Clinical Characteristics, Management, and Treatment Outcomes of Primary Hypophysitis: A Monocentric Cohort

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ABSTRACT

Primary hypophysitis (PH) is a rare autoimmune inflammatory disease of the pituitary gland. The aim of the study was to evaluate clinical characteristics, disease management, and outcomes of cases with PH. Medical records of PH patients admitted to Hacettepe University Hospital between 1999 and 2017 were analyzed retrospectively. Paraffin-embedded pathology blocks were obtained for both re-examination and IgG4 immunostaining. Twenty PH patients (15 females, 5 males) were evaluated. Mean age at diagnosis was 41.5 ± 13.4 years. Some form of hormonal disorder was present in 63.2% of cases, hypogonadism (66.6%) being the most common. Panhypopituitarism was present in 36.8%. All patients had pituitary gland enlargement on magnetic resonance imaging; stalk thickening and loss of neurohypophyseal bright spot were present in 17.6 and 23.5%, respectively. Lymphocytic hypophysitis was the most common histopathological subtype (50%). Among pathology specimens available for IgG and IgG4 immunostaining (n = 10), none fulfilled the criteria for IgG4-related hypophysitis. Four patients were given glucocorticoid treatment in diverse protocols; as initial therapy in 3. Sixteen cases underwent surgery, 7 of whom due to neuro-ophthalmologic involvement. Only 1 patient was observed without any intervention. Reduction of pituitary enlargement was seen in all surgical and glucocorticoid treated cases. None of the surgical patients showed hormonal improvement while one case in glucocorticoid group improved. PH should be considered in the differential diagnosis of sellar masses causing hormonal deficiencies. MRI findings are usually helpful, but not yet sufficient for definitive diagnosis of PH. Treatment usually improves symptoms and reduces sellar masses while hormonal recovery is less common.

Introduction

Primary hypophysitis (PH) is a rare autoimmune disease caused by inflammatory infiltration of the pituitary gland, which can result in transient or permanent endocrine dysfunction. The annual incidence was reported to be 1 in 7–9 million cases, and several studies of retrospective re-analysis of surgical pituitary specimens confirmed the low overall incidence of 0.4% [1].

Histopathological examination is the gold standard for PH diagnosis, however, 'clinical' diagnosis can be made by assessment of symptoms, hormonal profile and magnetic resonance imaging (MRI) characteristics together. It is reported that about one third of the cases are diagnosed in this manner [2]. Natural course of the disease has a very large spectrum: either spontaneous resolution or permanent endocrine dysfunction are possible [3]. Medical therapy (most commonly glucocorticoids) has been increasingly used

by clinicians, therefore the role for surgery has been gradually decreasing in recent years [4].

Here we aim to contribute to current literature by analyzing clinical features of *primary* hypophysitis cases over a time frame of 18 years diagnosed in a single tertiary medical center which serves approximately 1600 patients with pituitary disorders annually. We evaluated diagnostic challenges and our therapeutic management experiences of both histopathologically and 'clinically' identified cases.

All procedures performed in the study were in accordance with the ethical standards of the institutional research committee (GO 17–170) and with the Helsinki declaration.

Subjects and Methods

Medical records of 20 PH patients admitted to Hacettepe University Hospital between August 1999 and September 2017 were analyzed retrospectively. Considering the low incidence of the disease, we included all cases regardless of follow-up duration. Four out of 20 PH cases were diagnosed according to clinical, hormonal and radiological findings whereas 16 had histopathological confirmation. Secondary causes of hypophysitis were ruled out with appropriate tests in all clinically diagnosed PH patients; granulomatous vasculitis, sarcoidosis and Langerhans cell histiocytosis were excluded by related diagnostic criteria [5] and PPD or Quantiferon test was performed to rule out tuberculosis. None of the subjects were receiving immune check point inhibitors or other targeted therapies associated with hypophysitis. Anti-pituitary antibodies were regrettably not checked. Due to retrospective nature of the study, some of the patients lacked detailed evaluations for accompanying autoimmune diseases.

MRI and hormone test results were reviewed from patient files. Assessment of pituitary hormonal disorders were made according to accessible data, dynamic tests if present. Hormonal replacement therapies for hypocortisolism, hypothyroidism, and hypogonadism were set correspondingly. Paraffin-embedded pathology blocks were obtained from pathology archive for both re-examination and IgG4 immunostaining. IgG4-related disease was evaluated according to related criteria [6]: (1) Characteristic organ involvement, (2) Elevated serum IgG4 levels, and (3) Histopathological findings showing (i) marked lymphocyte and plasmocyte cell infiltration and fibrosis; (ii) IgG4-positive plasma cell infiltration: IgG4 to IgG ratio > 40 % and IgG4-positive plasma cells per high-powered field (HPF) > 10 %. According to these criteria, cases meeting all three are defined as definite, cases meeting first and second criteria as possible, and cases meeting first and third criteria as probable IgG4-related disease.

We assessed treatment outcomes according to symptom recovery and follow-up MRI as well as hormonal findings. Disease recurrence was defined as returning symptoms and/or progression in follow-up MRI.

SPSS-23 program was used for statistical analysis. Normally distributed variables were given as mean values with standard deviations while non-normally distributed variables were given as median values with ranges. p-Values less than 0.05 were considered statistically significant.

▶ **Table 1** Characteristics, pre-treatment endocrine findings, and magnetic resonance imaging (MRI) findings of primary hypophysitis patients.

		Total n
Mean age at diagnosis (years ± SD)	41.5 ± 13.4	20
Female sex (n, %)	15 (75 %)	20
Median time to diagnosis (months)	18 (1–120)	19
Referral symptoms (n, %)		19
Headache	12 (63.2 %)	
Decreased libido/menstrual irregularities	9 (47.4 %)	
Visual disturbance (any)	7 (36.8 %)	
Polyuria/polydipsia	6 (31.6 %)	
Nausea	2 (10.5 %)	
Fatigue	2 (10.5 %)	
Hormonal disorders, any (n, %)	12 (63.1 %)	19
Panhypopituitarism	7 (39 %)	19
Hypogonadism	12 (66 %)	18
Hypothyroidism	11 (61 %)	18
Hypocortisolism	7 (39 %)	18
Hyperprolactinemia	6 (31.5 %)	19
Diabetes insipidus	5 (28 %)	18
GH deficiency	4 (21 %)	19
MRI contrast pattern		17
Homogenous contrast enhancement	4 (23.5)	
Heterogeneous contrast enhancement	2 (11.7)	
Peripheral contrast enhancement	2 (11.7)	
Infundibular contrast enhancement only	1 (5.9)	
Hypo-enhancement	2 (11.7)	
Not reported [*]	6 (35.3)	
Other MRI findings		
Infundibular thickening	3 (17.6)	
Loss of neurohypophyseal bright spot	4 (23.5)	
Optic chiasm or nerve compression (any)	7 (41.2)	

SD: Standard deviation, GH: Growth hormone. [*] Pre-operative MRI was not performed in our center and/or did not report contrast enhancement pattern.

Results

Clinical presentation and endocrinological evaluation

Twenty patients (15 females, 5 males) with PH were included (▶ **Table 1**). Mean age at diagnosis were 34.6 ± 15.0 vs. 43.9 ± 12.5 years in male and female patients, respectively; p = 0.19. Median time from symptom onset to diagnosis was 18 months (1–120). Since all data except pathological examination and age was miss-

ing for one patient, 19 patients were included in further analysis. Most common presenting symptoms were headache (n = 12, 63.2 %) and symptoms associated with hypogonadism; such as decreased libido in male and menstrual irregularities in female patients (n = 9, 47.4 %). Visual disturbance (photophobia, hemianopsia, etc.) and polyuria/polydipsia were also common (▶ **Table 1**). Among six patients examined for accompanying autoimmune disorders, only one had autoimmune thyroiditis with normal thyroid functions.

At least one form of hormonal disorder was present in 12 out of 19 patients (63.2 %), hypogonadism (66.6 %) and hypothyroidism (61.1 %) being the most common (▶ **Table 1**). Seven out of 19 patients had panhypopituitarism (36.8 %). Hypocortisolism was found in 38.9 % of the patients (n = 7). Posterior hypophyseal involvement was present in five patients (27.8 %): Two of these patients did not have any concurrent anterior pituitary hormonal deficiencies but elevated PRL. Overall, six patients had mildly elevated levels of prolactin (PRL) (31.6 %) ranging between 39.0–69.6 ng/ml (Reference range: 5.18–26.5 ng/ml).

Only one patient was diagnosed subsequent to pregnancy. This 34-year-old patient was admitted with symptoms of visual disturbance one month after child delivery. MRI findings suggested pituitary macroadenoma measuring 14 × 16 × 24 mm which compressed optic chiasm, normal adenohypophysis gland was not visible while neurohypophyseal bright spot was in usual location. The patient was undergone urgent surgery under glucocorticoid coverage, in which only decompression could be made due to very hard pituitary tissue structure. Pathology report came back as lymphocytic hypophysitis. The patient needed prednisolone and levothyroxine replacement postoperatively.

Radiological findings

MRI findings were obtainable for 17, but missing for remaining three patients, and they are presented in ▶ **Table 1**. According to the radiologic score defined by Gutenberg et al. [7] (age ≦ 30 years: –1, relation to pregnancy: –4, pituitary volume ≧ 6 cm³: + 2, medium/high gadolinium enhancement: –1, asymmetry: + 3, loss of posterior pituitary bright spot: –2, enlarged stalk size: –5, mucosal thickening: + 2) which suggested scores between –13 to + 2 (median –5) indicative of PH, only five of our patients were compatible with autoimmune hypophysitis. One out of these 5 cases had a score of –4 due to related pregnancy (as described above) but did not meet any of the other criteria. Remaining four patients had scores ranging –5 to –8, all of whom were diagnosed 'clinically' as primary hypophysitis: Three cases were given glucocorticoid treatment and one was observed without intervention (described below).

Notably, 'possible hypophysitis' was more frequently reported by radiologists in the recent years compared to early 2000s. It is also noteworthy that radiological diagnosis was more accurate in patients whose clinical information was provided as 'panhypopituitarism' and preliminary diagnosis as 'hypophysitis' by clinicians. Loss of posterior pituitary bright spot also appeared to be important in radiologists' decision making. Three out of four MRIs showing loss of neurohypophyseal bright spot were reported as possible hypophysitis.

Pathological examination findings

Pathological assessments of all patients were made by the same experienced neuropathologist (F.S.). Lymphocytic hypophysitis was the histopathological subtype in eight out of 16 patients (50 %). Six cases were diagnosed as granulomatous hypophysitis (37.5 %) while one patient was reported as xantho-granulomatous and one as lymphogranulomatous hypophysitis.

Breakdown of the reticulin fiber network was reported in seven cases. Fibrosis, granuloma formations and multinuclear giant cells were detected in 7 (43.7 %), 7 (43.7 %) and 8 (50 %) patients; respectively. Neither histopathological subtype of PH nor existence of fibrosis had any association with hormonal deficiencies. Pathological findings indicating the presence of accompanying Rathke's cleft cysts were reported in three lymphocytic hypophysitis cases (18.7 %); none of which was reported in preoperative MRI.

We have examined the pathology specimens prepared from paraffin embedded blocks for IgG and IgG4 immunostaining. Out of ten specimens available for this process, none fulfilled the criteria for IgG4-related hypophysitis. However, two patients (31-year-old male and 40-year-old female) had > 10 IgG4 positive plasma cells per one high powered area. Male patient with panhypopituitarism and DI was classified as lymphocytic hypophysitis, pathological findings included fibrosis and marked stromal infiltration with lymphocytes. Histopathology of the female patient with DI and mild hyperprolactinemia was compatible with both granulomatous and lymphocytic hypophysitis; fibrosis was present. Since serum IgG4 levels were regrettably not available in these two cases, these patients may be diagnosed as *probable* IgG4-related hypophysitis.

Treatment

Glucocorticoid treatment was given to four patients, as initial therapy in three cases who were diagnosed 'clinically'. Patients treated with glucocorticoid are presented in ▶ **Supplementary Table 1S**.

Case 1

Only male patient in this group received methylprednisolone at an initial dose of 60 mg/day intravenous for two weeks, followed by 60 mg/d orally; the dose was tapered down in a monthly basis to a final dose of 8 mg/day and was stopped after 6 months. Radiologic improvement was detected after 6 months; however, hormonal situation did not improve. Serum IgG4 levels were found to be higher than normal (IgG4: 1100 mg/l, N: 39–864; IgG: 1480 mg/dl, N: 751–1560). No other organ or system involvement associated with IgG4-related disease has emerged at diagnosis or during follow-up. Therefore, this case was considered as possible IgG4 related hypophysitis. Progression was detected on MRI after 72 months of follow up regarding infundibular thickening (6 mm), although no further immunosuppressive treatment was planned due to lack of clinical significance. The patient continued hormone replacement therapy for panhypopituitarism and DI.

Case 2

This female patient was given methylprednisolone 60 mg/day initially, and the dose was tapered down in 3 months. She rapidly became Cushingoid in appearance with concurrent elevated blood glucose and rhabdomyolysis. Although the infundibular thickening shrank to 5 mm at the end of 3 months, panhypopituitarism and DI

remained. Due to lack of improvement and Cushingoid adverse effects, cessation of treatment was decided while hormone replacement therapy was sustained.

Case 3

The other female patient was treated with pulse methylprednisolone 1 g/day for three days and 60 mg/day deflazacort as maintenance therapy, which was tapered down to as low as 6 mg/day. Desmopressin was given for accompanying DI. After one year of treatment, MRI findings of the patient were completely normal, and both deflazacort and desmopressin therapies were stopped.

Case 4

Glucocorticoid was given as secondary treatment in this female patient presenting with decreased visual acuity and diplopia. She was given to surgery, which provided decompression of optic chiasm. Pathology report came back as granulomatous hypophysitis. Two months after surgery she was admitted to hospital with headache and relapsed decline in visual acuity of the right eye and was given pulse glucocorticoid treatment which rapidly improved symptoms. However, panhypopituitarism remained.

A total number of 16 cases underwent surgery. Preliminary diagnosis was non-functioning pituitary macroadenoma in nine (56.2 %); macroadenoma, Rathke's cleft cyst or other kind of sellar mass (e. g. craniopharyngioma) in five (31.2 %) patients (data not available in one). Surgery related minor complications such as mild bleeding, cerebrospinal fluid leak, arachnoid membrane rupture was seen in three cases; all were repairable.

One female patient among clinically diagnosed cases presented with headache and diagnosed as PH according to symptoms and MRI findings (expanded pituitary gland with homogenous contrast enhancement and thickened infundibulum, radiologic score of –5 according to radiologic criteria by Gutenberg et al. [7] at the age of 50. Hormonal evaluation was completely normal and she was not given any treatment. Her medical history revealed several previous examinations for headache in a time range of 84 months and MRI findings were stable comparing to one year earlier.

Patient Outcomes

Median follow-up period was 12 months (range: 0–132 months). Among 15 patients who underwent operation radiological improvement and symptom relief occurred in all, yet none showed hormonal improvement (data not available in one). New hormonal deficiencies emerged in 4 surgical patients: Panhypopituitarism emerged in one of the two patients with completely normal pre-operative endocrine evaluation, and DI in the other. The other two patients with partial endocrine deficiencies needed additional hormone replacements post-operatively (▶ **Table 2**, **Supplementary Table 1S**). Radiologic and symptomatic relapse arose in 1 patient two months after surgery who was treated effectively with glucocorticoid.

Three 'clinically' diagnosed patients received initial glucocorticoid therapy but in diverse protocols. Pituitary enlargement regressed in all, as well as symptoms related to mass effect. The only patient to benefit from glucocorticoid treatment regarding endocrine outcomes was initially given pulse glucocorticoid and long-term low dose glucocorticoid as maintenance therapy. Radiologic

recurrence was seen in one patient after 72 months without symptoms (▶ **Supplemantary Table 1S**).

Discussion

In this retrospective study, we evaluated characteristics, presenting signs and symptoms, management modalities and treatment outcomes of 20 PH patients diagnosed in our center. In addition, we examined the pathology specimens for IgG and IgG4 staining. Main findings of our cohort are presented in ▶ **Table 3** comparably with previous single-center case series.

Most common presenting symptom related to PH has indisputably been headache, as in our series. Visual disturbances according to mass effect are also common, while other symptoms vary depending mainly on existing hormonal deficiencies. Hypogonadism and hypothyroidism were the most common endocrine deficiencies in our series, similar to some previous case series [8, 9]; but more common than that reported in a recent PH case review (66 % and 61 % vs. 55 % and 52 %, respectively) [10]. Although hypocortisolism has generally been defined as the most common endocrine disorder in PH (60 %) [10], some case series reported lower incidence as in our cohort [9, 11]. DI, growth hormone deficiency and mild hyperprolactinemia were also less common in our series than general [10]. Median time from onset of symptoms to diagnosis ranged from 3.5 to 16 months in previous case series [8, 9, 12–15], while it was 18 months in ours (▶ **Table 3**).

Formerly higher female to male ratios in PH has recently been given as 2.5:1, which was 3 in our case series. Mean age at the time of diagnosis (41.5 years) was also consistent with literature [10]. In our series, female cases were older than males at the time of diag-

▶ **Table 2** Treatment, outcomes, and follow-up of primary hypophysitis patients.

		Total n
Preliminary diagnosis (n, %)		20
Hypophysitis	4 (20 %)	
Other	16 (80 %)	
Preoperative endocrinology consultation (n, %)		19
Yes	8 (42.1 %)	
No	11 (57.9 %)	
Surgery (n, %)		20
Yes	16 (80 %)	
No	4 (20 %)	
Surgical complications, any (n, %)		15
Yes	3 (20 %)	
No	12 (80 %)	
Post-operatively emerging hormonal disorders, any (n, %)	4 (26.6 %)	15
Improvement of hormonal disorders in cases treated by steroid (n, %)	1 (20 %)	4
Median follow-up (months, range)	12 (0–132)	

▶ **Table 3** Characteristics, treatment modalities and treatment outcomes of PH patients comparably with previous single-center case series.

	Leung, GK. 2004 [8]	Park, SM. 2014 [11]	Khare, S. 2015 [13]	Imber, BS. 2015 [12]	Chiloiro, S. 2017 [15]	Wang, S. 2017 [9]	Ange-lousi, A. 2018 [16]	Korkmaz, OP. 2019 [14]	Current case series
Number of patients	16	22	24	21	21	50	22	17	20
Mean age at diagnosis (years)	47.6	48	31.5	37	40	37	42	31	41.5
Female to male Ratio	1	3.4	7	1.6	4.2	1.9	3.4	1.4	3
Pregnancy-related cases (n)	3		1	4	0	8	0	0	1
Most common presenting symptom/s (%)	Head-ache 75 % Lethargy 62 % Gonadal dysfunc-tion 50 %	Polyuria/polydipsia 82 % Headache 27 %	Headache 83 %	Polyuria/polydipsia 52 % Headache 57 % Visual disturbance 52 % Gonadal dysfunction 48 %	Polyuria/polydipsia 47 % Headache 24 % Gonadal dysfunc-tion 47 %	Headache and visual distur-bance	Head-ache 59 % Gonadal dysfunc-tion 59 % Visual distur-bance 32 %	Headache 53 % Polyuria/Polydipsia 47 % Fatigue 41 %	Headache 63 % Gonadal dysfunc-tion 66 % Visual distur-bance 37 % Polyuria/Polydipsia 32 %
Time to diagnosis (months)	15.8 (1–60)		10	3.5 (0.5–60)		4 (1–60)		12 (1–96)	18 (1–120)
Hormonal deficiencies (%)									
Adrenal	58	36	75		(Any kind of anterior hormonal deficiency in 81 %)	26	(Any kind of anterior hormo-nal deficien-cy in 77 %)	59	39
Thyroid	50	36	58.3			38		53	61
Gonadal	91.6	32	50			60		47	66
GH	43	23				22		6	21
DI	31	82	16.7	14	47.6	30.5	32	47	28
Hyperprolactinemia	37.5	23	41.6	48	42.8	48		41	31
Panhypopituitarism				57	4	10	23	23.5	39
Co-existing autoim-mune diseases (n)	5	2		5	13	3	8	2	2
Histopathological type %									
LH	77	73	100 (?)	76		100	86	75	50
GH	23	18		14					37.5
XGH		9					6	12.5	6
Mixed								12.5	6
IgG-4 related	1			5			6		
Clinically diagnosed cases (n/%)	3	11	15	2	19	22	8	9	4
Surgery (n)	13	5	5	19	2	15	9	7	16
Steroid treatment (n)	8	5	4	All	All	26	8*	5**	4
Observation (n)		12	11	None	None	9	5	10	1
Duration of follow-up (months)	30 (2–107)	57 (7–138)	18	28.9	12	≥6	60	24 (6–84)	12 (0–132)

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	Leung, GK. 2004 [8]	Park, SM. 2014 [11]	Khare, S. 2015 [13]	Imber, BS. 2015 [12]	Chiloiro, S. 2017 [15]	Wang, S. 2017 [9]	Angelousi, A. 2018 [16]	Korkmaz, OP. 2019 [14]	Current case series
Relief of symptoms after treatment %									
Surgery	100	100	100		72.2 % in all group	100			100
Medical	60	100				100			100
Observation						22.2			
Radiological improvement in non-surgical patients	NA	Pituitary mass reduction in 4 steroid treated patients (80 %)	Pituitary mass regressed in all, both steroid and observational groups	Mass reduction in 8 (50 %)	Radiologic improvement in 13 (72.2 %)	Mass reduction in all steroid treated patients	Normal imaging findings in 27 % of treatment group	Improvement in 40 % and 30 % of steroid and observation groups, respectively	Pituitary mass regressed in all steroid treated patients
		No change in observation group	Persistent stalk thickening in 13 (68.4 %)	Stable or worse in 50 %	(All group evaluated, regardless of surgery)	Spontaneous mass reduction in 22.2 % of observation group			
			Near normal MRI findings in 2 (10.5 %)	(All group evaluated, regardless of surgery)					
			Empty sella with thinning of stalk in 4 (21 %)						
Endocrine improvement, %				19 % in all group	85.7 % in all group				
Surgery			25			0	16.6	14.3	0
Medical	0	40	100			40.9	44.4	20	20
Observation		17	100			22	5.5	10	NA
Recurrence (n)	2	3		6		46 % in medical, 11 % in surgical group	4	1	2

* Five out of 8 patients received other immunosuppressive agents. ** None received steroid as initial treatment. NA: Not available.

nosis; which is a finding mostly incompatible with previous publications [2, 10, 16]. Although female patients were also older in the case series reported by Khare et al., mean age at diagnosis of overall group was younger than ours (31.5 years) [13]. Even though PH is highly associated with pregnancy [2], only one of our cases was pregnancy-related.

Other autoimmune diseases co-exist with PH up to 18 % of cases, autoimmune thyroiditis being the most common [2]. However, we could only define one case with concomitant autoimmune thyroiditis.

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Lymphocytic hypophysitis is the most common histological subtype of PH, reported in 68 % of cases. Granulomatous hypophysitis is the second most common variant (20 %) while IgG4-related and xanthomatous hypophysitis are reported in 4 and 3 % of patients, respectively. Mixed pathological characteristics were reported in 4 % [10]. Our findings were consistent with these data. Notably, concurrent Rathke's cleft cysts were defined in three lymphocytic hypophysitis cases in our series. None of these cases had cystic appearance on MRI, but recognized by pathological examination. Simply explained by the triggered inflammatory reaction occurring secondary to cyst rupture, this co-existence was previously reported in other cases of both lymphocytic and xantho-granulomatous hypophysis [17, 18]. Adrenal insufficiency was reported to be common in patients with Rathke's cleft cysts [19]; however, only one out of three of our cases had adrenal hormone deficiency. Although we performed IgG4 immunostaining in available pathology specimens, it was not achievable to fully evaluate patients regarding IgG4-related hypophysitis due to the retrospective nature of our study.

Previous studies suggested that histopathological confirmation is not always mandatory to diagnose PH, especially if no alternative diagnoses are considered which could change treatment [20]. Cases of 'clinically diagnosed' PH have been reported more frequently in the literature in recent years, possibly due to expanded awareness. However, the majority of patients are still diagnosed after surgical procedures [10], as in our series. The most common indications for surgery in PH have been symptoms related to mass effect, such as headache and visual disturbances; but also, diagnostic difficulties. Our study exposed that radiological diagnosis was more accurate when clinicians provide more clinical knowledge for radiologists. Also, loss of posterior pituitary bright spot and thickened infundibulum were associated with more precise diagnosis of PH, like previously been identified as indicative radiological findings for PH [21]. Nevertheless, yet the best imaging technique available, pituitary MRI alone may not be enough to distinguish PH from pituitary adenomas [22].

Treatment of PH targets both hormonal deficiencies and symptoms associated with mass effect. Conservative management has been suggested in asymptomatic patients [2], which was appropriate for one case in our series. While glucocorticoids are the first choice of medical treatment in PH, surgery should be reserved for severe cases having neuro-ophthalmologic findings or cases who are non-responsive to medical treatment [22]. Overall, mass reducing treatments, either surgical or medical, have been reported to improve symptoms and radiological findings in 70–80 % of patients but endocrine deficiencies in only 18 % [2, 10, 23], compatible with our findings. Used in variable doses and duration, Honegger et al. reported radiologic and hormonal improvement in 65 % and 18 % of cases with glucocorticoid treatment, respectively [23]. All glucocorticoid treated patients in our series showed radiologic response. Although some previous case series reported better hormonal response rates to glucocorticoid therapy than ours [9, 11, 13, 16], our rates were similar with others [12, 14, 23] and better than one [8] (▶ Table 3). Out of 16 surgical patients in our series, seven had optic chiasm compression. Although 14 to 25 % recovery of endocrine function in surgical cases was reported in some previous reports [8, 13, 16], none of our patients showed im-provement in this manner. There was only one case relapsed after surgery, though Honegger et al. reported 25 % recurrence in surgically treated PH cases [23]. None of our subjects received third-line treatments such as other immunosuppressive agents or radiotherapy.

Our study has some limitations; first of which is the rather high surgery rate. This is mainly a consequence of high occurrence of neuro-ophthalmological involvement, but also of diagnostic difficulties. Another limitation is that glucocorticoid treated patients received different treatment regimes. However, we think that the distinguished regimes may be explicable by the retrospective nature of the study.

In conclusion, we have reported a series of PH including 20 cases mostly confirmed by histopathology. We have reviewed clinical characteristics and presentations, radiological and endocrine findings as well as disease management and outcomes of the patients comparatively with previous reports. Although few patients received glucocorticoid therapy, we have discussed each case in detail regarding treatment modalities and therapy responsiveness.

Conflict of Interest

The authors declare that they have no conflict of interest.

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