News

1995 — The Centenary of Rontgen's Discovery of X-Rays

To celebrate this auspicious event, a major international congress, organised jointly by the British Institute of Radiology, the College of Radiographers, the Institute of Physical Sciences in Medicines, the Royal College of Radiologists and the Royal Society of Medicine, will be held between 12 and 16 June 1995 in Birmingham, U.K. Current radiological science and future developments shall be included in a programme that will incorporate eminent national and international speakers. For more information, please contact Vanessa Whitehead or Elizabeth Carruthers, British Institute of Radiology, 36 Portland Place, London W1N 4AT, U.K. Tel: 071 436 7807; Fax: 071 255 3209.

Cancer in the Elderly

The Second International Conference on Geriatric Oncology will take place between 19 and 21 September 1994 in Genoa, Italy, and will involve collaboration with the University of South Florida, the National Institute of Aging and the Brown University, U.S.A. The focus of the meeting is to increase awareness and sensitivity of the scientific community to issues of geriatric oncology, to increase the knowledge of specialists involved in managing cancer in the aged and to disseminate the information internationally. Broad topic areas for discussion include epidemiology, aetiology, diagnosis and treatment, and specific tumour symposia. For more information, please contact the Organizing Secretariat, Service Point Srl, Largo San Giuseppe 3/19, 16121 Genoa, Italy. Tel: 0039 10 586066 or 590159; Fax: 0039 10 590160.

Advanced Course on Cell Differentiation and Death

Following the great success of the first advanced course entitled "Cell Growth, Differentiation and Death" in 1992, a second course on the same subject is being organised by the Paediatric Haemotology and Oncology Department of the International School of Medical Sciences at the Ettore Majorana Centre for Scientific Culture in Italy. The course, which will be held between 1 and 4 May 1994, will cover a diverse range of topics including neuropeptides and cytokines, retinoic acid, oncogene expression, apoptosis, and skin, neuronal and immuno-haematological differentiation. Participants shall be limited to fifty. For more information please contact Professor Luisa Massimo, Department of Paediatric Haematology and Oncology, G. Gaslini Childrens Hospital, Largo G. Gaslini, 16148 Genoa, Italy. Tel: (39) 10 5636331 or 5636227; Fax: (39) 10 3776590.

Twelfth Asia–Pacific Cancer Conference

The general theme of this conference is "Towards Total Cancer Control", and it will be held in Singapore between 17 and 20 October 1995. All relevant and important aspects of cancer control, with particular reference to the Asia-Pacific region, are expected to be addressed in both presentations and teaching sessions. For more information, please contact Dr Eng-Hen NG, Secretary General, 12th Asia–Pacific Cancer Conference, Singapore Cancer Society, 15 Enggor Street 06-03/04, Realty Centre, Singapore 0207. Tel. 65-2219577, Fax 65-2227424.

Eur J Cancer, Vol. 29A, No. 16, pp. 2332–2333, 1993.
Printed in Great Britain
0959–8049/93 $6.00 + 0.00

Letters

Response to Increasing Doses of Octreotide in a Patient with Carcinoid Syndrome

Jaffer A. Ajani and Jennifer R. Chesnut

NEUROENDOCRINE TUMOURS can originate in various organs, but are derived from the neural crest cells dispersed during human development [1, 2]. These cells are capable of synthesising, accumulating and releasing a variety of peptides into the bloodstream. Thus, tumours derived from these cells can secrete one or more peptides in quantities capable of causing debilitating hormonal syndromes. The most common type of neuroendocrine neoplasm is the carcinoid tumour which accounts for approximately 65% of all neuroendocrine tumours [3]. Most patients with advanced carcinoid tumours develop carcinoid syndrome, which is characterised by abdominal cramps, diarrhoea, flushing of face and upper torso, bronchospasm, cardiac valve involvement, telangiectasias and hypotension. Serotonin, bradykinins and substance P are considered responsible for the carcinoid syndrome [4]. Abnormal serum levels of serotonin and its urinary metabolite, 5-hydroxy indole acetic acid (5-HIAA),

Correspondence to J.A. Ajani.
The authors are at the Department of Gastrointestinal Oncology and Digestive Diseases, Division of Medicine, University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas, U.S.A.
Received 3 Sep. 1993; accepted 13 Sep. 1993.

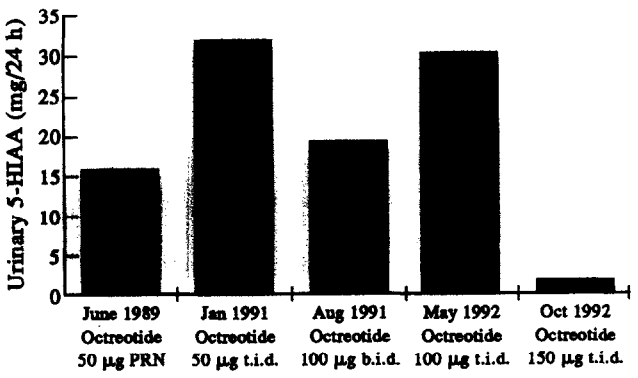

Fig. 1. A bar graph demonstrating urinary levels of 5-HIAA with various doses of octreotide. The level of urinary 5-HIAA does not necessarily reflect the effect of the octreotide dosages listed. PRN, as necessary; b.i.d., twice daily; t.i.d., three times per day.

can be assessed routinely; 5-HIAA has played a particularly important role in monitoring patients with carcinoid syndrome.

Kvols *et al.* reported on the effectiveness of a somatostatin analogue, octreotide (Sandostatin®), in 25 patients with carcinoid syndrome [5]. A marked reduction in symptoms, as well as biochemical responses, was observed in most patients. Although patients initially responded for a median of 12 months to the maximum dosage of 150 μg given subcutaneously three times a day, most of them eventually experienced a recurrence of their symptoms. This "escape" phenomenon is currently not understood, but is perhaps related to somatostatin receptor regulation. In a follow-up study, Kvols *et al.* [6] administered 500 μg of octreotide subcutaneously three times a day to 28 patients with carcinoid syndrome, and documented the biochemical, symptomatic and objective tumour responses. Considering the potential utility of sequential dose increments, we have administered increasing doses of octreotide to a patient with carcinoid syndrome, and the patient has, in fact, been responding. We describe here a treatment strategy that we believe has not yet been reported.

A 62-year-old woman presenting with postprandial abdominal cramping and loose stools in March 1988 was admitted to the hospital in April 1989 with a diagnosis of small bowel obstruction. She underwent an exploratory laparotomy, and an obstructing malignant carcinoid tumour was found in the terminal ileum. Postoperatively, her urinary 5-HIAA level was elevated (13.5 mg/24 h, normal range 0–10).

In June 1989, her diarrhoea worsened (approximately 16 bowel movements over 24 h). She continued to receive symptomatic therapy, and the severity of symptoms decreased. A computerised tomographic (CT) scan of the liver revealed metastases. Her urinary 5-HIAA level was 15.8 mg/24 h. Because symptoms were worsening, treatment with octreotide 50 μg subcutaneously once daily was begun; it completely stopped her diarrhoea. Because of constipation associated with the daily injection of octreotide, the patient administered the octreotide only occasionally—one 50-μg dose, two to three time per week.

Conjugated oestrogenic hormone (Premarin®) therapy was begun in June 1989, and resulted in symptom improvement until January 1991, when the patient's symptoms worsened significantly. The urinary 5-HIAA level increased to 32 mg/24 h. At this time, she was instructed to give herself 50 μg of octreotide subcutaneously three times daily. Her symptoms improved again.

In August 1991, although her urinary 5-HIAA level had decreased to 19.5 mg/24 h, a CT scan of the abdomen revealed slightly progressive liver metastases. Shortly thereafter, she again reported a worsening of her symptoms. The dosage of octreotide was increased to 100 μg twice daily. Her symptoms improved and she did well until May 1992, when her diarrhoea and flushing worsened, and she developed bronchospasms. Another CT scan revealed progressive liver metastases and her urinary 5-HIAA level had increased to 30 mg/24 h. After once more increasing the total daily dose of octreotide, this time to 300 μg (100 μg three times daily), her symptoms improved.

In September 1992, the patient increased the dosage of octreotide to 150 μg three times daily, and by October 1992 her urinary 5-HIAA levels had become normal (1.7 mg/24 h; Fig. 1). At the time of this report, the patient's octreotide dosage has been increased to 200 μg three times daily due to another period of worsened symptoms. However, she once more became asymptomatic, and for the past 4 months has been working full time. If her symptoms recur, our plan is to increase the octreotide dosage gradually to 500 μg three times daily, the maximum recommended dosage.

The presence of somatostatin receptors in carcinoid tumours has been reported [7]. The effectiveness of somatostatin or its analogues appears related to the presence or absence of somatostatin receptors [8]. In some patients, the improvement of symptoms with the administration of octreotide can be remarkable but not necessarily sustainable. The reason for the transient nature of the response in some patients is not understood. It is also not clear why some patients respond again when the dose of octreotide is increased. Our case also demonstrates that octreotide has a wide therapeutic dose range. It would be interesting to study a group of patients receiving octreotide or a similar somatostatin analogue with a predetermined schedule of dose increases. It is conceivable that a patient's duration of response might be prolonged if a step-wise dose increase approach were taken.

1. Pearce AGE. The diffuse neuroendocrine system and the APUD concept: related endocrine peptides in brain, intestine, pituitary, placenta and cutaneous glands. *Med Biol Eng Comput* 1977, **55**, 115–125.
2. Gower WR, Fabri PJ. Endocrine neoplasms (nongastrin) of the pancreas. *Sem Surg Oncol* 1990, **6**, 98–109.
3. Moertel CG. An odyssey in the land of small tumors. *J Clin Oncol* 1987, **5**, 1503–1522.
4. Moertel CG. Treatment of carcinoid tumors and the malignant carcinoid syndrome. *J Clin Oncol* 1983, **1**, 727–740.
5. Kvols LK, Moertel CG, O'Connell MJ, *et al.* Treatment of the malignant carcinoid syndrome: evaluation of a long-acting somatostatin analogue. *N Engl J Med* 1986, **315**, 663–666.
6. Kvols LK, Moertel CG, Schutt AJ, Rubin J. Treatment of the malignant carcinoid syndrome with a long acting somatostatin analogue (SMS 201-995): preliminary evidence that more is not better. *Proc ASCO* 1987, **6**, 95.
7. Reubi JC, Kvols LK, Waser B, *et al.* Detection of somatostatin receptors in surgical and percutaneous needle biopsy samples of carcinoids and islet cell carcinomas. *Cancer Res* 1990, **50**, 5969–5977.
8. Kvols LK, Reubi JC, Moertel CG, *et al.* Somatostatin receptors may predict responsiveness of malignant neuroendocrine syndromes to therapy with somatostatin analogue (SMS 201-995, octreotide). *Proc Am Soc Clin Oncol* 1989, **8**, 101.