Acromegaly etiology

Acromegaly is usually caused by a pituitary somatotroph adenoma. The other main diseases causing acromegaly are ectopic GH-producing pancreatic tumors and tumors producing GHRH, a hypothalamic hormone that stimulates GH secretion from the anterior pituitary. Among them are pancreatic tumors, pulmonary tumors, and hypothalamic gangliocytomas, and the endocrine mechanism stimulating GH secretion has well been documented. GHRH production or gene expression in pituitary somatotroph adenomas has been demonstrated by several investigators [1) 2) 3) 4)]

The cause of acromegaly could be determined after the discovery of growth hormone (GH) and insulin-like growth factor I (IGF-I) and demonstrating an association with GH hypersecretion and elevated circulating IGF-I. Usually caused by pituitary neuroendocrine tumors.

In > 95 % of cases GH secreting pituitary neuroendocrine tumor.

In >75 % macroadenomas with cavernous sinus invasion and/or suprasellar extension.

A duplication event in GPR101 is implicated in cases of gigantism and acromegaly.

AHR gene rs2066853 polymorphism is significantly more frequent in acromegalic patients than in healthy subjects, regardless of gender, pituitary tumor size, age at diagnosis and prevalence of colonic tumours and is associated with increased disease aggresivity. Moreover, the rs4986826 variant was detected in few patients with rs2066853 polymorphism, but its role is to be cleared [5)].

Pituitary carcinomas are exceedingly rare. Extremely infrequently acromegaly occurs as a result of ectopic secretion of growth hormone releasing hormone (GHRH) from a peripheral neuroendocrine tumour, or from excessive hypothalamic GHRH secretio. Approximately 5% of cases are associated with familial syndromes, most commonly multiple endocrine neoplasia type 1 (MEN1) syndrome, but also McCune-Albright syndrome, familial acromegaly, Carney’s syndrome and Familial Isolated pituitary neuroendocrine tumor (FIPA) [6)].

Co-secretion of growth hormone (GH) and prolactin (PRL) from a single pituitary neuroendocrine tumor is common. In fact, up to 25% of patients with acromegaly may have PRL co-secretion. The prevalence of acromegaly among patients with a newly diagnosed prolactinoma is unknown. Given the possibility of mixed GH and PRL co-secretion, the current recommendation is to obtain an insulin-like growth factor-1 (IGF-1) in patients with prolactinoma at the initial diagnosis. Long-term follow-up of IGF-1 is not routinely done [7)].

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