Somatotroph adenoma case series

Six patients diagnosed with Somatotroph adenoma in the Department of Neurosurgery at Huashan Hospital were enrolled in the study. Primary pituitary neuroendocrine tumor tissues and adjacent normal pituitary specimens with no morphologic abnormalities from these six patients were obtained at surgery. RNA sequencing (RNA-seq) and assay for transposase-accessible chromatin with high-throughput sequencing (ATAC-seq) were applied to investigate the underlying relationship between gene expression and chromatin accessibility changes in somatotroph adenoma.

Totally, 1528 differential expression genes (DEGs) were identified by transcriptomics analyses, including 725 up-regulated and 803 down-regulated. Further, we obtained 64 significant DEGs including 10 DEGs elevated and 54 DEGs that were negligibly expressed in tumor tissues. The up-regulated DEGs were mainly involved in terms related to synapse formation, nervous system development, and secretory pathway. In parallel, 3916 increased and 2895 decreased chromatin-accessible regions were mapped by ATAC-seq. Additionally, the chromatin accessible changes were frequently located adjacent to transcription factor CTCF and Rfx2 binding site.

The results are the first to demonstrate the landscape of chromatin accessibility in somatotroph adenoma, which may contribute to illustrating the underlying transcriptional regulation mechanism of this disease [1].

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24 patients bearing large Somatotroph adenomas.

Clinical data and somatostatin receptor ligands (SRLs). SRLs response both before and after surgical debulking were collected and 21 molecular biomarkers of SRLs response were studied in tumor samples by gene expression.

From the 21 molecular markers studied, only two of them predicted enhanced SRLs response after surgery. Tumors with improved response to SRLs after surgical debulking showed lower levels of Ki-67 (MKI67, FC=0.17, and p=0.008) and higher levels of RAR-related orphan receptor C (RORC) (FC=3.1 and p˂0.001). When a cut-off of no detectable expression was used for Ki-67, the model provided a sensitivity of 100% and a specificity of 52.6% with an area under the curve of 65.8%. Using a cut-off of 2 units of relative expression of RORC, the prediction model showed 100% of sensitivity and specificity.

High levels of RORC and low levels of Ki-67 identify improved SRLs response after surgical debulking in large somatotropic adenomas. To determine their expression would facilitate medical treatment decision making after surgery [2].

A total number of 159 patients with acromegaly were included in a study, as well as two control groups (150 patients with non-GH-secreting adenomas and 50 patients without pituitary neuroendocrine tumors). Magnetic resonance images of all patients were evaluated for the presence of an empty sella, downward and lateral tumor extension, and maximum superoinferior diameter of the mass. Additionally, these values were correlated with growth hormone and IGF-1 levels.

The empty sella phenomenon was detected significantly more often in patients with a GH-secreting adenoma with a prevalence of 22% vs. 5.3% in non-GH-secreting adenomas ($p < 0.001$) or 8% in the healthy control group ($p = .036$). Moreover, GH-secreting adenomas presented with a significant rate of downward tumor extension (74.8% vs. 35.5%; $p < 0.001$), whose extent correlated inversely but weakly with the GH hormone level ($r = -0.17$; $p = .036$). It was also found that a decreased superoinferior diameter and higher ratio of intrasellar to suprasellar extension are predictive quantitative values for the presence of a GH-secreting adenoma (area under curve, 0.712).

Somatotroph adenomas are frequently associated with an empty sella phenomenon. Moreover, GH-secreting adenomas are frequently accompanied by an enhanced, quantitatively measurable impression of the sellar floor. Hypothetically, this is caused by tumor-induced local bone remodeling processes [3].

Park et al., classified 132 patients with GH-secreting pituitary neuroendocrine tumors invading CS into 4 groups. The patients underwent surgery using a microsurgical transsphenoidal approach (TSA) with the assistance of an endoscope. For adenomas with CS invasion confined to the medial compartment of ICA (internal carotid artery), they were divided into type A (without radiological evidence) and B (with radiological evidence). For adenomas with ICA encasement, tumors were divided according to the surgical approach: type C (standard TSA) and D (far-lateral TSA). Surgical and endocrinologic outcomes were compared between each group.

Gross total resection rates were 100%, 73.6%, 14.7%, 0% and endocrinologic remission rates by surgery alone were 100% , 62.3%, 26.5%, 0% for type A, B, C, and D tumors, respectively. There was no endocrinologic remission by surgery alone for type D tumors. Nevertheless, it showed marked reduction of postoperative nadir GH at 1 week, 6 months, 1 year, and IGF-I at 1 year compared to type C tumors.

For tumors with CS invasion confined to the medial compartment of ICA, total resection should be attempted by direct visualization of the entire medial wall of CS. Even for tumors with ICA encasement, aggressive tumor resection by far-lateral TSA can increase the chance of remission with the help of adjuvant treatment [4].

A retrospective review of 53 patients who had follow up endocrinologic data at least 3 months post-surgery was performed among patients who were treated by EEA between 1998 and 2012. Data were analyzed for remission using GH and IGF-I levels based on 2010 consensus criteria. We also analyzed the outcomes using 2000 consensus criteria for ease in comparison to prior studies of outcomes of surgery for acromegaly. In this series of mostly large (88.2% macroadenomas), invasive (46.9% Hardy-Wilson C, D, E) adenomas, there were 27 patients (50.9%) who achieved remission after EEA only. For patients who had no remission with EEA alone, RS and/or medical therapy were used and 37 patients (69.8 %) achieved remission overall. Statistical analysis showed larger tumor size, Hardy Stages C, D, E and Knosp Scores 3, 4 to be predictive against remission for EEA only and EEA with other modalities. The volume of residual tumor after EEA was not found to be predictive of remission with additional therapies. We used stringent consensus criteria from 2010 in a series which included a high proportion of invasive GH secreting adenomas to show that EEA alone or combined with other modalities results in comparable remission rates to earlier studies which used less strict criteria, while retaining low complication rates [5].

1)
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