Does Radiation Therapy for Brain Tumor Affect Pituitary Function, Resulting in Isolated ACTH Deficiency?

Key words: autoimmune, genetic defect, enzyme defect, POMC

Isolated ACTH deficiency is well known to be a rare cause of secondary adrenocortical insufficiency. The diagnosis is made by the demonstration of low cortisol production with low plasma ACTH, absent adrenal responses to stimulation for pituitary or hypothalamus with intact adrenal response to exogenous ACTH, and normal secretory indices of other pituitary hormones. It has been frequently reported that some cases with isolated ACTH deficiency are associated with lymphocytic thyroiditis, suggesting an autoimmune etiology of isolated ACTH deficiency (1–4). Moreover, Takao et al recently demonstrated that autoantibodies to a 22-kDa human pituitary cytosolic protein were frequently found to be existed in sera from patients with lymphocytic hypophysitis (73.3%) and isolated ACTH deficiency (77.8%), compared with Hashimoto thyroiditis, Grave’s disease and normal control subjects (5). It was also reported that the prevalence of a 22 kDa band of anti-pituitary antibodies was significantly higher in patients with isolated ACTH deficiency than in the controls (6). Those reports suggest that pituitary autoantibodies could be involved in the pathogenesis of isolated ACTH deficiency.

In this issue of the Journal, Sakai et al described that radiation therapy for brain tumor may induce isolated ACTH deficiency (9).

They also emphasized that an autoimmune endocrine disease was unlikely in the present case since neither anti-thyroid nor anti-pituitary autoantibodies were found. It is difficult to propose the exact mechanism inducing isolated ACTH deficiency in that case, while we should carefully follow-up pituitary functions, especially the pituitary adrenal axis after radiation therapy for brain tumor.

It is also well known that sequential cleavage of the precursor protein pre-pro-opiomelanocortin (POMC) generates melanocortin peptides such as ACTH, MSH and beta-endorphin. A genetic defect within the POMC gene inducing an interference with the appropriate synthesis of ACTH [2 mutations in exon 3 (G7013T, C7133 delta)], or abolishing POMC translation by a mutation in exon 2 (C3804A) has recently been reported (7). It was also hypothesized that isolated ACTH deficiency may be induced by enzyme defect or chimeric enzyme for biosynthesis of ACTH (8).

Finally, it is possible to consider that the radiation therapy for brain tumor can induce a genetic defect within the POMC gene or abnormal functions of enzymes such as defect enzymes and chimeric enzyme for biosynthesis of ACTH, although further investigations concerning the pathogenesis of isolated ACTH deficiency will be needed.

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References