TJEM TURKISH JOURNAL OF ENDOCRINOLOGY AND METABOLISM

CASE REPORT
Turk J Endocrinol Metab. 2022;26(2):97-99

Postpartum Lactation Failure Secondary to Isolated Prolactin Deficiency: A Case Report and Literature Review

ABSTRACT

Prolactin deficiency can occur alone, as can be seen by the deficiency of 1 or more of the other anterior pituitary hormones. Isolated prolactin deficiency is an extremely rare condition, and the only known symptom is the lack of lactation in postpartum women. A 29-year-old female presented in 2 weeks postpartum for evaluation of lactation failure. On the postpartum 16th day, the prolactin level was very low. Since there were no other pituitary abnormalities, we considered the diagnosis of isolated prolactin deficiency. In this case, we presented lactation failure due to isolated prolactin deficiency, which is extremely rare in the literature. In isolated prolactin deficiency, most of the patients are diagnosed with the absence of lactation and there are no other concurrent pituitary pathologies. In the treatment, recombinant human prolactin stands out as an option, but it is unavailable in many countries. In most cases, baby formula is used to feed babies.

Keywords: Hormone deficiency, isolated prolactin deficiency, lactation, lactation failure, r-hPRL

Introduction

Prolactin (PRL) is a hormone synthesized from the lactotrophic cells in the anterior pituitary and is required for the initiation and maintenance of lactation after birth. During pregnancy PRL secretion begins increasing and, along with many other hormones (estrogen, progesterone, insulin, and cortisol), contributes to the development of breasts for milk production.[1,2] Despite its importance during pregnancy, the role of PRL in the development of normal breast tissue in non-pregnant women is fully unknown. Prolactin deficiency develops because of the loss of the function of anterior pituitary cells secreting PRL and results in decreased serum PRL levels. Prolactin deficiency can occur alone, as can be seen by the deficiency of 1 or more of the other anterior pituitary hormones. Isolated PRL deficiency is an extremely rare condition, and the only known symptom is the lack of lactation in postpartum women.[3] No symptom of PRL deficiency has been reported in males.

Case Presentation

A 29-year-old G1P1 female presented in 2 weeks postpartum for evaluation of lactation failure. Her pregnancy was spontaneous, and she experienced no complications during pregnancy and delivery (cesarean section). Although the mother breastfed her baby with an interval of 2 hours and used a breast pump 9 times a day, during the previous 2 weeks, there was no milk or colostrum. There was no family history of problems with lactation. Her breasts were Tanner Stage V, and her body mass index was 27 kg/m^2. Her medical history was significant for hypothyroidism due to Hashimoto's thyroiditis diagnosed 4 years before her pregnancy. She was maintained on a stable dose of levothyroxine of 75 µg before pregnancy. During the pregnancy, the dosage of levothyroxine was increased to 125 µg/day.

On the postpartum 16th day, the PRL level was 1.45 µg/L (reference range: 3.2-20 µg/L). Other laboratory findings found at 9:00 AM in the morning were as follows: adrenocorticotropic hormone 32.6 pg/mL (reference range: 7.2-63.3 pg/mL), cortisol 19 µg/dL (reference range: 6.7-22.6), thyroid-stimulating hormone 0.6 µIU/mL (reference range: 0.34-5.6), macroprolactin 1.23 µg/L (reference range: 3.34-26.72 µg/L), dilutional prolactin 1.52 µg/L, insulin-like growth factor I 128 ng/mL (reference range: 117-329), basal growth hormone (GH) 1.97 ng/mL (reference range: <10), luteinizing hormone 4.95 mIU/mL (reference range: 0.5-76.3 mIU/mL),

Arzu Bilen[1]
Habib Bilen[2]
Esra Güngör Albayrak[1]
Yusuf Karadeniz[2]
Naile Gökkaya[2]

[1]*Department of Internal Medicine, Atatürk University Faculty of Medicine, Erzurum, Turkey*
[2]*Division of Endocrinology and Metabolism, Department of Internal Medicine, Ataturk University Faculty of Medicine, Erzurum, Turkey*

Corresponding author:
Arzu Bilen
✉ arzu.bilen@atauni.edu.tr

Received: April 28, 2022
Accepted: June 13, 2022

Cite this article as: Bilen A, Bilen H, Güngör Albayrak E, Karadeniz Y, Gökkaya N. Postpartum lactation failure secondary to isolated prolactin deficiency: A case report and literature review. *Turk J Endocrinol Metab*. 2022;26(2):97-99.

DOI: 10.5152/tjem.2022.22048

Table 1. Characteristics of Women with Isolated Prolactin Deficiency

Cases	Age, Years	Parity	Maternal History	Medical History	Pre-gestational Breast Tissue	Gestational Breast Enlargement	Menstrual Cycle
Turkington et al (1972) (2 cases)	27	2	Not mentioned	None	Normal	Normal	Not mentioned
	29	2	Not mentioned	None	Normal	Normal	Not mentioned
Kauppila et al (1987)	30	2	Normal	Not mentioned	Normal	Normal	Normal
Falk (1992)	36	2	Normal	Normal	Normal	Normal	Irregular
Zargar et al (2 cases) (1997)	25	2	Maternal history	Normal	Normal	Not mentioned	Normal
	58	6	Not mentioned	Normal	Normal	Not mentioned	Normal
Doichi et al (2001)	26	1	Normal	Not mentioned	Atrophic	None	Secondary amenorrhea
Iwama et al (2013)	39	2	Normal	Hashimoto's disease	Normal	Normal	Normal
Collejas et al (2 cases) (2015)	32	1	Not mentioned	Polycystic ovary syndrome	Atrophic	None	Irregular
	24	1	Not mentioned	Polycystic ovary syndrome	Normal	Normal	Irregular
Akel et al (2016)	31	1	Normal	Hashımato's Disease	Normal	Normal	Normal
Pamela et al. (2018)	32	1	Not mentioned	Mild intermittent asthma, seasonal allergies	Normal	None	Normal
Bilen et al (2020)	29	1	Normal	Hashimoto's disease	Normal	None	Normal

follicle-stimulating hormone 6.33 mIU/mL (reference range: 33.4-171.5 mIU/mL), estradiol 352 pg/mL (reference range: 95-433 pg/mL), and other laboratory tests were normal.

The pituitary gland was evaluated as normal in magnetic resonance imaging. Since there were no other pituitary abnormalities, we considered the diagnosis of isolated PRL deficiency. The PRL autoantibodies and genetic tests, which may be useful for the etiology of the disease, could not be performed because the patient did not give consent. Recombinant human prolactin (r-hPRL) usage was recommended as a possible treatment option for the patient, who was informed that she would be unable to give her milk. However, the patient declined r-hPRL treatment and preferred to use baby formula.

Discussion

Prolactin is a hormone secreted from lactotroph cells in the anterior pituitary. It is inhibited by dopamine, a neurotransmitter in the hypothalamus. Although the primary function of the PRL hormone is breast development and milk production during pregnancy, prolactin receptor is found in many tissues.[4] Prolactin is secreted physiologically in a pulsatile manner. Its level increases especially with sleep, stress, nipple stimulation, and lactation. During pregnancy, together with some hormones (insulin, cortisol, thyroid hormone, estrogen, and progesterone), it plays a role in breast development and provides milk production. Lactation is prevented with the dominance of estrogen and progesterone during pregnancy and starts with the withdrawal of these 2 hormones after birth. Prolactin levels remain at an average value to maintain lactation (200 ng/mL) and decrease over time. As seen in our case, although the PRL hormone has a significant effect in increasing the size of the breast tissue during pregnancy, it does not seem to be an essential hormone for breast development that occurs in women with puberty.

MAIN POINTS

- Isolated prolactin deficiency is extremely rare in the literature.
- In isolated prolactin deficiency, most of the patients are diagnosed with the absence of lactation and there are no other concurrent pituitary pathologies.
- In this article, we presented both other very rare cases in the literature and our own case.

Many reasons may lead to a lack of pituitary hormones. Prolactin deficiency can be seen after pituitary surgery or radiotherapy, in pituitary insufficiency due to Sheehan's syndrome, inflammato ry-infiltrative diseases affecting the pituitary gland, pituitary interruption syndrome, and the use of dopamine agonists. Isolated PRL hormone deficiency is an extremely rare condition, and to date, less than 20 cases have been reported in the literature. Although there are a few case reports of genetic transmission, information about genetic transmission in humans related to isolated PRL deficiency is limited.[5] Regarding the control of PRL production, in female mice, the effect of transient receptor potential channel Trpc5 on dopaminergic neuroendocrine neurons was investigated. In this study, severe PRL deficiency was shown to occur in Trpc5-mutant female

mice.[6] However, the genetic relationship regarding isolated PRL deficiency in humans has not yet been elucidated. It is known that autoimmunity can also cause various pituitary hormone deficiencies.[7] The presence of Hashimoto's thyroiditis in most cases supports that autoimmunity may play a role in the isolated PRL deficiency etiology.[8] However, it is extremely rare in the literature that the autoimmune process affects only cells that secrete PRL. Anti-PRL antibodies have been identified in 1 case with isolated PRL deficiency in the literature.[9] As in some of the existing cases, our patient had autoimmune thyroid disease.

In patients with isolated PRL deficiency, features such as spontaneous pregnancy, menstrual cycle patterns, and normal breast development before pregnancy vary from patient to patient.[10-14] In our case, pregnancy was spontaneous. Pre-pregnancy menstrual cycles were regular, and breast development was normal. Table 1 presents the patients' characteristics in case reports previously published. As seen in the table, unlike in our case, some patients may have menstrual irregularities, breast tissue development disorders, and infertility complaints. In mothers with isolated PRL deficiency-related lactation failure, the use of medicines, also called galactagogues, is being tried for treatment.[2] Galactagogues are drugs such as domperidone, metoclopramide, sulpiride, GH, thyrotropin-releasing hormone, metformin, oxytocin, and r-hPRL. In the treatment of isolated PRL deficiency, the most reasonable option among galactagogues seems to be the use of r-hPRL. It is reported that milk volume can be increased in women with lactation failure with the r-hPRL treatment applied twice daily.[15,16]

Conclusion

In this case, we presented lactation failure due to isolated PRL deficiency, which is extremely rare in the literature. Autoimmunity and genetic mechanisms may play a role in the etiopathogenesis of isolated PRL deficiency. In isolated PRL deficiency, most of the patients are diagnosed with the absence of lactation and there are no other concurrent pituitary pathologies. In the treatment, r-hPRL stands out as an option, but it is unavailable in many countries. In most cases, baby formula is used to feed babies.

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.B., H.B., G.E.A., Y.K., N.G.; Design – A.B., H.B.; Supervision – A.B., H.B.; Resources – A.B., H.B.; Materials – A.B., H.B., G.E.A., Y.K., N.G.; Data Collection and/or Processing – A.B., H.B., G.E.A.; Analysis and/or Interpretation – A.B., H.B.; Literature Search – A.B., H.B.; Writing Manuscript – A.B., H.B.; Critical Review – A.B., H.B.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: This study received no funding.

References

1. Tabares FP, Jaramillo JVB, Ruiz-Cortés ZT. *Pharmacological Overview of Galactogogues*. Veterinary Medicine International; 2014.
2. Russo J, Russo IH. Development of the human breast. *Maturitas*. 2004;49(1):2-15. [CrossRef]
3. Berens PD, Villanueva M, Nader S, Swaim LS. Isolated prolactin deficiency: A possible culprit in lactation failure. *AACE Clin Case Rep*. 2018;4(6):e509-e512. [CrossRef]
4. Ben-Jonathan N, LaPensee CR, LaPensee EW. What can we learn from rodents about prolactin in humans? *Endocr Rev*. 2008;29(1):1-41. [CrossRef]
5. Zargar AH, Masoodi SR, Laway BA, Shah NA, Salahudin M. Familial puerperal alactogenesis: possibility of a genetically transmitted isolated prolactin deficiency. *Br J Obstet Gynaecol*. 1997;104(5):629-631. [CrossRef]
6. Blum T, Moreno-Pérez A, Pyrski M, et al. Trpc5 deficiency causes hypoprolactinemia and altered function of oscillatory dopamine neurons in the arcuate nucleus. *Proc Natl Acad Sci U S A*. 2019;116(30):15236-15243. [CrossRef]
7. De Bellis A, Colella C, Bellastella G, et al. Late primary autoimmune hypothyroidism in a patient with postdelivery autoimmune hypopituitarism associated with antibodies to growth hormone and prolactin-secreting cells. *Thyroid*. 2013;23(8):1037-1041. [CrossRef]
8. Akel BM, Feuerstein BL, Charlamb JR, Desimone ME. Failure of postpartum lactogenesis due to isolated prolactin deficiency. Case Rep. *Intern Med*. 2016;3:43-46.
9. Iwama S, Welt CK, Romero CJ, Radovick S, Caturegli P. Isolated prolactin deficiency associated with serum autoantibodies against prolactin-secreting cells. *J Clin Endocrinol Metab*. 2013;98(10):3920-3925. [CrossRef]
10. Turkington RW. Phenothiazine stimulation test for prolactin reserve: the syndrome of isolated prolactin deficiency. *J Clin Endocrinol Metab*. 1972;34(1):246-249. [CrossRef]
11. Callejas L, Berens P, Nader S. Breastfeeding failure secondary to idiopathic isolated prolactin deficiency: report of two cases. *Breastfeed Med*. 2015;10(3):183-. [CrossRef]
12. Douchi T, Nakae M, Yamamoto S, Iwamoto I, Oki T, Nagata Y. A woman with isolated prolactin deficiency. *Acta obstet gynecol Scand*. 2001;80(4):368-370.
13. Falk RJ. Isolated prolactin deficiency: a case report. *Fertil Steril*. 1992;58(5):1060-1062. [CrossRef]
14. Kauppila A, Chatelain P, Kirkinen P, Kivinen S, Ruokonen A. Isolated prolactin deficiency in a woman with puerperal alactogenesis. *J Clin Endocrinol Metab*. 1987;64(2):309-312. [CrossRef]
15. Powe CE, Allen M, Puopolo KM, et al. Recombinant human prolactin for the treatment of lactation insufficiency. *Clin Endocrinol (Oxf)*. 2010;73(5):645-653. [CrossRef]
16. Grzeskowiak LE, Wlodek ME, Geddes DT. What evidence do we have for pharmaceutical galactagogues in the treatment of lactation insufficiency?—A narrative review. *Nutrients*. 2019;11(5):974. [CrossRef]