CLINICAL IMAGE

Ectopic acromegaly due to growth hormone–releasing hormone secretion from bronchial carcinoid causing somatotroph hyperplasia and partial pituitary insufficiency

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Acromegaly due to ectopic growth hormone–releasing hormone (GHRH) secretion from a neuroendocrine tumor (NET) is very rare, and up to 100 cases have been reported in the literature.[1] Pancreatic or bronchial NETs are the primary sources of GHRH, but pheochromocytomas were also described.[2-5] To the best of our knowledge, we report the first case of acromegaly due to GHRH-producing NET causing pituitary hyperplasia and resulting in partial pituitary insufficiency.

A 43-year-old woman was referred to our department with symptoms suggesting acromegaly for about 5 years and amenorrhea for 2 years. The patient presented with typical acromegaly symptoms: coarsened facial features, macroglossia, enlarged hands and feet, soft tissue swelling, marked interdental spacing, and excessive sweating (FIGURE 1A). Her medical history was notable for bilateral surgery for carpal tunnel syndrome. Hormonal evaluation revealed normal thyroid function, normal prolactin levels, hypogonadotropic hypogonadism (luteinizing hormone [LH], 1.3 U/l; follicle-stimulating hormone [FSH] 6.3 U/l, and estradiol <10 pg/ml), secondary hypocortisolism (adrenocorticotropic hormone [ACTH] 08:00 AM, 6.2 pg/ml; cortisol 8:00 AM, 3.5 μg/dl), elevated fasting growth hormone (GH) levels (44 μg/l), and insulin-like growth factor 1 (IGF-1) levels exceeding 3.3-fold the upper limit of normal (ULN). Nonsuppressed GH levels during the 75-g oral glucose tolerance test were noted (nadir, 17 μg/l).

Pituitary magnetic resonance imaging revealed an enlarged gland (24 × 13 × 12 mm), with extrasellar extension, and homogenous

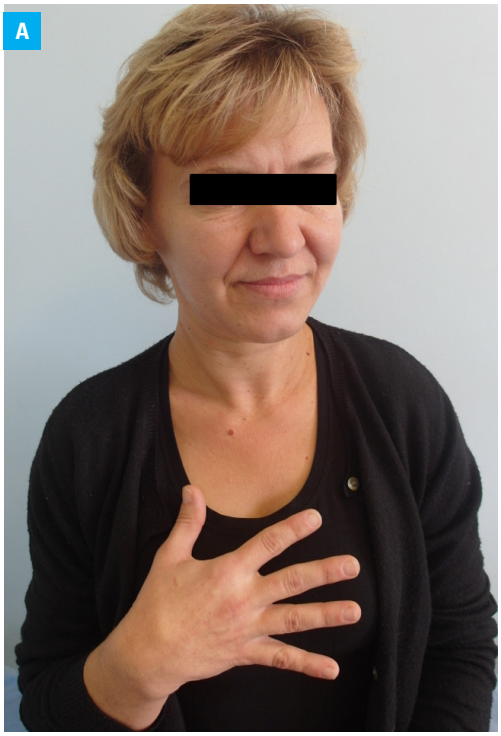

FIGURE 1 A – acromegaly symptoms: typical facial features (a wide nose, prognathism, a prominent eyebrow, thickened lips), a large right hand (patient consent obtained)

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Received: November 22, 2018.
Revision accepted: December 27, 2018.
Published online: January 4, 2019.
Pol Arch Intern Med. 2019; 129 (3): 208-210
doi:10.20452/pamw.4413

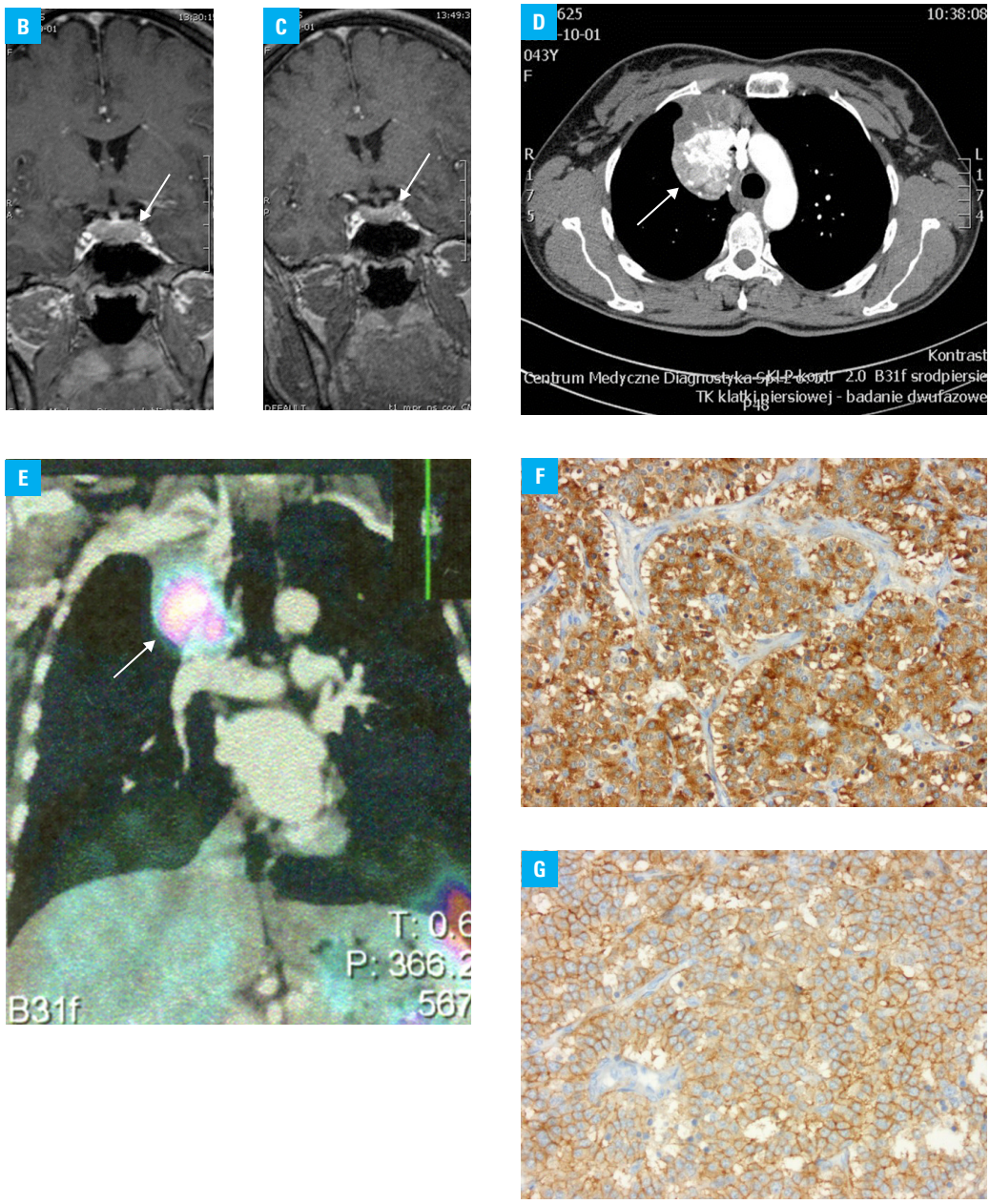

FIGURE 1
B – magnetic resonance imaging of the pituitary gland after gadolinium enhancement showing symmetrical pituitary enlargement (24 × 13 × 12 mm) without focal lesions (arrow); **C** – magnetic resonance imaging of the pituitary gland after gadolinium enhancement 3 months after long--acting somatostatin analogue therapy, showing a decrease in the pituitary size (19 × 13 × 8 mm) (arrow); **D** – chest computed tomography showing a 5-cm tumor with calcifications and strong enhancement after contrast in the upper right lung lobe (triangle); **E** – somatostatin receptor scintigraphy indicating an abnormal high radiolabel uptake of the lung tumor revealed by computed tomography; **F** – growth hormone–releasing hormone cytoplasmic immunostaining in 80% of tumor cells (original magnification ×200). **G** – moderately intense somatostatin receptor type-2 membranous immunopositivity in 80% of tumor cells (original magnification ×200).

gadolinium enhancement without focal lesion (FIGURE 1B). As no pituitary adenoma could be detected, a chest X-ray was performed. A tumor (56 × 40 mm) in the right anterior mediastinum was identified. Chest computed tomography (CT) confirmed the presence of a 5-cm tumor with calcifications and strong contrast enhancement (FIGURE 1C). Somatostatin receptor scintigraphy showed abnormal radiolabel uptake of the tumor revealed by CT (FIGURE 1D). Long-acting somatostatin analogue treatment with lanreotide Autogel (120 mg) was started while awaiting surgery. A significant improvement in acromegaly symptoms was observed. After 3 months of treatment, pituitary imaging showed a reduction in the pituitary size (19 × 13 × 8 mm) (FIGURE 1E) associated by a decrease in GH and IGF-1 levels (GH, 6 μg/l; IGF--1, 1.4 × ULN), normalization of corticotroph function (ACTH 8:00 AM, 14 pg/ml; cortisol 8:00 AM, 9.4 μg/dl) and gonadotrophic function (LH, 8.9 U/l; FSH, 7.9 U/l; estradiol, 177 pg/ml) with regular menstrual cycles. No reduction in the pulmonary tumor size on CT was noted. The patient underwent a right upper lobectomy with clear tumor margins. A pathological report revealed a typical carcinoid with a mitotic count of less than 2 mitoses/2 mm^2 and absence of necrosis. Immunostaining was positive for chromogranin and CD56. Additional staining of the tumor showed high expression of GHRH and SSTR2 (80% of the cells) (FIGURE 1F and 1G). The concentrations of GH and IGF-1 normalized after surgery (GH, 0.57 μg/l; IGF-1, 0.97 × ULN). No recurrence of acromegaly symptoms during a 3-year follow-up was observed.

In summary, we reported a case of acromegaly with transient pituitary insufficiency due to GHRH-producing bronchial carcinoid causing somatotroph hyperplasia. A distinction between a pituitary somatotroph adenoma and ectopic GHRH secretion is important, as pituitary

hyperplasia may be misdiagnosed as a pituitary tumor, leading to unnecessary pituitary surgery.[2] Long-standing pituitary hyperplasia may lead to a deficiency in one or more pituitary hormones.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

HOW TO CITE Stelmachowska-Banaś M, Głogowski M, Vasiljevic A, et al. Ectopic acromegaly due to growth hormone–releasing hormone secretion from bronchial carcinoid causing somatotroph hyperplasia and partial pituitary insufficiency. Pol Arch Intern Med. 2019; 129: 208-210. doi: 10.20452/pamw.4413.

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