LETTER TO THE EDITOR

False elevation of chromogranin A due to proton pump inhibitors

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Dear Editor,

In their review on the diagnostic approach of neuroendocrine tumours (NET) Kuiper *et al* state that chromogranin A (CgA) is the most specific (86%) and sensitive (68%) diagnostic serum marker.[1] However, CgA may be elevated in a number of other endocrine, gastrointestinal, malignant and even cardiovascular disorders. We want to draw attention to one of the most frequent causes of false elevation of CgA, namely the use of H2 blockers or proton pump inhibitors (PPI).[2]

Patient A, a 49-year-old woman, was evaluated for the presence of NET because of vegetative symptoms and profuse watery diarrhoea. The urinary excretion of 5-HIAA was normal, while serum CgA (4960 µg/l (normal 20 to 100)) and gastrin (0.67 µg/l (normal <0.15)) were strongly elevated. The subsequent somatostatin receptor scintigraphy was normal. After discontinuation of the long-term esomeprazol (40 mg twice daily), both serum CgA (84 µg/l) and gastrin (0.10 µg/l) levels normalised. Re-treatment with esomeprazol led to a serum CgA level of 3090 µg/l.

Patient B is a 58-year-old woman on long-term esomeprazol (20 mg) treatment because of gastro-oesophageal reflux. Because of profound flushes, palpitations and abdominal complaints, serum CgA was determined to exclude NET. The elevated (543 µg/l) serum CgA level prompted a somatostatin receptor scintigraphy without abnormalities. After discontinuation of the esomeprazol, the serum CgA level normalised (43 µg/l) with a marked increase to 1360 µg/l several weeks after reinstitution.

Patient C, a 35-year-old woman, was evaluated for NET because of episodes of sweating, palpitations and abdominal cramps. While taking 40 mg pantoprazol, the serum CgA level was 271 µg/l. No imaging studies were done as the serum CgA dropped to 44 µg/l after discontinuation of pantoprazol.

These three cases illustrate that CgA may strongly rise during long-term treatment with PPI. Treatment with gastric pH increasing drugs such as PPI and to a lesser extent H2 blockers leads to gastrin production by the antral G-cells with subsequent stimulation of the gastric enterochromaffin-like cells and release of CgA. In most patients treated with PPI a two- to fourfold increase in CgA is found.[3,4] The increase in CgA seems related to the dosage and duration of PPI treatment. A more than tenfold increase in CgA levels, as in two of our patients, has occasionally been reported.[2] One to two weeks after discontinuation of PPI the CgA levels return to normal. It is therefore advocated to stop PPI treatment for at least two weeks before determination of CgA to avoid unnecessary imaging studies.

REFERENCES

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