Plasma Chromogranin A and Chromogranin B Concentrations in Untreated Patients with Mid Gut Carcinoid and their Biochemical Response to Octreotide.

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INTRODUCTION

In our centre patients with neuroendocrine tumours (NETs) that have been shown to be receptor positive on Octreotide scan may be treated with somatostatin analogues (SSA). Prior to initiation of this therapy, patients may undergo an Octreotide suppression test (OST).This is performed to assess tolerance to SSA therapy and also potential biochemical/symptomatic response to long term therapy.

PATIENT DETAILS & METHODS

During an OST blood samples are taken at 15 and zero minutes before and then serially for 3 hours after a subcutaneous bolus injection of 50 micrograms Octreotide. For this study we recorded basal and 1 hour post injection chromogranins A and B (CgA, CgB) concentrations in 36 patients (21 male, 15 female), median age 61 years (range 28-76). Our reference ranges are ≤30U/L for CgA (Dako ELISA) and ≤1.8 nmol/L for CgB (Euria RIA). For comparison, results were expressed as times the upper limit of normal (x ULN).

Basal concentrations (x ULN) and percentage change in CgA and CgB 1 hour after Octreotide injection in patients with a carcinoid tumour and their survival time after diagnosis.

Sex	Age	Basal CgA x ULN	% change in CgA	Basal CgB x ULN	% change CgB	Survival years
m	67	46.7	-92	1.9	-1	>4
f	61	16.7	-89	1.6	-86	>4.5
m	60	6.0	-64	2.8	-58	>5
f	72	333.3	-62	18.7	-14	<1
m	68	9.7	-57	1.0	-42	<1
f	48	22.7	-51	0.0		<1
m	59	5.0	-47	1.4	-7	>3
m	69	5.0	-43	0.3	11	>5
m	69	47.7	-33	5.7	-43	>2
f	67	52.3	-33	13.0	-6	>6
f	59	5.7	-29	0.6	-69	>2
f	60	2.0	-28	0.6	-8	>3
m	42	4.7	-22	0.0		>3
m	73	5.5	-21	2.4	-36	<2
m	62	2.1	-19	0.5	-8	>4
m	76	6.0	-19	0.3	-44	>2
m	38	3.2	-16	0.0		>3
m	53	3.5	-14	0.5	22	>3
f	58	4.7	-7	0.3	57	>2
f	68	1.7	-4	1.1	-47	>3
m	64	4.3	0	0.4	1	>4
f	70	7.0	0	12.0	-49	>5
m	73	8.2	+4	3.4	-20	<1
m	28	27.0	+6	1.8	-33	<1
f	72	1.5	+7	0.2	0	>5
f	49	14.3	+7	4.0	0	<1
m	64	37.3	+11	0.6	-5	<2
m	61	16.3	+16	1.4	-26	(>1.5)
m	60	2.3		15.9		>2
f	62	33.7		6.6		>5
m	75	278.0	+22	5.2	-7	<1
m	58	17.3	+50	0.4	-49	<1
m	59	35.3	+138	1.5	-3	<2
f	63	0.8	-20	0.7		>8
f	38	0.7	-45	0.2	0	>5
f	53	0.5	0	0.5	-20	>7

Raised basal CgA and/or CgB

Normal basal CgA and/or CgB

>20% decrease in a raised basal 1hr after octreotide

<20% change in raised basal 1hr after octreotide

>20% increase in raised basal 1hr after octreotide

% change in normal result

< 2 year survival after diagnosis

RESULTS

Basal CgA ranged from 0.5 - 333.3 x ULN. Basal CgB ranged from zero (undetectable) to 18.7 x ULN.

Of 36 patients, 21 had highly elevated basal CgA (> 5 x ULN), 10 had moderately elevated CgA (2 x ULN - 5 x ULN) and 5 patients had normal or marginally raised CgA. Eleven patients had CgB > 2 x ULN, 7 patients had elevated CgB up to 2 x ULN and 18 had normal CgB. All patients with elevated CgB also had raised CgA.

Eleven of 36 patients survived less than 2 years. All of these had highly elevated basal CgA of > 5 x ULN and 7 also showed no notable reduction in CgA after Octreotide injection.

DISCUSSION

It is noted that, using these assay methods, in all patients who showed increased CgA and CgB, the scale of increase in CgB is much less than that of CgA. The largest rise observed in CgA was 333.3 x ULN and the largest rise in CgB was 18.7 x ULN.

*Massironi *et al* (2010) reported that a decrease in plasma CgA of greater than 30% in an OST is a predictor of response to somatostatin analogue therapy. Ten of 33 patients here with raised CgA showed >30% decrease.

In this study we have not yet fully assessed the value of these results as predictors of response to SSA treatment but we note that 8 of 11 patients who died within 2 years of diagnosis had a poor response to bolus Octreotide injection with <30% decrease (or an increase) in CgA.

In this set of 36 patients we found none with raised CgB only (using ref. range ≤1.8nmol/L).

Summary

Using these assay methods basal CgB shows a lower order of rise than CgA and fewer patients had elevated CgB than CgA.

Highly elevated basal CgA and little or no decrease 1 hour after injection of Octreotide may indicate a poor prognosis and shorter survival time.

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Plasma Chromogranin A Response to Octreotide Test: Prognostic Value for Clinical Outcome in Endocrine Digestive Tumors. Sara Massironi, Dario Conte, Valentina Sciola, Matilde Pia Spampatti, Clorinda Ciafardini, Luca Valenti, Roberta Elisa Rossi and Maddalena Peracchi.

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