# Sustained response to alpha interferon in a patient with advanced metastatic serotonin secreting endocrine tumour: case report.

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This 52 year old lady presented in 2001 at a GI clinic complaining of occasional abdominal cramps which could be severe and could last for several hours. Symptoms were not associated with constipation or diarrhoea. She had a history of migraine. She had suspected wheat allergy and had commenced on a coeliac diet, during which she had observed a weight loss of 2.25Kg (5lbs). A coeliac screen excluded coeliac disease and the gluten free diet was discontinued.

On review at 8 weeks she had developed post- prandial diarrhoea. A further weight loss of 2.25Kg (5lbs) was recorded. OGD and colonoscopy were performed with normal findings. A diagnosis of severe irritable bowel syndrome was made.

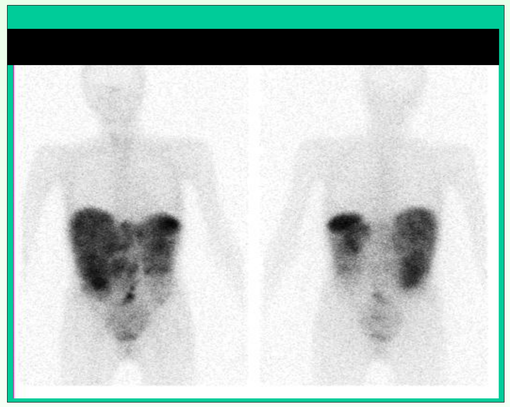
In January 2002 she returned to the GI clinic with a further weight loss of 3.2Kg (7lbs) (7.7Kg, 17lbs, since onset of symptoms). She reported cyclical symptoms of diarrhoea which persisted for 3-5 days. She also complained of occasional facial flushing.

Urinary 5HIAA/5HT and neuroendocrine tumour markers were measured:-

| | | |
|---|---|---|
| **Urinary 5HIAA** | **637.1umol/24h** | **(RR 10-47)** |
| **urinary 5HT** | **12.05** | **(RR 0.30-1.30)** |
| **Pancreastatin (PST)** | **1050ng/L** | **(RR 0-50)** |
| **Neurokinin A** | **350ng/L** | **(RR 0-20)** **(Specific marker for MGC)** |

CT and octreotide scintigraphy showed extensive hepatic metastases with para-aortic and iliac lymphadenopathy. No abnormal findings were identified in the ileum or colon suggestive of a primary lesion.

**Octreoscan at diagnosis** Images 24 & 48 hrs



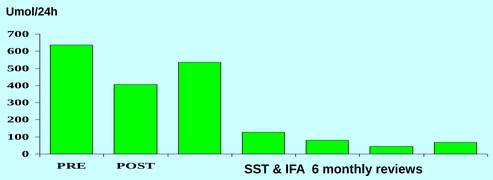
The surgical team considered the disease to be in-operable at thet time. The patient was not in favour of hepatic embolization. Somatostatin analogue treatment (SST) was commenced, Lanreotide Autogel 90mg. increased to 120mg. Symptoms continued and Autogel was replaced with Sandostatin LAR 30mg. Symptoms remained uncontrolled. After 4 months of SST symptoms had increased and tumour markers had continued to rise.

| | Initial | After SST (4 months) |
|---|---|---|
| **PST** | **1050** | **3400** |
| **NKA** | **350** | **1500** |

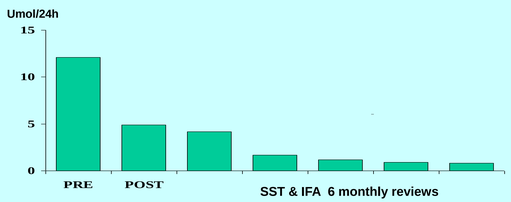
Alpha Interferon (IFA) was introduced concomitant with Sandostatin LAR, 1.5M units three times weekly and was increased incrementally to 9M units three times weekly.

Within 2 months symptoms eased and this regimen was continued. By 6 months symptoms had abated. The patient was reviewed monthly and haematology was monitored carefully. Plasma tumour markers were also measured. Over the following year tumour markers gradually fell. Urinary 5HIAA settled around the upper limit of normal and 5HT returned within the reference range after 18 months.

**Urinary 5HIAA pre-& post-treatment with SST & IFA**

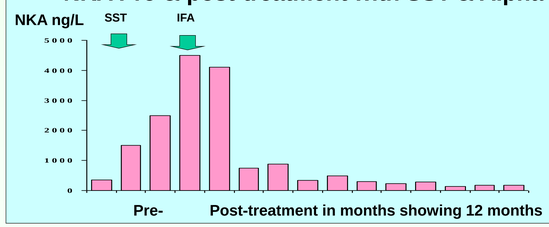



**Urinary 5HT pre-& post-treatment with SST & IFA**




Circulating NKA was secured below 100ng/l (RR 0-20) within a year and thereafter between 50-100ng/l

**NKA Pre-& post-treatment with SST & Alpha Interferon**

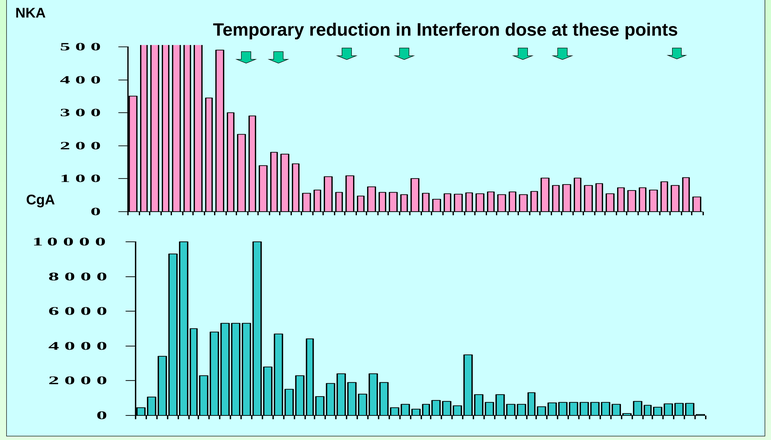



On IFA the patient experienced marked fatigue and suffered frequent migraine. Dosage was reduced from 9M units to 1.5M units three times weekly and occasionally the drug was discontinued for a few days, up to one week.

Side effects associated with IFA diminished.

Remaining on Interferon long term was tolerable for the patient under these conditions when IFA was reduced from time to time.

**Pre- & post-treatment circulating NKA & CgA concentrations**




During the brief periods of reduced IFA treatment NKA rose rapidly and significantly and carcinoid symptoms gradually re-developed.

For 7 years and with the co-operation of the patient a balance was achieved between side-effects associated with IFA and control of disease.

A comparison made between CT scans from January 2002 and January 2008 showed stable disease. Multiple hepatic metastases in both studies, appeared similar. One mass, anterior to the right common iliac vessels, in 2002 measured 3.8cms, in 2009 was reduced to 2.6cms. Para-aortic nodes were unchanged.

In the spring of 2009 the patient decided to reduce IFA and the drug was gradually withdrawn completely, at her request, by the summer of 2010. In the spring of 2010 she received three cycles of Y 90. PRRT. Her biomarkers markers rose steadily from 2008 and she died in June 2011.

| | June/08 | June/09 | June/10 | June/11 |
|---|---|---|---|---|
| **PST** | **615** | **950** | **>1,280** | **>1,280** |
| **CgA** | **1,900** | **5,500** | **10,480** | **>15,000** |
| **NKA** | **90** | **374** | **1,000** | **2,210** |
| **Urinary 5HIAA** | **331** | **790** | **1,985** | **-** |

## Comment

1 Considerable controversy surrounds the efficacy of IFA treatment in NETs. This case report illustrates that IFA, concomitant with SST, offers an effective treatment for advanced metastatic carcinoid disease. When this regimen can be tolerated control may be long-term. Dosage of IFA can be titrated to maintain a balance between disease control and side-effects. Subsequently we have used this regimen in many patients with about one third showing a similar response.

2 There is a delay in response to IFA treatment in carcinoid disease. For several month, symptoms may persist and tumour markers may continue to rise before improvement is observed.