

2차성 부갑상선 기능항진증 환자에서의 miRNA 발현과 p53, wnt 신호 전달 체계와의 연관성

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Genetic Profiling of miRNAs Reveals the Role of p53 and Wnt Signaling Pathway in Secondary Hyperparathyroidism

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Background: MicroRNAs (miRNAs) are small non-coding, single-stranded RNAs that regulate messenger RNAs at the post-transcriptional level. They have been identified as mediators of various signaling pathway such as cell proliferation and growth of neoplasm. Secondary hyperparathyroidism (SHPT) should be treated with surgery in some cases, however the exact mechanisms why the glands gains autonomy with poor response to medication remains unclear. We aim to investigate whether genetic profiling of miRNA of parathyroid gland in SHPT would be useful to predict the possibility for surgical treatment.

Methods: Patients were enrolled who needed to receive parathyroidectomy for SHPT irresponsive to medication. Parathyroid tissues for normal controls were accidentally obtained from patients receiving thyroid lobectomy. We performed a TaqMan low-density array-based RT-PCR miRNA profiling, and compared with expressions of 384 miRNA expression between patients and controls.

Results: In parathyroid nodular hyperplasia, mean pre-operative intact parathyroid hormone (PTH) levels were 1781.2 ± 864.2 pg/ml, and mean parathyroid volume was 4.5 ± 2.70 cm³. Twelve miRNAs (miR-103, miR-1271, miR-1275, miR-1291, miR-148b, miR-18a, miR-193a-3p, miR-21, miR-301, miR-425-5p, miR-532, and miR-532-3p) were significantly up-regulated (>2 fold change), and miRNA-139-5p, which had anti-tumorogenic and anti-metastatic activity, was significantly down-regulated in parathyroid nodular hyperplasia compared to normal controls. The p53 expression was negatively correlated with miRNA-139-5p expression significantly in parathyroid nodular hyperplasia ($r=-0.892$, $p=0.042$). Non-phospho β -catenin expression in nucleus was significantly increased in parathyroid nodular hyperplasia compared to normal control groups. But, there were no significant associations with p21 and p27 expression.

Conclusions: These results suggest that genetic profiling of miRNA in SHPT might be useful to predict surgical treatment of SHPT and miR-139-5p might have a role in the proliferation of parathyroid cell in SHPT through p53 pathway.

Key Words: 부갑상선 기능항진증, miRNA, p53
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