Case Report

DOI: 10.4274/tjem.3200
Turk J Endocrinol Metab 2016;20:144-147

Pituitary Abscess Due to *Staphylococcus Lugdunensis* in a Patient with Lymphocytic Hypophysitis

Lenfositik Hipofizit Zemininde Gelişen *Staphylococcus Lugdunensis* Apsesi

Alev Selek, Berrin Çetinarslan, İlhan Tarkun, Zeynep Cantürk, Özlem Akyay, Burak Çabuk*, Çiğdem Vural**

Kocaeli University Faculty of Medicine, Department of Endocrinology, Kocaeli, Turkey
*Kocaeli University Faculty of Medicine, Department of Neurosurgery, Kocaeli, Turkey
**Kocaeli University Faculty of Medicine, Department of Pathology, Kocaeli, Turkey

Abstract

Lymphocytic hypophysitis is a rare endocrine disease involving lymphocytic infiltration and chronic pituitary inflammation. Pituitary abscess is another rare disease which may be associated with underlying parasellar pathology. Here, we report a case of lymphocytic hypophysitis diagnosed with a pituitary abscess and recurrent suprasellar involvement after surgery. A 58-year-old female presented with headache, panhypopituitarism, and a pituitary lesion with thickening of the pituitary stalk. She had pituitary surgery and was diagnosed with lymphocytic hypophysitis associated with pituitary abscess. After antibiotic therapy, the lesion recurred with extension to the hypothalamus and compressive symptoms. She was operated in order to rule out recurrent abscess, and then, high dose glucocorticoid treatment was initiated. The headache and fever resolved within one week of glucocorticoid treatment and her visual field was completely normal. However, glucocorticoid treatment resulted in toxic hepatitis and had to be prematurely withdrawn limiting the entire treatment length to 12 weeks. 100 mg/day azothioprine was started after normalization of her liver enzymes. The pituitary lesion reduced more than 50% on the third month magnetic resonance imaging and she is still on follow-up without any recurrence. Lymphocytic hypophysitis may cause neurological deficits and complete loss of pituitary functions. The disease may rarely be complicated with abscess, therefore, careful evaluation and surgical treatment should be performed.
Keywords: Lymphocytic hypophisitis, pituitary abscess, *Staphylococcus lugdunensis*

Öz

Lenfositik hipofizit, kronik hipofizer lenfositik infiltrasyon ile karakterize nadir bir endokrin hastalıktır. Hipofizer apse ise, altta yatan parasellar patolojiler ile ilişkili olabilecek hipofizin diğer nadir hastalıklarındandır. Bu olgu takdiminde, hipofizer apse ile prezente olan ve cerrahi sonrası süprasellar tutulum ile nüks eden bir lenfositik hipofizit olgusu sunulmaktadır. Elli sekiz yaşında kadın hasta baş ağrısı, panhipopituitarizm ve hipofiz sapında kalınlaşmaya neden olan sellar lezyon ile başvurdu. Cerrahi tedavi sonrası lenfositik hipofizit ve hipofizer apse tanısı konuldu. Antibiyotik tedavisi sonrası lezyon, hipotalamusa yayılım ve bası bulguları ile nüks etti. Apse rekürrensini ekarte etmek için yapılan ikinci cerrahi sonrası yüksek doz glukokortikoid tedavisi başlandı. Glukokortikoid tedavisinin ilk haftasında baş ağrısı, ateş ve görme alanı daralması tamamen düzeldi. Fakat glukokortikoid tedavisinin neden olduğu toksik hepatit nedeniyle tedavi 12 haftada kesildi. Karaciğer fonksiyonlarının normale dönmesinin ardından 100 mg/gün dozunda azotioprin başlandı. Üç ayda lezyonda %50'den fazla küçülme sağlandı ve komplikasyon görülmedi. Lenfositik hipofizit tüm hipofiz fonksiyonlarının kaybı ve ciddi nörolojik kayıplara neden olabilir. Nadiren apse ile komplike olabilir, bu nedenle dikkatli değerlendirme ve cerrahi tedavi düşünülmelidir.
Anahtar kelimeler: Lenfositik hipofizit, hipofizer apse, *Staphylococcus lugdunensis*

Introduction

Lymphocytic hypophysitis (LH) is a rare inflammatory disease of the pituitary gland. It is generally accepted as an autoimmune disease, because of the existence of antipituitary antibodies and concomitant autoimmune diseases, especially Hashimoto's thyroiditis (1,2). Definitive diagnosis relies on tissue biopsy (2). However, a homogenous enhancing sellar mass coincides with pregnancy, diabetes insipidus or hypopituitarism with or without hyperprolactinemia and a coexisting autoimmune disease may predict a presumptive diagnosis (3). Clinical course of the disease is a spectrum; from spontaneous resolution resulting in empty sella, to recurrent invasive pituitary mass with severe compressive symptoms. This case is interesting for different aspects; to the best of our knowledge, pituitary abscess formation secondary to preexisting LH has not been described yet. *Staphylococcus lugdunensis* has also not been described as a causative agent for pituitary abscess.

Address for Correspondence: Alev Selek MD, Kocaeli University Faculty of Medicine, Department of Endocrinology, Kocaeli, Turkey
Phone: +90 262 303 81 98 E-mail: alevselek@gmail.com **Received:** 15/06/2015 **Accepted:** 13/09/2015

Case Report

A 58-year-old female was admitted to our hospital with one-year history of headache and a pituitary adenoma. The pituitary lesion had been diagnosed during her evaluation for intractable headache with fever before admission to our hospital. At that time, the pituitary lesion was 9 mm in diameter on initial magnetic resonance imaging (MRI). Cerebrospinal fluid (CSF) examination was sterile and pituitary functions were normal (Table 1). She was on levothyoxine treatment due to previous diagnosis of Hashimoto's thyroiditis. Headache and fever continued with spontaneous remission and relapse periods despite non-steroidal anti-inflammatory drugs. In the course of time, she had lost her anterior pituitary functions progressively resulting in panhypopituitarism (Table 1). On admission to our hospital, she was on levothyroxine, hydrocortisone and desmopressin replacement treatment. Pituitary MRI revealed a heterogeneous pituitary lesion measuring 14x11 mm in diameter, with minimal peripheral contrast enhancement and thickened pituitary stalk (8 mm) (Figure 1a). According to the clinical course and MRI findings, hypophysitis was the preliminary diagnosis. She underwent transsphenoidal pituitary surgery in order to confirm the diagnosis and subtype of hypophysitis. During operation, a purulent discharge was seen (Figure 2) and after drainage of abscess, a pituitary biopsy was taken. Gram staining showed gram-positive cocci and *Staphylococcus lugdunensis* was cultured. Antibiotic therapy with meropenem and linezolid was initiated. The pituitary biopsy revealed pituitary abscess formation and lymphocytic infiltration of the remaining pituitary gland (Figure 3, 4). Langerin, S-100 and CD1a immunohistochemical stains were all negative. Immunoglobulin (Ig) G4/IgG ratio was 1/10 and serum IgG4 levels were normal. LH with pituitary abscess was diagnosed after other causes were excluded. Prednisolone treatment was not initiated due to abscess formation and she was discharged with hormone replacement treatments after completion of antibiotic treatment. Headache and fever recurred after six month of surgery. Sedimentation rate and C-reactive protein levels were normal and all viral and bacteriological investigations were negative. On imaging, it was found that the pituitary lesion relapsed with extension to the hypothalamus and optic chiasm (Figure 1b). Bitemporal hemianopsia was detected on visual field examination. Second surgery was done for decompression and ruling out recurrent pituitary abscess. There was no abscess formation and fibrotic tissue could have been partially excised. Intravenous infusion of 100 mg methylprednisolone for 3 days and oral administration of 60 mg/dL prednisone for two weeks were started. By the end of the second week, liver enzymes increased up to 20 times the normal values. Diagnostic tests for autoimmune hepatitis, *Brucella*, tuberculosis and hepatotropic viruses were negative and hepatobiliary ultrasound was normal. Therefore, the diagnosis of toxic hepatitis due to glucocorticoid treatment was established and the treatment had to be prematurely withdrawn limiting the entire treatment length to 12 weeks. Headache and fever resolved within one week of steroid treatment and her visual field was completely normal. 100 mg/day azothioprine was started after normalization of her liver enzymes. The size of the pituitary lesion was reduced by more than 50% on MRI on the third month of treatment and she is still on follow-up without any recurrence (Figure 1c). The patient is now at the sixth month of treatment, however, anterior pituitary functions are not recovered yet. She could not tolerate dose decrease in hydrocortisone and desmopressin replacement treatments.

Table 1. Laboratory values of the patient reflecting progressive loss of pituitary functions

	1st month	3rd month	10th month	Normal range
TSH	5.5	0.05	0.11	(0.5-5) mIU/L
fT_3	2.5	2.14	1.8	(2.8-4.7) pg/dL
fT_4	0.95	0.5	0.46	(0.6-1.75) ng/dL
Prolactin	16.5	16.9	16,4	(2.4-20) ng/mL
FSH	25.5	2.2	1.4	(23-119) mIU/mL
LH	16.7	2.7	0.1	(16-54) IU/L
E2	<5	<20	<20	(0-32) pg/mL
ACTH	18.7	-	8.6	(0-45) pg/mL
Cortisol	14.7	-	0.4	(5-22) ug/dL
IGF-1	154	-	51	(53-186)

*Bold written values are below normal range
TSH: Thyroid stimulating hormone, FSH: Follicle-stimulating hormone, E2: Estradiol, ACTH: Adrenocorticotropic hormone, IGF: Insulin-like growth factor, fT_3: Freetriiodthronine, fT_4: Freethyroxine

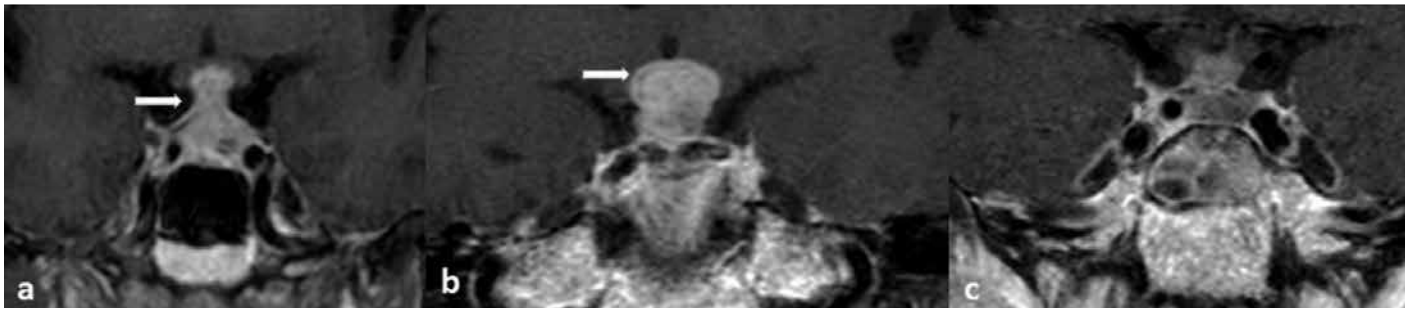

Figure 1. a) Pituitary magnetic resonance imaging of the patient on admission, thickened pituitary stalk (arrow) and heterogenic sellar enlargement, b) magnetic resonance imaging of the recurrent pituitary lesion extending to hypothalamus (arrow), c) magnetic resonance imaging of the pituitary lesion after glucocorticoid treatment

Discussion

LH is thought to be an autoimmune disease characterized by extensive lymphoplasmacytic infiltration of the pituitary gland. Although LH is predominantly seen in females aged 30-40 years, our case was a postmenopausal woman (4). Clinical course of the disease may be insidious or more rapidly progressive as in this case (4). Headache is present in more than 50% of cases and a high frequency of hypopituitarism has been reported (6). The current case has lost all the pituitary functions within 10 months after the diagnosis of diabetes insipidus.

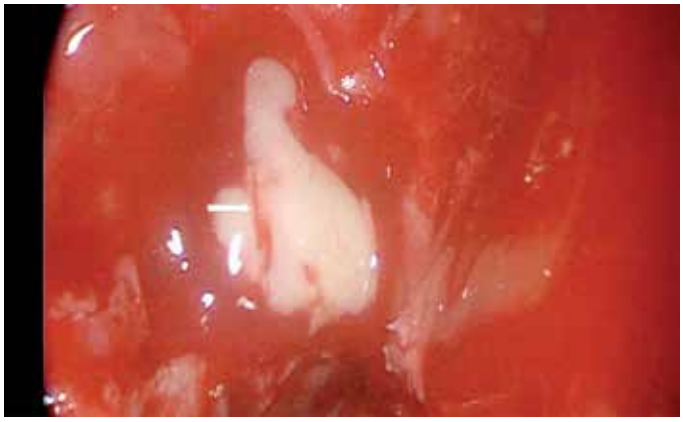

Figure 2. Sellar floor, dura matter (*) and purulent discharge during surgery (arrow)

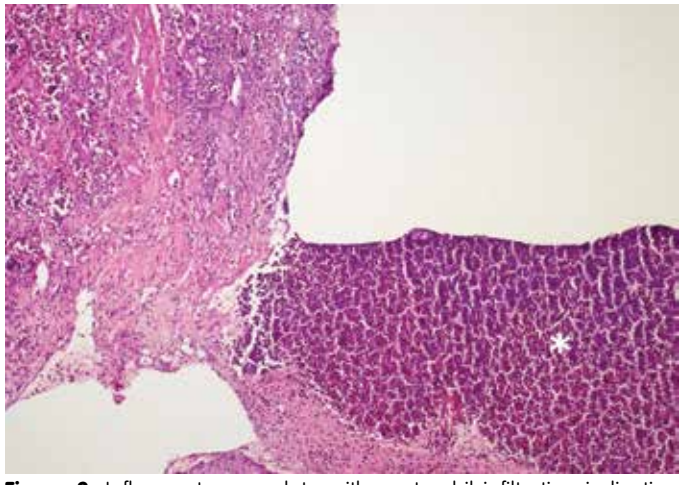

Figure 3. Inflammatory exudate with neutrophil infiltration indicating abscess formation (*) and surrounding pituitary tissue with lymphocyte infiltration (hematoxylin & eosin x200)

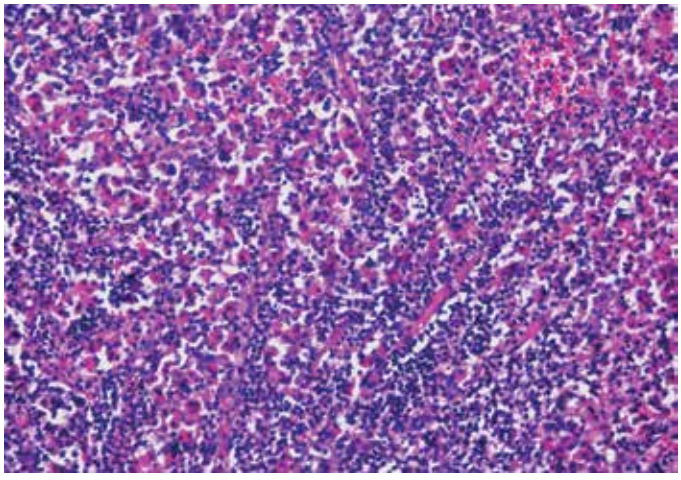

Figure 4. Lymphocytic infiltration of the pituitary tissue (hematoxylin & eosin x40)

Radiologic features of LH are variable from suprasellar extending mass to empty sella. Extrasellar disease is very rare but pituitary stalk thickening is seen in most cases (5). Our case presented with a sellar mass, but the recurrent lesion was extending into the suprasellar region, reaching the hypothalamus with optic chiasm compression. Definitive diagnosis of LH requires histopathological evaluation. Microscopically, a diffuse infiltrate of inflammatory cells, mostly lymphocytes, is seen with nests of normal acinar cells surrounded by necrosis and extensive fibrosis (6). Most likely, differential diagnosis of this case was Langerhans cell histiocytosis (LCH) according to the clinical course and radiologic features. Langerin, S-100 and CD1a immunohistochemical stains were performed as they are pathognomonic for LCH, and all were negative (7). The pathology of the first operation intra-operative pathological evaluation, revealed neutrophilic infiltration of the centre suggesting abscess formation and lymphocytic infiltration of the surrounding hypophysial cells. Therefore, LH with pituitary abscess was diagnosed (Figure 1).

Pituitary abscess is a rare clinical entity accounting for approximately 0.2-1% of all pituitary lesions (8,9). The abscess may arise as a primary pituitary lesion or be associated with an underlying parasellar pathology (8,10). Previous CSF examination and sphenoid sinusitis might be the leading causes of abscess formation in our patient. Underlying LH might also be a facilitating factor for the inoculation of microorganisms. The recommended managements of pituitary abscess are surgical drainage and administration of antibiotics (10). Meropenem and linezolid treatments were started parenterally following oral administration of ampicillin/sulbactam for 6 weeks. *Staphylococcus lugdunensis* is a coagulase-negative *Staphylococcus* known primarily as a cause of endocarditis, especially in immunocompromised patients (11). It has also been associated with septic arthritis, osteomyelitis, peritonitis, brain abscesses, and infections of the skin and soft tissues, urinary tract, and prosthetic medical devices. It has rarely been implicated in central nervous system infections (12). To the best of our knowledge, the current case is the first report describing *Staphylococcus lugdunensis* pituitary abscess.

Most symptomatic LH patients require pulse glucocorticoid therapy followed by a slow tapering over a period of weeks to months (13). Despite good response, relapses are common. Glucocorticoids combined with azathioprine constitute effective treatment for recurrent LH. Metotrexate, cyclosporine A and stereotactic radiation have also been reported in the management of recurrent patients (3). Due to abscess formation, we could not start glucocorticoid treatment initially. After exclusion of the abscess after the second surgery, high-dose glucocorticoid treatment was administered. After 12 weeks, azathioprine was added to the treatment since glucocorticoid treatment had to be discontinued earlier due to toxic hepatitis. The size of the pituitary lesion was reduced more than half at the third month of treatment.

In conclusion, the very rare presentation of coinciding pituitary abscess formation and LH requires very careful consideration of diagnosis, treatment, and monitoring. The reason for pituitary abscess is unknown in most cases. In the case presented here, it may be due to disruption of pituitary tissue by the lymphocytic inflammation rendering the pituitary gland susceptible to bacterial invasion and abscess formation.

Ethics

Informed Consent: Consent form was filled out by the participant.
Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Alev Selek, Özlem Akyay, Berrin Çetinarslan, Concept: Alev Selek, İlhan Tarkun, Zeynep Cantürk, Burak Çabuk, Design: Alev Selek, Özlem Akyay, Berrin Çetinarslan, Data Collection or Processing: Alev Selek, İlhan Tarkun, Zeynep Cantürk, Çiğdem Vural, Analysis or Interpretation: Alev Selek, İlhan Tarkun, Özlem Akyay, Berrin Çetinarslan, Literature Search: Alev Selek, Özlem Akyay, Berrin Çetinarslan, Writing: Alev Selek, Zeynep Cantürk, Burak Çabuk, Çiğdem Vural.
Conflict of Interest: No conflict of interest was declared by the authors.
Financial Disclosure: The authors declared that this study received no financial support.

References

1. Caturegli P, Lupi I, Landek-Salgado M, Kimura H, Rose NR. Pituitary autoimmunity: 30 years later. Autoimmun Rev. 2008;7:631-637.
2. Falorni A, Minarelli V, Bartoloni E, Alunno A, Gerli R. Diagnosis and classification of autoimmune hypophysitis. Autoimmun Rev. 2014;13:412-416.
3. Carmichael JD. Update on the diagnosis and management of hypophysitis. Curr Opin Endocrinol Diabetes Obes. 2012;19:314-321.
4. Caturegli P, Newschaffer C, Olivi A, Pomper MG, Burger PC, Rose NR. Autoimmune hypophysitis. Endocr Rev. 2005;26:599-614.
5. Gutenberg A, Hans V, Puchner MJ, Kreutzer J, Bruck W, Caturegli P, Buchfelder M. Primary hypophysitis: clinical-pathological correlations. Eur J Endocrinol. 2006;155:101-107.
6. Molitch ME, Gillam MP. Lymphocytic hypophysitis. Horm Res. 2007;68 Suppl 5:145-150.
7. Ghafoori S, Mohseni S, Larijani B, Mohajeri-Tehrani MR. Pituitary stalk thickening in a case of langerhans cell histiocytosis. Arch Iran Med. 2015;18:193-195.
8. Vates GE, Berger MS, Wilson CB. Diagnosis and management of pituitary abscess: a review of twenty-four cases. J Neurosurg. 2001;95:233-241.
9. Altas M, Serefhan A, Silav G, Cerci A, Coskun KK, Elmaci I. Diagnosis and management of pituitary abscess: a case series and review of the literature. Turk Neurosurg. 2013;23:611-616.
10. Kuge A, Sato S, Takemura S, Sakurada K, Kondo R, Kayama T. Abscess formation associated with pituitary adenoma: A case report: Changes in the MRI appearance of pituitary adenoma before and after abscess formation. Surg Neurol Int. 2011;2:3.
11. Vandenesch F, Etienne J, Reverdy ME, Eykyn SJ. Endocarditis due to Staphylococcus lugdunensis: report of 11 cases and review. Clin Infect Dis. 1993;17:871-876.
12. Spanu T, Rigante D, Tamburrini G, Fiori B, D'Inzeo T, Posteraro B, Policicchio D, Sanguinetti M, Fadda G. Ventriculitis due to Staphylococcus lugdunensis: two case reports. J Med Case Rep. 2008;2:267.
13. Yamagami K, Yoshioka K, Sakai H, Fukumoto M, Yamakita T, Hosoi M, Ishii T, Sato T, Tanaka S, Fujii S. Treatment of lymphocytic hypophysitis by high-dose methylprednisolone pulse therapy. Intern Med. 2003;42:168-173.