychotic (risperidon 6mg/day), anxiolytic (alprozolam 1.5mg/day) and antidepressant (mirtazapine 30 mg/day) drug therapies were added, and the dose of citalopram was increased. Treatment with antipsychotics, anxiolytic and antidepressive drugs was associated with a reduction of the psychiatric symptoms. The patient was discharged with minor complaints 2 weeks later. One month later, the control interview revealed an absence of psychotic symptoms, decreased anxiety and decreased major depressive disorder symptoms, and antipsychotic and anxiolytic drug therapies were stopped and the dose of mirtazepine lowered to 15 mg/day. Citalopram therapy continued at the same dosage level.

The patient has received antidepressive treatment as well as interferon alpha-2b and

cytarabine for one year following the suicide attempt. His mental condition has remained stable, and the CML has been in remission. We did not observe any wound healing problem due to the CML, mental disorders or drugs he received. The cooperation of the patient was excellent in the rehabilitation period of the surgical interventions.

DISCUSSION

Interferons, with their antiviral and antineoplastic activities, stand as a reference point both in oncology and virology. They have been used in the treatment of various disorders such as hepatitis, multiple sclerosis, leukemia, renal cancer and malignant melanoma. However, numerous somatic and neuropsychic side effects complicate interferon therapy and limit its efficiency. Although interferon has been reported present in the central nervous system during systemic interferon therapy and electroencephalographic abnormalities have been associated with it, the mechanism of interferon in psychiatric complications needs to be clarified (18, 19). Presently, interferon-alpha and interferon-beta are not believed to differ in their potential to induce psychiatric complications (20).

Personality disorders, mood disorders, anxiety, suicidal tendencies and manic and psychotic symptoms are the main psychic complications of interferons and are detected in 17% to 30% of the patients receiving interferon therapy (5, 10). Psychiatric side effects are the most frequent reason for discontinuing interferon therapy (10). Moreover, some of these side effects can lead to suicidal behavior. Suicidal behavior among patients receiving interferon have ranged from 0.02% (6) to 3.4% (10) and fit into three main clinical entities: complication of a severe depressive syndrome, confusional context and disorder of impulse control. Depressive disorders are the most common interferon-related psychiatric diagnosis and are detected in 5% to 15% of the patients (8, 20). The majority of interferon-related psychiatric complications develop within 1 to 6 months of the initiation of interferon therapy. However, we should add that Mulder and coworkers studied prospectively the psychiatric side effects of interferon alpha in 63 consecutive patients with hepatitis C and found that interferon treatment was not associated with

a worsening of psychiatric symptoms (21).

Although Renault et al. (10) believe that psychiatric problems are generally seen in patients receiving high doses, others state that such effects are not related to the dose or duration of interferon therapy (6, 20, 22). Fattovich (6) and Fukunishi (7) have described psychiatric symptoms occurring in patients with no psychiatric or substance-abuse history, but some authors have found that such problems with interferon tend to occur in patients who have shown drug or alcohol abuse or a past history of psychiatric disorder (10, 20, 22). Patients receiving interferon should be screened and monitored for depression (23). In cases of severe depression or organic personality changes with increased risk of suicide, immediate discontinuation of interferon therapy and close psychiatric supervision for 6 months has been recommended since suicidal behavior was reported, even in the interferon withdrawal period (24).

In the case of our patient, depression was diagnosed two months before the suicidal behavior and 10 months after the CML diagnosis. The depressive status of the patient could be endogenous, an adjustment disorder with a depressed mood or a side effect of interferon. Since the patient had no past or family history of mental disorders and no history of substance abuse, the probability of endogenous depression is low, although we cannot fully rule it out. An adjustment disorder (subtype: "with depressed mood") can be considered as an alternative diagnosis. However adjustment disorders begin within three months of the onset of a stressor (17); our patient had no remarkable psychiatric reaction to his sickness for 10 months following the announcement of the diagnosis (the CML diagnosis is the stressor in our case), and the leukemia had been in complete remission from the beginning of interferon therapy. So it appears the depression and suicidal behavior of our patient were probably related to the interferon therapy. Cytarabine is the other drug used in combination with interferon to treat our patient's leukemia, and to our knowledge, no serious psychiatric side effects from cytarabine have been reported.

In the presented patient, the interferon therapy was re-instituted with close psychiatric

monitoring after a 5-day pause since interferon has vital importance for leukemia treatment. The other alternative drug for leukemia, imatinib mesylate (25), has recently been approved in Turkey. The patient's oncologist does not plan to change the interferon treatment protocol since the disease has been in remission and the psychiatric status of the patient has also been stable.

In conclusion, patients receiving interferon therapy should be carefully monitored for the psychiatric side effects of the therapy, and reconstructive surgeons should consider the psychiatric and medical management of such patients, as well as their reconstruction.

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