GH-secreting pituitary adenoma in the course of McCune-Albright syndrome in a 21-year-old patient complicated by hepatocellular carcinoma

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McCune-Albright syndrome is caused by a postzygotic, somatic, activating mutation of the GNAS1 gene. The most characteristic clinical features are fibrous dysplasia, café-au-lait spots, and peripheral precocious puberty. To diagnose the syndrome, it is necessary to identify at least 2 out of the 3 aforementioned symptoms, which may vary in severity [1]. Increased hormonal secretion by the thyroid, pituitary, parathyroid, and adrenal gland hormones is less common. Acromegaly develops in approximately 30% of cases of McCune-Albright syndrome [2].

We present the case of a 21-year-old man with McCune-Albright syndrome, with pituitary macroadenoma secreting growth hormone (GH) and prolactin, in whom hepatocellular carcinoma appeared after many years of treatment.

At the age of 9 years, the boy was diagnosed with McCune-Albright syndrome due to the presence of fibrous bone dysplasia, café-au-lait spots, and early puberty. At the age of 11 years (in 2014), his growth velocity accelerated (his height was 190 cm), and elevated levels of insulin-like growth factor-1 (IGF-1) (1079 ng/mL) and a lack of GH suppression (GH > 40 ng/mL) in the oral glucose tolerance test were found. Additionally, significantly increased prolactin secretion (> 470 ng/mL) was noted. A magnetic resonance imaging (MRI) scan revealed the presence of a pituitary tumour measuring 28 × 33 × 30 mm, extending into the sphenoid sinus, involving the right internal carotid artery, and compressing the optic nerve chiasm. Massive remodeling of the sphenoid bone was also observed. Treatment with subcutaneous lanreotide (120 mg every 28 days) and oral cabergoline (0.5 mg twice weekly) was initiated to reduce tumour size before the planned surgical intervention. After 3 months of therapy, a reduction in pituitary tumour size to 11 × 21 × 20 mm was observed, and neurosurgical tumour resection was performed. However, complete tumour excision was not possible due to its location. Therefore, the aforementioned medical treatment was continued postoperatively. Follow-up examinations showed normalization of prolactin levels (7 ng/mL), but GH secretion (31.7 ng/mL) and IGF-1 levels (1600 ng/mL) remained significantly elevated. Due to massive dysplasia in the sphenoid bone region and the tumour’s proximity to the carotid artery, the patient was disqualified from further surgical treatment as well as radiotherapy. Therefore, lanreotide and cabergoline treatment was continued, but with inadequate control of GH/IGF-1 levels. At that point, available therapeutic methods for treating gigantism had been exhausted.

After turning 18 years of age, the patient was qualified for pasireotide treatment, which is available in Poland as part of a drug program for adults. At that time, the patient had a height of 220 cm and a body mass...
index (BMI) of 24.5 kg/m², while a MRI pituitary scan revealed a similar adenoma size as in previous examination (7 years earlier). Abdominal ultrasound showed no abnormalities.

Pasireotide treatment was initiated at a dose of 40 mg intramuscularly every 28 days. Due to a gradual decrease in IGF-1 levels (though without reaching a satisfactory level within the normal range or slightly above), the medication dose was increased to 60 mg intramuscularly (i.m.) every 28 days after 3 months of therapy.

After 6 months of treatment, during which satisfactory control of acromegaly was still not achieved, a decision was made to initiate pegvisomant treatment [3, 4]. At the same time, a subsequent abdominal ultrasound performed 6 months after the previous one revealed a 3.5-cm tumour in the liver. Abdominal MRI findings suggested a malignant lesion. The patient underwent tumour resection, and the histopathological examination confirmed hepatocellular carcinoma grade 2 according to the World Health Organization (WHO) classification, pT1b (Fig. 1).

The patient is now one year post-surgery without complications. He is receiving pegvisomant (25 mg daily) and lanreotide, his IGF-1 level is 724.6 ng/mL, and his GH concentration is 21.85 ng/dL.

Treating gigantism/acromegaly in patients with McCune-Albright syndrome is a clinical challenge, primarily due to fibrous bone dysplasia [5]. The presented patient was disqualified from surgery and radiotherapy due to massive fibrous dysplasia of the skull bones.

Despite administering maximum doses of pasireotide, our patient did not achieve control of acromegaly. Therefore, the decision was made to switch to pegvisomant, which acts peripherally to reduce IGF-1 levels but does not exert an inhibitory effect on GH secretion or pituitary adenoma mass. Within the currently approved drug program in Poland, it is not possible to use pegvisomant and pasireotide concurrently. Consequently, to control the tumour mass, a first-generation somatostatin analogue preparation was added to the treatment regimen. However, this treatment still did not result in the normalization of GH and IGF-1 secretion or disease control.

Hepatocellular carcinoma is extremely rarely reported in this age group, and its occurrence may be associated with prolonged elevated IGF-1 levels. The presented case demonstrates the difficulty in achieving control of acromegaly in the context of McCune-Albright syndrome and highlights the need for increased oncological vigilance in these patients.

Statement concerning ethics
The research was conducted in accordance with the principles of ethics of the World Medical Association Declaration of Helsinki. Data were collected retrospectively. Written informed consent was obtained from the patient for the publication of this case report (including all laboratory data and images).

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Conflict of interest
The authors declare that they have no conflict of interest.

References