IFN & SIDE EFFECTS KIDS

1: Pediatr Infect Dis J. 1997 Oct;16(10):984-90.

Side effects of alpha-interferon therapy and impact on health-related quality of life in children with chronic viral hepatitis.

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BACKGROUND: Interferon (IFN) is standard therapy for chronic viral hepatitis in children. The aim of this study was to evaluate the side effects of alpha-interferon (IFN) in 94 consecutive children (58 males; age range, 3 to 14 years) affected by chronic viral hepatitis treated with different schedules ranging from 3 to 10 MU and from 3 to 12 months, and the impact of this therapy on health-related quality of life. METHODS: Side effects were evaluated with clinical and laboratory examinations and were recorded on a diary card. The health-related quality of life was evaluated with a modified version of the Sickness Impact Profile. RESULTS: All patients experienced at least one adverse reaction to IFN treatment; 80% had more than five side effects.There were no life-threatening reactions. Three children experienced severe reactions (febrile seizure, severe hypertransaminasemia and relapsing episodes of epistaxis, respectively) that required permanent IFN withdrawal. Another child had a febrile seizure requiring temporary IFN withdrawal. In seven children the neutrophil count fell below 1000/mm3 and promptly increased when IFN was temporarily discontinued. The remaining children had mild or moderate clinical and/or laboratory adverse reactions. Age, sex, viral etiology of chronic hepatitis and response to therapy were not significantly associated with the appearance of side effects. The pre-IFN health-related quality of life was good in all children; it deteriorated significantly during IFN therapy and returned to basal standards within 3 months after IFN withdrawal. No patient required suspension of IFN therapy because of worsening of health-related quality of life. CONCLUSION: Children have a low risk of developing severe IFN-induced side effects. Adverse reactions and worsening of health-related quality of life were tolerable and did not seem to be a limiting factor for IFN

therapy in young candidates.

PMID: 9380477 [PubMed - indexed for MEDLINE]

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Interferon Therapy in Patient With History of Seizures?

Question

Is a past or current history of seizures/epilepsy a contraindication to the use of interferon (IFN), pegylated or not, for the treatment of hepatitis?

Alvaro Gonzalez-Koch, MD

Response from Roshan Shrestha, MD
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A history of seizures or epilepsy is a relative contraindication to the treatment of hepatitis C virus (HCV) infection with IFN. However, an individual with a history of a seizure disorder who (1) has been on antiseizure therapy without any episodes of recurrent seizure activity within the past 1-2 years, (2) has been followed by a neurologist, and (3) has a favorable HCV genotype with active disease by both laboratory and liver histology could be considered for treatment with IFN. The patient should be counseled about the possibility of seizures during treatment, despite being on antiseizure medication with therapeutic levels. However, if there is ongoing seizure disorder, the patient should not be considered for IFN therapy.

Posted 06/27/2003

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Note: Performing your original search, ***interferon seizure***, in PubMed will retrieve *128* records.

1: Rev Med Chir Soc Med Nat Iasi. 2000 Apr-Jun;104(2):135-7.

[Seizures during the treatment with interferon for chronic C hepatitis]

[Article in French]

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Interferon alpha (IFN-alpha) is a well-established first-line treatment for chronic viral hepatitis. Side effects of IFN-alpha therapy are common but generally mild and self-limited. Generalized seizures during IFN-alpha therapy are very uncommon and are present in clinical isolated cases and usually in association with high doses of IFN-alpha. In our case a female of 39 years old, seizures have occurred at low doses of IFN-alpha used as therapy for chronic C viral hepatitis. As it comes to our knowledge, till now, there were published only 4 cases of generalized seizures that occurred during treatment with IFN-alpha for chronic C viral hepatitis. The physiopathology of this complication is unknown. Generalized seizures can be reasonable due to IFN-alpha therapy, as long as the patient didn't have any seizure history, or other factors, which can develop seizures. Neurological examination, EEG and brain scan were normal. The recurrence of these seizures was absent stopping IFN-alpha therapy without any other seizure treatment.

PMID: 12089978 [PubMed - indexed for MEDLINE]

Note: Performing your original search, ***interferon alpha seizure melanoma***, in PubMed will retrieve 4 records.

1: Ann Dermatol Venereol. 2003 Feb;130(2 Pt 1):202-4.

[Seizures during interferon alpha therapy: three cases in dermatology]

[Article in French]

Legroux-Crespel E, Lafaye S, Mahé E, Picard-Dahan C, Crickx B, Sassolas B, Descamps V.

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INTRODUCTION: Interferon alpha has many side effects. Among them the risk of occurrence of seizures is not well known by dermatologists. We report three cases of seizures that occurred in patients treated with interferon alpha in two dermatological diseases: mycosis fungoides and melanoma. OBSERVATIONS: A 68 year-old man, treated for mycosis fungoides, and two men aged 47 and 52 years, treated for melanoma, were under interferon alpha. After 11 months, 3 weeks and 9.5 months, respectively, the three patients had seizures without any past history of epilepsy. Anamnesis and assessment of each patient (brain CT, biological results) suggested the responsibility of interferon alpha. After withdrawal of the treatment, no relapse was observed after 3 months, 6 months and 1 year later, respectively. DISCUSSION: Seizures during treatment with interferon alpha have already been reported. According to the series their prevalence would be of 1 to 4 p. 100. Their pathophysiology is not well known, but apparently interferon alpha lowers the epileptogenic threshold by affecting the central nervous system either directly or through cytokines or neuromediators. The risk of occurrence of seizures must be known by the prescribing physician who must systematically search for past history of epilepsy or risk factors for seizures. This rare but existing side effect raises the problem of information to be supplied to the patient by the prescribing physician.

PMID: 12671585 [PubMed - indexed for MEDLINE]

PSYCHOSOMATICS

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Case Report

Neuropsychiatric Complications Associated With Interferon-Alpha-2b Treatment of Malignant Melanoma

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Key Words: Malignant Malinoma • Complications

Malignant melanoma is a common skin neoplasm; it accounts for 3% of all cancers.[1] Each year, approximately 40,000 new cases are diagnosed in the United States. Treatments for this potentially lethal cancer include lesion excision, lymph node dissection, and surgical adjuvant therapy with chemotherapy or with an immunomodulatory agent. [1] More recently, interferon-alpha-2b (IFN-A), an immunomodulatory drug produced by recombinant DNA techniques, has become the agent of choice for patients with resected lesions and a high risk of disease recurrence. [2,3] Unfortunately, a variety of neuropsychiatric side effects can result from use of IFN-A.

This is the case of a 51-year-old man who underwent a course of high-dose intravenous (IV) IFN-A to treat malignant melanoma. During IFN-A therapy, he developed severe depression, which was effectively treated with electroconvulsive therapy (ECT). To the author's knowledge, this is the first such case report. A review of the relevant literature on malignant melanoma, IFN-A, and interferon-related mood disorders and their treatments is provided.

Case Report

Mr. A, a 51-year-old mechanic, was diagnosed with malignant melanoma 1 month after he noted spots of blood on the back of his shirt. Treatment included a wide excision of the lesion and a left axillary node dissection (after a positive sentinel node biopsy). He underwent a course of high-dose IFN-A (20 million units/square meter [MU/m^2] IV five times a week for 4 weeks). After 1 week of IFN-A, Mr. A became depressed. Although he had a history of major depressive disorder (MDD) with a suicide attempt 5 years earlier, obsessive-compulsive disorder (OCD), and posttraumatic stress disorder (PTSD) related to combat experience, his psychiatric symptoms had been stable until interferon administration. After the first week

of interferon, olanzapine 2.5 mg twice daily was added to his regimen of citalopram 40 mg daily to target his excessive ruminative thoughts. By the end of the fourth week, Mr. A was severely depressed and had intense thoughts of suicide with a plan to drive his car into a bridge abutment; this prompted referral for inpatient psychiatric treatment.

He reported no history of alcohol or substance abuse. Medications on admission included citalopram (40 mg daily), olanzapine (2.5 mg twice daily), a multivitamin (daily), as well as a nonsteroidal anti-inflammatory drug for pain and temazepam for sleep when needed.

Mr. A had a burly physique and appeared in good health. Surgical scars over the back and axillae were the only remarkable findings; there was no evidence of infection. Laboratory studies revealed normal levels of electrolytes and glucose; liver function tests, a complete blood count, and folate and B_{12} levels were also normal. The urinalysis and urine screen for drugs of abuse were unremarkable. Thyroid stimulating hormone (TSH) was elevated at 30.31 μU/mL (normal range: 0.50–5.00 μU/mL). This was rechecked three times at several intervals during Mr. A's hospital course; each value (8.41, 9.30, and 11.40 μU/mL) was elevated. The remainder of the thyroid panel was also repeatedly checked and was within normal limits, except for a slightly decreased free T4 index of 3.6 (normal range: 4.5–10.9) at the time of discharge. Rapid plasma reagin (RPR) test was nonreactive. An electrocardiogram (EKG) revealed mild sinus bradycardia; the EKG was otherwise unremarkable. A chest X ray was normal. Computed tomography (CT) scans of the head, thorax, abdomen, and pelvis (completed 3 months before admission at another hospital) were reportedly normal. The mental status examination revealed depressed mood, anxious and dysphoric affect, obsessive rumination, and suicidal ideation (with a plan), but there was no evidence of homicidal ideation, mania, psychosis, or abnormal cognition.

The initial diagnostic impression was that Mr. A was experiencing a major depressive episode as well as obsessive symptoms. Given the severity of his depression, which had continued to worsen despite ongoing treatment with antidepressant medication, ECT was planned. Four unilateral ECT treatments were performed. Mr. A was continued on citalopram (40 mg/day), his olanzapine dose was decreased (to 2.5 mg/day), and he was given a benzodiazepine as needed for sleep and anxiety. Initiation of thyroid hormone supplementation was not recommended by endocrinology consultants, who suspected that Mr. A's thyroid function abnormalities were interferon related and could be followed as an outpatient.

Mr. A was discharged in good condition; he was without depressed mood, severe anxiety, or suicidal ideation. His outpatient oncology team recommended termination of IFN-A therapy (which had been scheduled to proceed with a maintenance phase of 10 MU/m^2 subcutaneously three times a week for 48 weeks) because of presumed interferon-induced depression and suicidal ideation, and he was followed in the oncology clinic. He received no subsequent immunotherapy or chemotherapy for his melanoma, and there has been no evidence of cancer recurrence.

Mr. A continued to have a stable mood until 15 months later, when he was readmitted to an inpatient psychiatric facility for a recurrence of depressive symptoms with suicidal ideation in the setting of 3 months of alcohol abuse. The medical workup included a brain magnetic resonance imaging (MRI) study with and without gadolinium contrast; there was no evidence of metastasis. Physical examination and contrast-enhanced chest CT similarly showed no evidence of melanoma recurrence. The remainder of the comprehensive laboratory workup was unremarkable except for an elevated TSH of 20.45 μU/mL. This was rechecked the next day, and the value remained elevated at 19.22 μU/mL with normal thyroid indices. Given the patient's prior response, consultation for ECT was obtained. However, the consultants chose not to proceed with ECT because Mr. A's symptoms were not severe enough during this hospitalization. In fact, Mr. A's mood stabilized quickly with milieu support, alcohol detoxification, and small medication adjustments, and he has since remained in good condition.

Discussion

With the incidence of melanoma rising more rapidly than any other form of cancer, malignant melanoma now represents 3% of all cancers. [1] The American Cancer Society has estimated that 41,600 new cases of melanoma were diagnosed in the United States in 1998 alone; the U.S. lifetime disease risk for melanoma

has increased sharply from 1/1,500 persons in 1935 to (an estimated) 1/75 persons in 2000. [1]

Surgical excision remains the principal treatment for primary melanoma; treatment for regional metastasis includes additional surgery, lymph node dissection, and regional chemotherapy limb perfusion. Adjuvant therapies include radiation, chemotherapy, and administration of biologic response modifiers (e.g., interferons and interleukins). As a result of the protocol titled Eastern Cooperative Oncology Group (ECOG) 1684, high-dose IFN-A emerged as the agent of choice for surgical adjuvant therapy in melanoma patients meeting specific criteria (i.e., [1] American Joint Commission on Cancer stage IIB or III melanoma, [2] absence of disease after surgical excision, [3] high risk for recurrence). [1,4] In these patients, IFN-A increased the median time to relapse, improved the estimated 5-year relapse-free survival rate (37% vs. 26% observation controls), and lengthened the estimated 5-year overall survival rate (46% vs. 37%). [4] ECOG 1684 established the following regimen for high-dose IFN-A in malignant melanoma: 4 weeks of 20 MU/m^2 of body surface area administered IV five times per week, followed by 48 weeks of 10 MU/ m^2 SC three times per week.

As interferons (immunomodulatory proteins with antimicrobial and antitumor properties) have been increasingly used in the treatment of melanoma and other diseases (e.g., chronic hepatitis B and C, AIDS-related Kaposi's sarcoma, hairy cell leukemias, and non-Hodgkin's lymphoma), awareness of their central nervous system (CNS) side effects has grown. [5] These effects can be grouped into two categories: early-onset constitutional reactions (e.g., fever, flulike symptoms, and malaise) after treatment initiation and late-onset reactions following sustained treatment. [5] Psychiatric complications include depression, anxiety, mania, and suicidal ideation; neurologic and neuropsychiatric complications include headaches, visual changes, paresthesias, hyperkinesia, decreased attention and concentration, and impairments in visual scanning, verbal memory, executive function, and motor control. [5,6] In addition, Greenberg and colleagues[3] described a syndrome of mood instability associated with IFN-A. This syndrome included unipolar depression, mania, and mixed affective states (either with or without psychotic features). Overall, 40% of interferon-treated melanoma patients report depressed mood; 8% endorse severe depression with functional impairment or suicidal ideation. [2,3] Attempted and completed suicides have been reported as adverse events to the Food and Drug Administration.[7]

The mechanisms by which interferon, which is similar in structure and function to adrenocorticotropic hormone and beta-endorphin, causes neuropsychiatric effects are unclear. IFN-A does not cross the blood-brain barrier, so its effects likely derive from indirect actions on the CNS. Proposed etiologies include direct stimulation or inhibition of the hypothalamic-pituitary axis, interferon-induced changes in thyroid function, indirect effects of IFN-A on the opioid receptor system, interferon-mediated alterations in neurotransmitter (e.g., serotonin, norepinephrine, and dopamine) levels, and toxic effects of secondary cytokines (e.g., interleukin-1). [6]

This case (Mr. A) provides an opportunity to consider the complex potential etiologies of his depression. Possibilities include recurrence of his primary mood disorder, depression secondary to CNS infiltration of his melanoma, depression secondary to the complications of treatment (interferon-induced vs. secondary to interferon-related hypothyroidism), and a reactive depression associated with having cancer. [6]

Mr. A's depression could have represented a recurrence of MDD that was completely independent of interferon therapy. However, the temporal relationship between IFN-A initiation and his development of mood symptoms suggests an interferon-induced recurrence of depression. Furthermore, the intensity of dysphoria was new to Mr. A and not consistent with prior episodes.

Since malignant melanoma is known to metastasize to the brain, this complication could have caused Mr. A's depression. The clinical literature reveals an estimated incidence of CNS metastases of 6%–11% (36%–54% in autopsy series). [8] CNS sites of involvement in order of frequency are as follows: cerebrum, usually the frontal lobe (no hemispheric preference), > cerebellum > base of brain > spinal cord. [9] Herald symptoms of CNS metastases include headaches, motor and sensory problems, psychological changes, and seizures. [9] As a Stage III patient, Mr. A underwent an extent-of-disease workup (including CTs of the head, chest, abdomen, and pelvis) that was unremarkable by report, and the inpatient psychiatry team was

satisfied with this evaluation. Unfortunately, since repeat brain imaging was not completed, CNS involvement could not be definitively excluded during the first hospitalization; a subsequent admission revealed no evidence of melanoma recurrence. The possibility of CNS metastasis underscores the importance of comprehensive workups, including head imaging and detailed neurologic examination. This has special significance in ECT, where increases in intracranial pressure due to space-occupying lesions could cause serious complications.

Another important factor was Mr. A's elevated thyroid stimulating hormone; it is unclear to what degree his thyroid abnormalities contributed to his mood changes. Although the increase in his TSH was presumed to be due to IFN-A treatment (since it fell rapidly following withdrawal of IFN-A), no baseline values were available for comparison. Furthermore, Mr. A's subsequent thyroid testing revealed an elevated TSH (with normal thyroid indices) 15 months after the termination of IFN-A. Thus, a causal relationship between interferon therapy and hypothyroidism cannot be clearly established in this case. The role of thyroid changes in the high incidence of depression among interferon-treated melanoma patients is difficult to discern. Trask and co-workers[5] noted that among studies reporting psychiatric side effects of IFN-A, only three studies mentioned any tests of thyroid function. The role of thyroid hormone augmentation in the treatment of depressed patients like Mr. A requires further inquiry.

Finally, while the temporal relationship between the start of interferon therapy and the onset of depressive symptoms suggests causality, it is also possible that Mr. A suffered from a reactive depression. In fact, depressed mood is commonly reported in patients before the initiation of any cancer treatment, [6] and it is thought to be precipitated by the stress of a life-threatening diagnosis.

Fortunately, Mr. A's depression, regardless of its etiology, responded to ECT. An established treatment for severe mood disorders for decades, ECT is considered safe and effective, and it is indicated in cases involving a serious risk of suicide. [10] Furthermore, "not a single controlled trial has shown another form of treatment to be superior to ECT in the short-term management of severe depressions." [11,12] In the case of Mr. A, ECT's impact may have been lifesaving. However, it is unclear how the patient might have responded to discontinuation of IFN-A alone. Case reports suggest that patients can either improve, remain unchanged, or become worse following the discontinuation of interferon. [3,13]

The occurrence of depression with suicidal ideation is felt to limit interferon treatment; in fact, the development of suicidal ideation is recognized as an absolute contraindication to continued therapy with IFN-A. [2] In our case, Mr. A's scheduled course of 48 weeks of subcutaneous IFN-A was terminated for this reason. In a case described by Ademmer and associates, [14] a patient treated with the IFN-A and ribavirin combination for hepatitis C made a suicide attempt while on an inpatient psychiatry unit; the treatment team chose to discontinue interferon because of the suicidal behavior. However, the authors concede that the literature is limited and does not provide consistent guidance on whether or when to stop interferon following the emergence of depressive symptoms. [14]

The presence of an effective and rapidly acting antidepressant treatment for interferon-induced depression not only would reduce the risks associated with depression and suicidal ideation but also would allow patients to continue treatment that can greatly improve prognosis. ECT should be considered such a treatment, but its role in the therapy of interferon-induced mood disorders requires further investigation. One may wonder if maintenance ECT could be an option for patients who are at high risk not only for fatal melanoma recurrences but also for depression and suicidal behavior while on interferon. While it was possible for Mr. A to be rechallenged with IFN-A and treated for depression with additional courses of ECT or other antidepressants, his outpatient oncology team elected to avoid the risk of another interferon-induced suicidal episode and discontinued IFN-A.

Effective treatment of interferon-induced psychiatric symptoms has been achieved with tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), psychostimulants, opioid-antagonists, and anxiolytics. [5,6] In addition, Greenberg and associates[3] reported the successful use of gabapentin for interferon-related mood instability in four patients with melanoma. To date, there have been no published controlled trials of antidepressant treatments that follow the initiation of IFN-A. [6]

Recently, Musselman and co-workers[15] published a randomized, double-blinded, placebo-controlled trial of paroxetine as prophylactic treatment for interferon-induced depression in patients receiving high-dose interferon for malignant melanoma. Significant findings in the paroxetine group included reduced incidence of major depression, decreased severity of mood symptoms when they did occur, and decreased likelihood of IFN-A discontinuation due to depressive symptoms. [15] Furthermore, the study found that baseline mood and anxiety ratings were predictive of depression and anxiety scores in the placebo group after IFN-A administration; [15] Capuron and Ravaud[16] have shown similar findings. These studies point to the importance of careful screening and prevention. Effective screening methods could play a critical role in identifying those at risk for severe depression.

Conclusion

The incidence of malignant melanoma is rapidly rising. As a result, more individuals will receive state-of-the-art immunomodulatory treatments (e.g., IFN-A). Since neuropsychiatric complications of this treatment are prevalent, we need to remain vigilant for their manifestations. Mr. A's case provides a compelling example of the neuropsychiatric symptoms associated with IFN-A therapy and presents a strategy for reviewing the differential diagnosis and treatment alternatives. Systematic study of preventive treatments as well as interventions for IFN-A psychiatric side effects is required. If we can diagnose and treat IFN-A psychiatric complications in a timely and effective fashion, we will be providing a valuable and lifesaving service.

REFERENCES

1. Langley RGB, Barnhill RL, Mihm MC Jr, et al: Neoplasms: Cutaneous melanoma, in Fitzpatrick's Dermatology in General Medicine. Edited by Freedberg IM et al. New York, McGraw-Hill, 1999, pp 1080-1116
2. Physicians' Desk Reference,® 54th Edition. Montvale, NJ, Medical Economics Company, Inc., 2000, pp 2808-2817
3. Greenberg DB, Jonasch E, Gadd MA, et al: Adjuvant therapy of melanoma with interferon-alpha-2b is associated with mania and bipolar syndromes: Gabapentin may serve as a mood stabilizer. Cancer 2000; 89:356-362[CrossRef][Medline]
4. Kirkwood JM, Strawderman MH, Ernstoff MS, et al: Interferon alfa-2b adjuvant therapy of high-risk resected cutaneous melanoma: The Eastern Cooperative Oncology Group trial EST 1684. J Clin Oncol 1996; 14:7-17[Abstract]
5. Trask PC, Esper P, Riba M, Redman B: Psychiatric side effects of interferon therapy: Prevalence, proposed mechanisms, and future directions. J Clin Oncol 2000; 18;2316-2326
6. Valentine AD, Meyers CA Kling MA, et al: Mood and cognitive side effects of interferon-α therapy. Seminars in Oncology 1998; 25 (Suppl 1):39-47
7. Dieperink E, Willenbring M, Ho SB: Neuropsychiatric symptoms associated with hepatitis C and interferon alpha: A review. Am J Psychiatry 2000; 157:867-876[Abstract/Free Full Text]
8. Amer MH, Al-Sarraf M, Baker LH, Vaitkevicius VK: Malignant melanoma and central nervous system metastases: Incidence, diagnosis, treatment and survival. Cancer 1978; 42:660-668[CrossRef][Medline]
9. Myers ML, Balch CM: Diagnosis and treatment of metastatic melanoma, in Cutaneous Melanoma. Edited by Balch CM, Houghton AN, Sober AJ, Soong S. St. Louis, MO, Quality Medical Publishing, Inc., 1998, pp 325-372
10. Crowe RR: Electroconvulsive therapy—A current perspective. New England Journal of Medicine 1984; 311:163-167[Medline]
11. Electroconvulsive therapy—Consensus conference. JAMA 1985; 254:2103-2108[Abstract]
12. Weiss AP, Welch CA: Electroconvulsive therapy, in Psychiatry Update and Board Preparation. Edited by Stern TA, Herman JB. New York, McGraw-Hill, 2000, pp 359-363
13. Prior TI, Chue PS: Psychotic depression occurring after stopping interferon-α. J Clin Psychopharmacol 1999; 19:385-386[CrossRef][Medline]
14. Ademmer K, Beutel M, Bretzel R, et al: Suicidal ideation with IFN-α and ribavirin in a patient with hepatitis C. Psychosomatics 2001; 42:365-367[Free Full Text]
15. Musselman DL, Lawson DH, Gumnick JF, et al: Paroxetine for the prevention of depression induced by high-dose interferon alfa. New England Journal of Medicine 2001; 344:961-966[Abstract/Free Full Text]
16. Capuron L, Ravaud A: Prediction of the depressive effects of interferon-alfa therapy by the patient's initial affective state. New England Journal of Medicine 1999; 340:1370[Free Full Text]

Interferon - Research + Literature
8/15/08 - 8/17/08 Print Outs

D ADVERSE EFFECTS

A review article (Quesada) concluded that with alfa interferons, doses of 1-9 MU are generally well tolerated, but doses of 18-36 MU yield moderate to severe toxicity. Doses greater than 36 MU can induce significant toxicity and significantly alter the performance status of the patient. Side effects can be minimized by administering ***interferon at bedtime***.

The most common adverse effect is ***flu-like syndrome*** consisting of fever, chills, fatigue, myalgias, anorexia and headache. These effects are transient, dose-related and reversible within 72 hours of cessation of treatment. Acetaminophen 500-1000 mg (10 mg/kg/dose for children) given 30 minutes before administration of interferon and q4h after alleviates the flu-like symptoms. Chills and rigors can be managed with meperidine 50 mg IV (1 mg/kg/dose in children) or chlorpromazine 25-50 mg IM before dose. Tolerance to the flu-like syndrome develops over several months on continued dosing. There are data to suggest that symptoms may be less pronounced if the interferon is given as a continuous infusion over a prolonged period of time such as 12-18 hours.

The significance of developing ***neutralizing antibodies*** to interferon remains controversial. The incidence of antibody formation to interferon alpha is approximately 0-10% but may be as high as 38% in patients with renal cell cancer. The issue of neutralizing antibodies has clinical relevance since patients have been described who lose their response to therapy after the formation of antibodies.

Elevation in liver function tests occur frequently, especially at doses greater than 10 MU daily, but generally decrease despite continued treatment and return to pre-existing levels within two weeks following cessation of treatment. Severe toxicity and liver failure can occur rarely.

The ***CNS toxicity*** is dose related and generally reversible, but resolution may take up to three weeks. Emotional and/or psychiatric problems have been reported in patients receiving >20 MU/m^2. At doses ≥100 MU, marked lethargy, confusion, dysphagia and overall mental and motor slowing occurs. Rarely, seizures have occurred at high doses. Suicidal ideation has been reported; interferon should be discontinued.

Cardiovascular adverse events, especially arrhythmias, are correlated with pre-existing cardiac dysfunction and prior cardiotoxic therapy. Hypotension may occur during, or up to two days after, interferon therapy. Patients should be adequately hydrated during therapy.

Adverse reactions to the ***intralesional administration*** of interferon are common (80%, severe 9%), but mild to moderate in severity, transient and rapidly reversible, usually within 24 hours. The most common reactions are flu-like symptoms and local reactions such as pruritis, paresthesia, swelling or pain.

Because the toxicity of high-dose interferon can be severely debilitating in ***patients with AIDS-related Kaposi's sarcoma***, it is advisable to escalate dose levels slowly in 3 MU/m^2 increments over several weeks and to immediately reduce doses by 50% when serious toxicity is encountered.

W Date: 8/18/08

Father's Notes Post my Seizure

ANTI-SEIZURE MEDS: Keppra
Topamax
Lamictal
Trileptal

INTERFERON alpha-2b Schering Corp. (Intron A)

Hi dose → 20 MU/m² 5x/wk 4 wks
Lo " → 10 MU/m² 3x/wk 48 wks

CHANCE MEL ↓ BY ___ & W/1 MO hi-dose?

CHANCE MEL ↓ BY ___ & W/11 MO lo-dose?

SEIZURE DUE HI-DOSE OR THE LO-DOSE?
NO WAY TO TELL (MORALES 8/18/08)

IF KEEP KEPPRA & RESTART IFN, CHANCE MORE SEIZURES?

OTHER SIDE EFFECTS IFN PERMANENT OR STOP WHEN STOP IFN (e.g. MEMORY PROBLEMS)?

→ Per Morales (8/18/08), 10 → 20% More people survive 5 yrs if go thru entire IFN treatment.

Per Herzog (4/21/08) – IF ADULT 50% CHANCE RECURRENCE, INT ↓ TO ABOUT 20%. SOME DRS THINK BETTER W/KIDS