Dramatic response of a metastatic carcinoid tumour to a combination of interferon and octreotide

Heikki Joensuu, Kalevi Kätäkä and Harry Kujari

Department of Oncology and Radiotherapy, Turku University Central Hospital and Department of Pathology, Turku University, Turku, Finland


The combination of alpha-interferon and octreotide has rarely been tested in the treatment of carcinoid syndrome. We describe a patient who was moribund when treated with interferon alone, but enjoyed a dramatic response leading to disappearance of all symptoms, normalization of 5-HIAA, and restoration of his normal life-style when octreotide was initiated. Neither interferon nor octreotide could be withdrawn without reappearance of the symptoms, suggesting that the combination of alpha-interferon and octreotide may have synergistic effects in carcinoid syndrome.

Heikki Joensuu, Department of Oncology and Radiotherapy, Turku University Central Hospital, SF-20520 Turku, Finland

Both alpha-interferon and the somatostatin analogue octreotide are efficient drugs in the treatment of the carcinoid syndrome. Although objective tumour shrinkage occurs in less than 10% of patients treated with either agent, the 24-h urinary 5-HIAA level decreases > 50% from the pretreatment value in 30 to 80% of cases (1-11), and the majority of patients experience an improvement in flushing and/or diarrhoea. However, octreotide rarely decreases the 24-h urinary 5-HIAA excretion within the normal limits (1, 2) and, similarly, only 3 of the 135 patients described in the literature treated with interferon were complete responders (3–11).

Here we describe a patient with metastatic carcinoid tumour who obtained a dramatic response to the combination of interferon and octreotide.

Case report

A 43-year-old man developed abdominal and back pain, palpitations and occasional flushes and diarrhoea in 1987–88. In addition, he had claudication and was able to walk only about 50 m without pain. Although he had difficulty in lying down, para-aortal tumours could be demonstrated in computed tomography. In January 1989, multiple mesenteric and para-aortal metastases that could not be removed were found at laparotomy. The location of the primary tumour was not found, despite a careful search at laparotomy and several X-ray examinations, including a small bowel series and computed tomography.

The histological appearance of the removed tumour was characteristic of a carcinoid tumour. Grimelius argyrophil staining gave a positive reaction as well as an immunohistochemical staining for synaptophysin, whereas stainings for gastrin, growth hormone, insulin, pancreatic polypeptide and vasoactive intestinal peptide were negative; an equivocal result was obtained when the tumour was stained for calcitonin, chromogranin and neuron specific enolase. dU-5-hydroxyindoleacetic acid (dU-5-HIAA) was elevated, 164 μmol/l (reference range, < 40 μmol/l).

The patient obtained some relief from radiotherapy to the para-aortal region (40/38 Gy), which was begun in February 1989. Because of exacerbation of the symptoms, recombinant interferon alpha-2b (Intron A) was started in August 1989. the dose increased to 10 × 10⁶ IU sc thrice weekly. During interferon treatment, flushing subsided, and dU-5-HIAA decreased from 189 to 129 μmol/l, but the patient continued to lose weight. His abdominal pain worsened, and in February 1990 he had cachexia and weighed only 50 kg after losing 26.5 kg within six months. Because of severe abdominal pain he received buprenorphine and morphine, and because of dehydration caused by vomiting, diarrhoea and inability to eat. iv hydration was commenced.

Octreotide (Sandostatin) 100 μg b.i.d. was started in February 1990 and diarrhoea and abdominal pain disappeared rapidly within 24 h of starting the drug. Interferon was continued. By March 1990 his weight had increased by 10 kg and dU-5-HIAA was < 40 μmol/l. He resumed his usual life-style. gained weight up to 67.5 kg, had no symptoms from the carcinoid tumour and only minor side effects from the treatment (a slight taste disturbance). His walk was no longer limited by claudication. The tumour tissue had decreased in size in computed tomography, but the decrease was less than 50% when estimated as the sum of the products of two perpendicular diameters of the tumours.

An attempt to reduce the octreotide dose to 50 μg b.i.d.
was accompanied by the reappearance of the back pain and a rise in \( \text{dU-HI} \) to 47 \( \mu \text{mol/l} \) in August 1990, which were overcome by increasing the dose to 150 \( \mu \text{g/d} \). Similarly, an attempt to gradually withdraw interferon while continuing octreotide resulted in the reoccurrence of abdominal pain and flushing in February 1991, and acute gastric dilatation that, however, could be treated conservatively. The symptoms disappeared when interferon was resumed. The patient continues with octreotide 100 \( \mu \text{g} \) b.i.d. and interferon \( 5 \times 10^6 \) IU thrice weekly from the symptoms and with normal \( \text{dU-5-HIAA} \) in September 1991. \( \text{dU-5-HIAA} \) has been within the normal range in eight subsequent assays since April 1990.

**Discussion**

The present case illustrates the dramatic effect that octreotide may have in severely ill patients with the carcinoid syndrome. Moreover, it suggests that the combination of octreotide and interferon is of value in the treatment of metastatic carcinoid tumour, because neither drug could be withdrawn without the occurrence of the symptoms, and the \( \text{dU-5-HIAA} \) level fell within the normal range. The combination of octreotide and interferon was well tolerated, and the quality of life greatly improved. The same dose of octreotide (from 150 to 200 \( \mu \text{g/day} \)) has been in use for 19 months, since the start of the treatment, which might indicate that the combination may prevent the need to increase the dose of octreotide with time.

**References**


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