

Rucurrent IgG4-related hypophysitis treated with Rituximab

가톨릭대학교 의과대학 내과학교실

조환석, 모은영, 한제호, 문성대, 김은숙, 조관훈, 조윤정

Background: Primary hypophysitis is a rare disease entity that has a reported estimated incidence of one case per 9 million persons per year. Histopathologically, the disease is subclassified into lymphocytic, granulomatous, xanthomatous, necrotizing, or IgG4-related hypophysitis. To date, few cases of histologically confirmed cases of IgG4-related hypophysitis have been reported.

Case: Here, we report a 31-year-old female patient with visual disturbance and polyuria as the initial presentation. In the laboratory test, there was panhypopituitarism and an elevation of blood sedimentation rate but, the IgG and IgG4 levels of the serum did not increase. Magnetic resonance imaging(MRI) revealed enlarged pituitary and thickened pituitary stalk. The patient responded to methylprednisolone pulse therapy but had two recurrences during the maintenance therapy using small-dose glucocorticoid hormones. So we planned to biopsy the pituitary gland and revealed IgG4-related hypophysitis. On pituitary biopsy, she was histologically diagnosed with IgG4-related hypophysitis. Considering the fact that two recurrences happened, we choose another immunosuppressant, which is azathioprine while tapering the glucocorticoid doses. Unfortunately, after one and half year or so later, her symptoms returned. Superoposterior enlarged lesion newly found on magnetic resonance imaging(MRI) represented 3rd recurrence as well. We decided to increase the dose of azathioprine, but the outcome was not what we were expecting. After 3rd methylprednisolone pulse therapy, we administered Rituximab, and her symptoms relieved.

Discussion and Conclusion: Although an elevated serum level of IgG4 is an important diagnostic indicator of IgG4-related hypophysitis, it is neither a necessary nor a specific one. In our care, the serum IgG4 level was normal but IgG4-related hypophysitis was confirmed by biopsy of the pituitary. Therefore, in the case of recurrent hypophysitis, IgG4-related disease should be ruled out by histological confirmation whether the serum IgG4 level is normal. After 3rd recurrence, we decided to administer Rituximab. Our patient showed a symptomatic response, pituitary problems persisted.

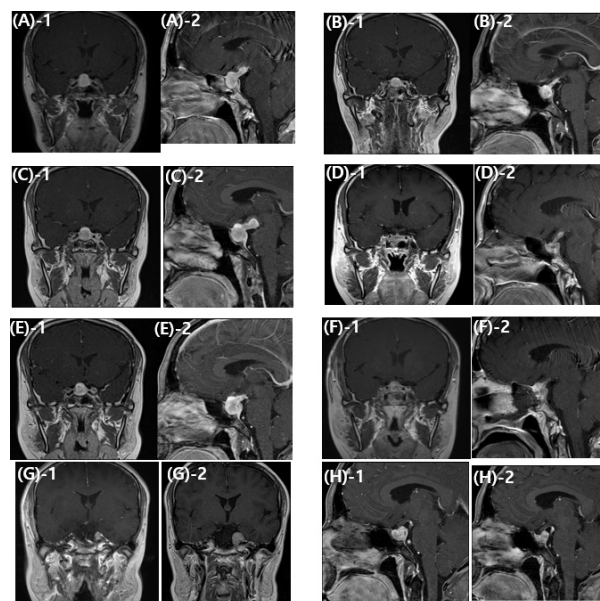


Figure 1. Changes on MRI after treatment with pharmacological doses of glucocorticoids or surgery for primary lymphocytic hypophysitis. Image (A) and image (B) showed the change in lesion size ; preglucocorticoids compared to postglucocorticoids treatments in a patient at 1st diagnosed. Image (C) and image (D) showed the change in lesion size ; preglucocorticoids compared to postglucocorticoids treatments in a patient at 1st recur. . Image (E) and image (F) showed the change in lesion size ; preglucocorticoids with azathioprine compared to postglucocorticoids treatments in a patient at 2nd recurrence. . Image (G) and image (H) showed the change in lesion size ; preglucocorticoids with azathioprine compared to postglucocorticoids treatments in a patient at 3rd recurrence.

Lab findings

		Basal	30min	60min	90min	120min
ACTH [pg/ml]	20-60	19.6	36.1	34.5	30.4	43.3
Cortisol [ug/dl]	2-25	0.92	3.02	1.73	2.39	3.48
TSH [mIU/L]	0.3-4.0	0.01	0.01	0.01	0.01	0.01
Prolactin[ng/ml]	1.5-13.0	31.43	83.04	64.68	45.06	41.34
LH [mIU/mL]	5-20	0.54	0.58	0.75	0.78	0.79
FSH [mIU/mL]	5-20	1.35	1.99	2.76	3.44	4.29
GH [ng/ml]	0-8	1.91	2.04	2.03	1.77	3.08

Table 1. Combined pituitary stimulation test (Cocktail test)

	6 am	8 am	9 am	10 am	11 am	12 am	Vaso op pres sion	30min	60min	90min
Urine Osm [mOsm/kg]	63	103	103	114	134	117		441	437	494
Serum Osm [mOsm/kg]	298	295	296	299	299	300		297	300	298
Serum Na [mEq/L]	146	145	146	145	147	145		146	147	147
Urine output [mL]		550	80	600	300	200		80	0	60

Table 2. Water deprivation test