

duplication to the complete doubling of all facial structures, as in diprosopus twins, it is questionable whether this type of anomaly is truly a conjoined twin or merely a regional duplication for some other reason [3]. The stomatodeal structures are most often affected in partial FD. Patients in the asymmetrical subgroup can have an accessory mouth at the side of the face or the head as seen in our case. There is a preponderance of female infants. Chromosomal analysis has usually shown normal karyotype. In infants with partial FD, the mandible and mouth are the most commonly duplicated craniofacial structures [4].

Although the aetiology of FD is unknown, several theories have been proposed. These include environmental factors, genetic mutations, abnormalities of the twinning process leading to incomplete twinning and inappropriate expression of the homeotic genes which control the spatial organization of developing structures [5]. Diprosopus is believed to be the result of an error related to neurulation of the embryo. Associated craniofacial abnormalities include cleft lip and palate, anencephaly, and abnormalities of the cranial nerve [6]. Severe cardiac abnormalities such as ventricular septal defects, double outlet right ventricle, transposition of the great arteries and patent foramen ovale have also been identified, as seen in our patient [7]. There are several case reports of reconstruction of FD [3,7,8]. Care must be taken to remove all duplicated mucosa; otherwise, a retention cyst can develop, necessitating re-operation.

References

- [1] Wu J, Staffenberg DA, Mulliken JB, Shanske AL. Diprosopus: A unique case and review of the literature. *Teratology* 2002;66: 282–7.
- [2] (No authors) Conjoined twins—an epidemiological study based on 312 cases. The International Clearinghouse for Birth Defects Monitoring Systems. *Acta Genet Med Gemellol* 1991;40:325–35.
- [3] Gilbert-Barness E, Debich-Spicer D, Opitz JM. Conjoined twins: morphogenesis of the heart and a review. *Am J Med Genet* 2003;120:568–82.
- [4] Verdi GD, Hersh JH, Russell LJ. Partial duplication of the face: case report and review. *Plast Reconstr Surg* 1991;87: 759–62.
- [5] Benirschke K, Temple WW, Bloor CM. Conjoined twins: nosology and congenital malformations. *Birth Defects Orig Artic Ser* 1978;14:179–92.
- [6] Rai VS, Gaffney G, Manning N, Grassi Pirrone P, Chamberlain PF. Antenatal diagnosis of complete facial duplication—a case report of a rare craniofacial defect. *Prenat Diagn* 1998;18: 618–20.
- [7] Borcakan C. An accessory mouth: case report. *Plast Reconstr Surg* 1978;61:778–80.
- [8] Beaty HG. A report of unusual embryologic defect of the face. *Plast Reconstr Surg* 1956;17:297–303.

N KILIC, B YAVASCAOGLU, A YESILYURT, H DOGRUYOL, Medical Faculty of Uludag University, Departments of Paediatric Surgery and Anaesthesiology and Reanimation, Bursa, Turkey. Correspondence: Nizamettin Kilic, Medical Faculty of Uludag University, Department of Paediatric Surgery, 16059, Görükle, Bursa, Turkey. Tel./Fax: +90 224 4429198. E-mail: nizam@uludag.edu.tr

Received April 1 2004; accepted May 17 2004

Death possibly associated with interferon use in a patient with chronic hepatitis

Sir,

Interferon α -2a (IFN α -2a) plays an important role in the treatment of chronic hepatitis. It inhibits viral protein synthesis and induces greater expression of class 1 major histocompatibility complex molecules in hepatocytes, resulting in increased efficiency of viral-directed cytotoxic actions [1,2].

Side effects of IFN treatment can be divided into two categories: constitutional reactions to the initiation of therapy and reactions after repeated high-dose administration. Some factors, including age, performance status and underlying disease, have been reported to have an impact on the severity of the side effects [1–3]. Initial reactions including chills, fever, fatigue, nausea, vomiting and malaise usually begin 30 to 120 min after IFN treatment and persist for several hours. Moreover, these side effects are not usually dose limited and can be relieved with acetaminophen or anti-inflammatory medications and can be seen at any time of the treatment [2,4–6]. Dose-dependent and

reversible neuropsychiatric toxicity was reported in some studies [4]. There are few reported cases of shock after IFN administration [2–4]. Here, we report the death of a 5-y-old girl with chronic hepatitis B probably induced by an allergic shock of interferon injection.

A 5-y-old girl with active hepatitis B infection had been followed-up for a year. The patient had two siblings who were 9 and 7 y old with the same diagnosis. They all had positive HBeAg and high copy of HBV DNA. Interferon treatment was planned for the three siblings. Her laboratory evaluation 2 d before admission revealed normal complete blood count, erythrocyte sedimentation rate, C-reactive protein, alkaline phosphatase and albumin levels but elevated serum activities of alanine transaminase (ALT, 91 U/l) and aspartate transaminase (AST, 84 U/l).

We planned to give 5 000 000 IU/m² interferon α -2a subcutaneously, three times a week. After the first dose of the IFN α -2a all of the siblings were quite well for 2 h at the hospital. They were also well 4 h

after the drug administration when they went to bed. At the eighth hour the mother had noticed that one of the siblings did not respond to stimulus, could not be awakened and was brought to our emergency department. She was unconscious, her extremities were cold and peripheral pulses were poor. Her blood pressure was 63/36 mmHg, and axillary temperature was 36.6°C. She had tachypnoea (44/min) and tachycardia (126/min). Neurological examination revealed hypotonia and hypoactive deep tendon reflexes. She did not experience an epileptic attack or seizure at home or at the hospital. She had no abnormal neurological history.

Complete blood count revealed haemoglobin 133 g/l, WBC count $22.3 \times 10^9/l$ (40% lymphocyte, 46% polymorphonuclear leucocyte, 10% eosinophil and 4% monocyte) and platelet count $255 \times 10^9/l$. Her arterial blood gases were normal. Biochemical evaluation revealed glucose 4.8 mmol/l, serum urea 23 mmol/l, creatinine 133 $\mu\text{mol/l}$, sodium 131 mmol/l, potassium 3.2 mmol/l, calcium 2.0 mmol/l, ALT 225 U/l, AST 201 U/l. The plasma ammonium level was normal (34 IU/l). Coagulation tests were normal. The interferon dose was checked, and it was not overdose.

She was treated with fluid replacement and inotropic support (dopamine and dobutamine). High volumes of fluid were required to correct the circulating volume. Her echocardiography and cranial tomography were normal. All cultures (blood, urine and cerebrospinal) were negative. Despite the aggressive treatment, including ceftriaxon 100 mg/kg/d for a possible septic shock, she died at the 16th hour after the admission. Her siblings had no complaint and continued their interferon treatment.

Generally, hypersensitivity reactions cannot be anticipated unless there is a history of being sensitive to the same drug. Beckman et al. [7] reported one patient who died from hypersensitivity to interferon after the second injection. They examined IgG and IgE antibodies to IFN. We could not examine IgG and IgE antibodies to IFN α -2a for technical reasons. Although side effects to IFN are generally minor, they are problematic for some patients. Life-threatening adverse events have been reported in large series [8]. Clinical presentations of drug reactions are often diverse and depending on the type of immune

response. The main question in the evaluation of the patient is whether the clinical problem is drug related. Anaphylaxis is an acute, systemic and life-threatening reaction usually following parenteral administration of drugs, and clinical findings usually develop within seconds to minutes but may be delayed for 30–60 min. Although the time from the interferon administration to the appearance of shock may be too long in our case for an anaphylactic reaction, there was no other clear cause other than interferon for the adverse event. In conclusion, our patient's death could not be explained by any other factor and may be attributed to her IFN treatment. Although the side effect spectrum of IFN α -2a is wide, there is no reported case of death in children associated with interferon with such a short time interval.

References

- [1] Okanoue T, Sakamoto S, Itoh Y, Minami M, Yasui K, Sakamoto M, et al. Side effects of high-dose interferon therapy for chronic hepatitis C. *J Hepatol* 1996;25:283–91.
- [2] Baluna R, Vitetta ES. Vascular leak syndrome: a side effect of immunotherapy. *Immunopharmacol* 1997;37:117–32.
- [3] Kansu A, Altuntaş B, Doğançlı T, Kalaycı AG, Girgin N. The efficacy and side effects of interferon alpha 2a (Roferon) on chronic virus infection in Turkish children. *Hepatol Res* 1999; 15:1–9.
- [4] Fontana RJ. Neuropsychiatric toxicity of antiviral treatment in chronic hepatitis C. *Dig Dis* 2000;18:107–16.
- [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;18:2316–26.
- [6] Ballauff A, Schneider T, Gerner P, Habermehl P, Behrens R, Wirth S. Safety and efficacy of interferon retreatment in children with chronic hepatitis B. *Eur J Pediatr* 1998;157:382–5.
- [7] Beckman DB, Mathisen TL, Harris KE, Boxer MB, Grammer LC. Hypersensitivity to IFN- α . *Allergy* 2001;56:806–7.
- [8] Fattovich G, Giustina G, Favaro S, Ruol A. A survey of adverse events in 11,241 patients with chronic viral hepatitis treated with alfa interferon. *J Hepatol* 1996;24:38–47.

TANIL KENDIRLI, EROL KISMET, ERKAN DEMIRKAYA, HALİL İBRAHİM AYDIN, VURAL KESİK & VEDAT KÖSEOĞLU, Department of Paediatrics, Gülhane Military Medical Academy, Ankara, Turkey. Correspondence: Erol Kismet, Department of Paediatrics, Gülhane Military Medical Academy, 06108, Ankara, Turkey. Tel: +90 312 304 4374. Fax: +90 312 304 2010. E-mail: kismeterol@yahoo.com

Received 30 November 2004; revised 13 December 2004; accepted 17 December 2004

Home nasal bilevel positive airway pressure therapy for diaphragmatic paresis in transverse myelitis

Sir,

We report a child with transverse myelitis, presenting with recurrent episodes of unilateral pneumonia

resulting from unilateral phrenic nerve paresis and respiratory muscle weakness, in whom bilevel positive airway pressure (BPAP) therapy via a nasal mask