Hirosaki Med. J. 59 (Suppl.) : S199—S201, 2007

CHANGES IN GLUCOSE TOLERANCE PARAMETERS AFTER SURGICAL TREATMENT OF ADRENAL PRECLINICAL CUSHING'S SYNDROME

Takeshi Nigawara, Satoru Sakihara, Kazunori Kageyama, Ken Terui, Yoshiko Fukuda, Shoko Kawashima, Shinobu Takayasu, Takako Moriyama, Masayuki Kawahara, Ayumi Korekawa, Maki Yamashita, Akira Kohsaka, Yoshifumi Kakizaki and Toshihiro Suda

Abstract Adrenal preclinical Cushing's syndrome (preCS) refers to adrenocortical tumor that secretes cortisol autonomously, and yet does not manifest a series of physical signs characteristic of Cushing's syndrome. In the Japanese guideline on preCS published in 1996, surgical resection is indicated in tumors larger than 5 cm in diameter, or in those suspected of malignancy. We have recommended surgery to a wider variety of patients who have metabolic complications such as glucose intolerance and hypertension in the background. In this study we surveyed whether parameters of glucose tolerance changed after resection of the tumor. From January 2001 to June 2005, 32 preCS cases were wrought up in our department, 17 of which were subsequently subjected to adrenalectomy. Seventy-five gram oral glucose tolerance test (OGTT) was performed both presurgically and postsurgically in 11 cases. After surgery, three patients showed improvement in plasma glucose profile. Homeostasis model assessment index of insulin resistance (HOMA-R), integrated insulin secretion during OGTT (ΣIRI) and insulinogenic index (II) made no significant change after surgery, but II showed a fairly plausible tendency of improvement. Our present data from small number of patients imply that surgical treatment of preCS may improve early-phase insulin secretion in OGTT. As preCS is most likely an insidious contributor to metabolic syndrome in the general population, its surgical indication should be extensively discussed in future studies.

Hirosaki Med. J. 59, Supplement : S199—S201, 2007

Key words: adrenal preclinical Cushing's syndrome; glucose tolerance; insulinogenic index

Background and objective

Adrenal preclinical Cushing's syndrome (preCS) refers to adrenocortical tumor that secretes cortisol autonomously, and yet does not manifest a series of physical signs characteristic of Cushing's syndrome. In the Japanese guideline on preCS (1996), surgical resection is indicated in tumors larger than 5 cm in diameter, or in those suspected of malignancy in morphological and functional aspects. However, we have recommended surgery to a wider variety of patients who have metabolic complications such as glucose tolerance and hypertension in the background, on the prediction that preCS is a fairly prevalent, potential exacerbating factor of metabolic syndrome.

In this study, we surveyed whether the parameters of glucose tolerance were altered after the resection of the tumor.

Subjects and methods

Of the 32 preCS cases that were hospitalized to our department from January 2001 to June 2005, 17 cases went under unilateral adrenalectomy. Pre- and postsurgical 75 g oral glucose tolerance test (OGTT) were performed in 11 cases (age 36 to 75 years, eight of whom were female). One of them had a family history of diabetes mellitus (DM).

Department of Endocrinology and Metabolism,
Hirosaki University Graduate School of Medicine
Fax: +81-172-39-5063,
E-mail: nigawara@cc.hirosaki-u.ac.jp

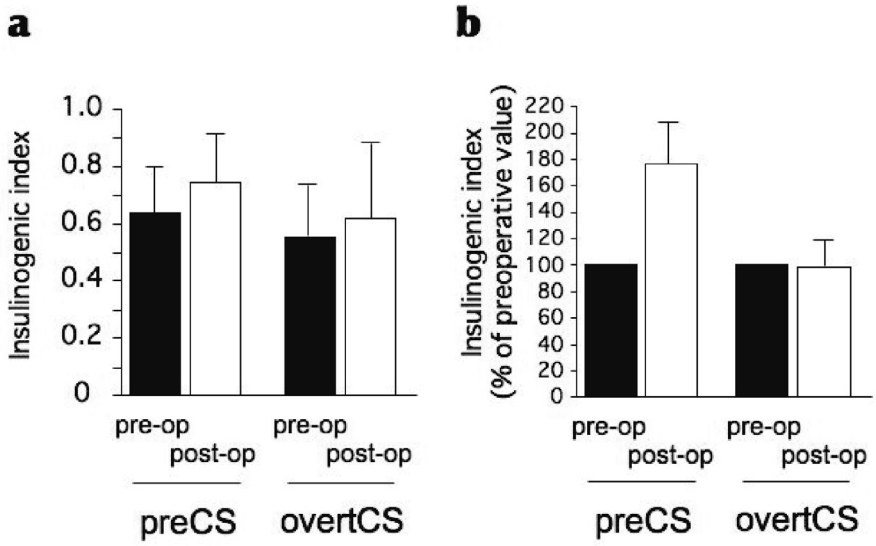

Figure 1 Insulinogenic index

For comparison, data were collected from three overt adrenal Cushing's syndrome (overtCS) cases treated in the same period (age 45 to 52 years, two of whom were female). One of them had a family history of DM.

Results

Unilateral adrenalectomy effectively eliminated the autonomous secretion of cortisol that was seen preoperatively in both preCS and overtCS cases, as confirmed by corticotropin-releasing hormone test and 8 mg dexamethasone suppression test.

The numbers of preCS cases ascribed in preoperative 75 g OGTT to normal glucose tolerance (NGT), impaired glucose tolerance (IGT), and DM were five, three and three, respectively. After surgery, total of three cases (two IGTs and one DM) migrated to NGT group, corroborating the beneficial effect of surgery in glucose metabolism. Based on the parameters obtained in pre- and postsurgical 75 g OGTT, homeostasis model assessment of insulin resistance (HOMA-R), cumulative insulin secretion during OGTT (ΣIRI) and insulinogenic index (II) were calculated. Neither of these indices made statistically significant changes, but only II showed a remarkable tendency of improvement (Figure 1b). Further looking into the severity of autonomous secretion of cortisol, improvement of II was prominent in patients who had scored serum cortisol≥2 μg/dl in preoperative 8 mg dexamethasone suppression test (Figure 2).

Discussion

Adrenal incidentaloma is found in approximately 5% of the general population. Ueshiba et al.[1] reported that preCS comprise only 2.3% of the incidentalomas in Japanese. In our experience, however, nearly half of the incidentalomas fall in the criterion of preCS formulated in 1996[2]. Thus, the significance of preCS as a prevalent, insidious exacerbating factor of metabolic syndrome is implied.

One of the mechanisms by which preCS facilitates metabolic syndrome may well be the augmentation of insulin resistance of excessive cortisol. On the contrary, our present data failed to demonstrate a concrete improvement of HOMA-R or ΣIRI after treatment of preCS. In turn, a tendency toward improvement in early-

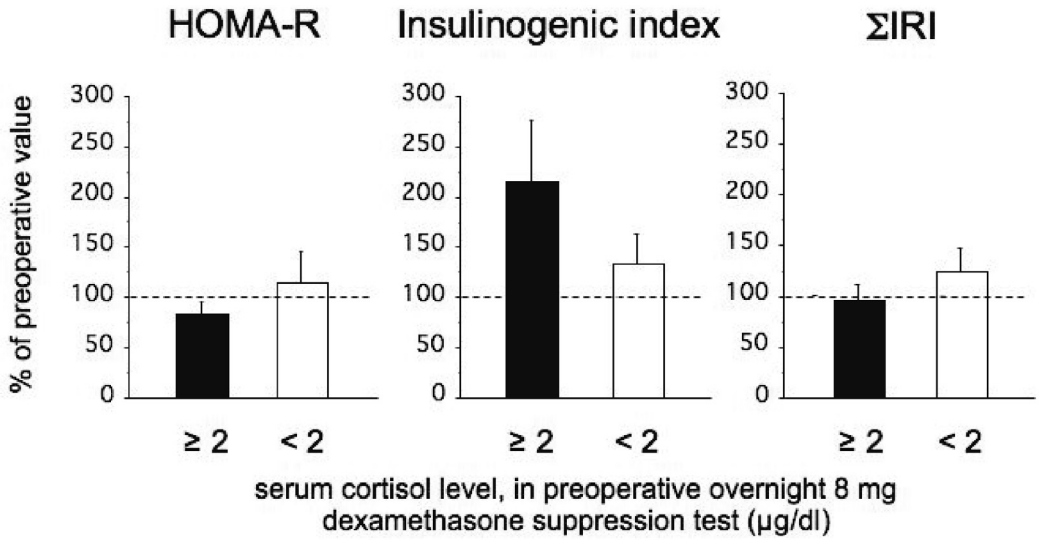

Figure 2 Parameters of insulin resistance/secretion according to cortisol suppressibility by 8 mg dexamethasone; change after treatment of preCS

phase insulin response (II) was observed.

In conclusion, our data from hitherto small number of patients suggest that surgical treatment of preCS may improve early-phase insulin secretion in OGTT, although it did not reach a statistical significance. A larger-scale study is necessary. In addition to glucose tolerance/insulin resistance, further evidence on the treatment of preCS in terms of blood pressure, lipid profiles, and atherosclerotic change need to be accumulated in order to discuss a proper treatment of preCS, which most likely is a common insidious contributor to metabolic syndrome.

Acknowledgment

We are grateful to Prof. Chikara Ohyama and his colleagues (Department of Urology, Hirosaki University School of Medicine) for surgical treatment of the patients, and also to Dr. Yoshimasa Kamata (Department of Clinical Pathology, Hirosaki University Hospital) for histological exploration of the specimen.

References

1) Ueshiba H, Ichijo T. Adrenal incidentaloma in Japan. J Clin Exp Med 2005;213:409-15.

2) Nawata H, Demura H, Suda T, Takayanagi R. Adrenal preclinical Cushing's syndrome. In: Annual report of "Disorders of adrenal hormones" Research Committee (fiscal year 1995). p223-226, Japanese Ministry of Health and Welfare, 1996.