Title

Identification of rabphilin-3A as a targeted autoantigen in lymphocytic infundibulo-neurohypophysitis (LINH)

Key Points

○ Identification of rabphilin-3A as a novel autoantigen in LINH

○ Clinical utility of anti-rabphilin-3A antibodies to diagnose LINH

○ Establishment of new method to identify autoantigens targeted by patient autoantibodies in liquid chromatography-tandem mass spectrometry on immunoprecipitates

Summary

Lecturer Yoshihisa Sugimura (Department of Endocrinology and Diabetes) in Nagoya University Graduate School of Medicine and Designated Lecturer Shintaro Iwama (Reseach Center of Health, Physical Fitness and Sports) in Nagoya University and their collaborators reported rabphilin-3A as a novel autoantigen in LINH and clinical utility of anti-rabphilin-3A antibodies to differentially diagnose LINH from other pituitary diseases. This work was published online in Journal of Clinical Endocrinology & Metabolism in April 28, 2015.

LINH is an increasingly recognized entity among cases of idiopathic central diabetes insipidus (CDI). The differential diagnosis of LINH from other pituitary diseases including tumors is difficult due to similar clinical and radiological manifestations. Invasive pituitary biopsy is required for the definite diagnosis of LINH. And the pathogenesis of LINH is unknown.

To identify autoantigen(s) in LINH, liquid chromatography-tandem mass spectrometry was used on immunoprecipitates obtained from rat posterior pituitary lysate incubated with IgGs purified from the sera of patients with LINH. Rabphilin-3A proved to be the most diagnostically useful autoantigen. The sensitivity of anti-rabphilin-3A antibodies was 76% (22 of the 29, including 4 of the 4 biopsy-proven samples) with LINH. In contrast, the specificity these antibodies was 100% in patients with biopsy-proven sellar/suprasellar masses without lymphocytic hypophysitis (n=34), including 18 patients with CDI.

In conclusion, rabphilin-3A is a major autoantigen in LINH. Autoantibodies to rabphilin-3A may become a biomarker for LINH and be useful for the differential diagnosis in patients with CDI.

Research Background

CDI can be caused by several diseases, such as tumors. The etiological diagnosis is still unknown in about half of the patients. LINH is an increasingly recognized entity among cases of idiopathic CDI; however, the differential diagnosis from other pituitary diseases is difficult due to similar clinical and radiological manifestations. Since the definite diagnosis of LINH requires invasive pituitary biopsy, a biomarker for LINH is required in clinical practice.

Research Results

Rat posterior pituitary lysate was immunoprecipitated with the sera of patients with LINH. The immunoprecipitates were searched by liquid chromatography-tandem mass spectrometry to screen for pituitary autoantigens. Rabphilin-3A was the most diagnostically useful autoantigen. Furthermore, anti-rabphilin-3A antibodies were detected in 76% (22 of the 29 patients, including 4 of the 4 biopsy-proven samples) with LINH. In contrast, these antibodies were absent (specificity; 100%) in patients with biopsy-proven sellar/suprasellar masses without lymphocytic hypophysitis (n=34), including 18 patients with CDI.

Research Summary and Future Perspective

Rabphilin-3A is a major autoantigen in LINH. Autoantibodies to rabphilin-3A may become a biomarker for the diagnosis of LINH and be useful for the differential diagnosis in patients with CDI.

Article

Iwama S, Sugimura Y, Kiyota A, Kato T, Enomoto A, Suzuki H, Iwata N, Takeuchi S, Nakashima K, Takagi H, Izumida H, Ochiai H, Fujisawa H, Suga H, Arima H, Shimoyama Y, Takahashi M, Nishioka H, Ishikawa SE, Shimatsu A, Caturegli P, Oiso Y. Rabphilin-3A as a targeted autoantigen in lymphocytic infundibulo-neurohypophysitis. J Clin Endocrinol Metab, Apr 28 2015 :jc20144209. [Epub ahead of print]

Japanese ver.

http://www.med.nagoya-u.ac.jp/medical/dbps_data/_material_/nu_medical/_res/topix/2015/RPH3A_20150520jp.pdf