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The rebound effect in the treatment of complex hemangioma with interferon alpha 2A

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The authors report the case of an infant with an extensive face hemangioma with subglottic airway obstruction which had been successfully treated with interferon alpha 2A but then reoccurred with the same dimensions and airway blockage after treatment was abruptly interrupted. The authors suggest the implementation of a standard procedure for the interruption of interferon alpha 2A treatment in order to avoid this rebound effect and advise on the need for further studies to properly evaluate dosage and administration parameters for interferon alpha 2A in the treatment of difficult hemangioma.

Uniterms: Hemangioma. Interferon. Vascular tumors.

INTRODUCTION

Hemangioma are tumors which are most frequently found in childhood. They grow very fast until the child attains one year of age, and then recede (in 90% of cases) until the child reaches 10. Most hemangioma are small but, in certain areas, can nevertheless create some complications such as airway blockages. The death toll of patients with hemangioma in the sub-glottic region varies - according to reports - from 20% to 50%.¹

Notwithstanding several treatment procedures already described, it is still difficult to restrain growth or accelerate recession of such tumors.² One of the options proving to be both efficient and promising is the use of interferon alpha 2A, initially described by White in 1989.³ In 1993 we started using interferon alpha 2A in difficult cases at the Social Pediatrics sector of Albert Einstein Israelite Hospital, and in 1997 we published our experiences.⁴ However, in one of the cases, after the initial success there was a reoccurrence of tumor growth and renewal of clinical consequences

immediately after the sudden stoppage of treatment. This is reported here, and the case is discussed with the aim of raising awareness about the possibility of rebound effects in the event of sudden stoppage of interferon alpha 2A treatment. We also suggest a procedure for the gradual removal of this medication.

CASE REPORT

I. M., female, was born on May 8, 1995, weighing 3680 grams. Within two weeks she developed a flat reddish blotch in the left periorbital and zygomatic regions which grew rapidly in area and presented an irregular shape while growing darker. By the age of 8 weeks this tumor already spanned the left side of the infant's face. At 12 weeks the infant developed difficulty in breathing with signs of airway obstruction. Dexametazone (1 mg/day) was administered orally. On September 5, 1995, the infant was interned for treatment of an acute breathing obstruction and submitted to a tracheotomy. On September 7, interferon alpha 2A treatment was started with the use of 3 million units per day, sub-cutaneously. By the third day, leukocytes had dropped from 11,200 to 4,700 and reached normal figures on the 12th day.

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From the third week after the treatment was started, a significant regression in hemangioma volume and a noticeable change to a lighter color were observed.

In a laryngoscopic exam performed in the third week, total blockage of the sub-glottis region by growths in the walls infiltrated by the hemangioma was observed. On November 25, 1995, a new laryngoscopic exam revealed that this abnormal growth had definitely reduced in size. On March 2, 1996, it was seen that the sub-glottic region no longer showed any invasion.

On April 6, 1996, the infant developed inflammatory signs around the tracheotomy orifice, associated with high body temperature, and a decision was made to intern her for treatment with antibiotic therapy and to stop the use of interferon. Her clinical condition improved within 5 days and the patient was released from hospital. The use of interferon was not resumed.

Thirty days later, the child showed signs of breathing obstruction and a laryngoscopic exam was performed which confirmed occlusion by hemangioma in the sub-glottic region, especially in the rear left part of the larynxes. Facial lesions were also observed to be darker and of greater volume, as well as having more irregular borders than before.

On August 12, 1996, the use of interferon alpha 2A was resumed at the same dosage of 3 million units per day. A laryngoscopic exam performed on November 11 showed the sub glottis region completely open and the tracheotomy cannula was removed. Interferon was, from then on, administered six times per week until Dec. 2, 1996, when the dosage was again reduced to 5 times per week and then was successively reduced by one dose per week until completely halted within four weeks.

DISCUSSION

Several reports have been published on the successful use of interferon alpha 2A in the treatment of hemangioma

since White's pioneering report in 1989.³ This medication has proved itself as an effective option in the effort to restrain growth of these tumors and also in influencing the regression process.

The dosage we used followed others' experiences^{2,6} and had the aim of safe utilization whilst avoiding collateral effects. As our daily administration of 3 million units subcutaneously proved to be adequate, it continues to be our reference for successful treatment. However, there are no specific studies aimed at determining the ideal dosage or establishing the best manner for its administration or termination of usage.

In the initial cases we attended to, we used dosages every three days until blood tests and clinical symptoms revealed improvement, especially regarding anorexia and nausea. Since occurrence of these collateral effects was rare and of light intensity, we then decided to use a daily dosage from the start of the treatment.

There is also no established recommendation for the duration of treatment, which depends on the patient's age and on the seriousness of the tumor's appearance. The difficulty lies in establishing when the growth of the hemangioma has become stabilized and when it is no longer capable of producing further complications. Comparisons or experimental studies are difficult due to the peculiar characteristics these tumors have, and no study has been published so far.⁵

We have not found any previous case report in the literature describing a rebound effect after successful treatment of a tumor by the use of interferon alpha 2A, although this possibility was previously discussed by Ezekowitz in 1992.⁶

The rebound effect we observed suggests that it is necessary to maintain the treatment with interferon for a longer period, particularly until the period of high risk potential for developing these tumors, i.e. 6 to 24 months, has passed.

From our experience in this case reported, we now remove medication gradually (one dose/week) to avoid any rebound effect. This procedure, however, is not yet objective and requires further clinical observation.

REFERENCES

- Mulliken JB, Young AE. Vascular birthmarks: hemangiomas and malformations. Philadelphia: WB Saunders Company; 1988.
- Ohlms LA, McGill TJ, Jones DT, Healy GB. Interferon alpha 2A: a therapy for airway hemangiomas. *Ann Otl Rhinol Laryngol* 1994;103:1-8.
- White CW, Sondeheimer HM, Crouch EC, Wilson H, Fan LL. Treatment of pulmonary hemangiomatosis with recombinant interferon alpha 2A. *New Engl J Med* 1989;320:1197-200.
- Anger J, Gomes VA, Ernesto JM, Pinus J, Faiwchow G. O tratamento de hemangiomas com interferon alfa 2A. *Arq Cient* 1997;2:3-6.
- The Cochrane Library 1997:Issue 3.
- Ezekowitz RAB, Mulliken JB, Folkman J. Interferon alpha 2a therapy for life-threatening hemangioma in infancy. *N Engl J Med* 1992;39:76-83.

RESUMO

Os autores relatam um caso de criança com hemangioma extenso de face com obstrução respiratória aguda provocada por hemangioma em região sub-glótica que foi tratada com sucesso com interferon alpha 2A mas que após a interrupção brusca de sua administração, apresentou uma recorrência das dimensões do hemangioma e da obstrução das vias aéreas superiores. Os autores sugerem uma padronização na retirada desta medicação e alertam quanto a necessidade de maiores estudos para indicar a dosagem e o tempo de manutenção do interferon alpha 2A no tratamento de hemangiomas complicados.