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Differences in Pathological Findings and Growth Hormone Responses in Patients with Growth Hormone-Producing Pituitary Adenoma

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Abstract. Plasma growth hormone (GH) responses to various stimuli were examined in 21 patients with GH-producing pituitary adenomas, classified into three types by the immunohistochemistry of cytokeratin and the glycoprotein hormone α-subunit distribution. Seven type 1 adenomas were exclusively composed of cells in which the cytokeratin formed a dot-like pattern; they were chromophobic to hematoxylin and eosin (H&E), occasionally positive for GH, and almost completely negative for the α-subunit. Thirteen type 2 adenomas were composed of cells with cytokeratin that had a perinuclear distribution; they were eosinophilic to H&E, and diffusely positive for both GH and the α-subunit. One patient had a type 3 adenoma which had a mixed pattern of intracellular cytokeratin distribution and was chromophobic and eosinophilic to H&E. Clinically, type 1 is characterized by earlier onset, larger tumor size, and more frequent aggressive extension. Paradoxical GH responses to TRH and OGTT were seen in 1 of 6 patients (16.7%) of type 1 and 8 of 9 patients (88.9%) of type 2, and 0% of type 1 and 62.5% of type 2, respectively. Type 2 cases showed higher plasma GH response to GH-releasing hormone, and a tendency to greater suppression of plasma GH by bromocriptine compared with type 1. Octreotide acetate administration revealed that the nadir/basal ratio of plasma GH levels was 42.9±6.6% in type 1 and 13.5±5.8% in type 2. These results suggest that there is a pathophysiological difference between these two distinct types of GH-producing pituitary adenomas.

Key words: Acromegaly, Cytokeratin, Immunohistochemistry, Growth hormone (GH), Somatostatin.
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SANO *et al.* recently reported that growth hormone (GH)-producing pituitary adenomas could be classified into at least two types according to the intracytoplasmic distribution of immunoreactive cytokeratin [1]. Cytokeratin is considered to have a certain unknown function within the cells besides forming their framework. In GH-producing pituitary adenomas, a distinct distribution of cytokeratin has been reported, and a functional abnormality of these cells has been suggested.

On the other hand, abnormalities of GH secretion in acromegalic patients include a high plasma GH level, impaired inhibition or paradoxical increase in GH after glucose ingestion [2], and stimulation of GH release by thyrotropin-releasing hormone (TRH) [3–5], or various GH response to GH-releasing hormone (GHRH) [6]. Bromocriptine [7, 8] and the somatostatin analogue octreotide acetate suppress GH release in patients with acromegaly [9, 10]. However, heterogeneous responses to these provocative and suppressive

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