



EFFECT OF SERUM PROLACTIN ON FERTILITY- A CASE REPORT

DR.S.V.MYTHILI AND DR.T.VIDHYA LOGINI

Department of Biochemistry, Sree Balaji Medical College And Hospital, Chrompet ,Chennai

ABSTRACT

Hyperprolactinaemia is the presence of abnormally high levels of prolactin in the blood. Normal levels are less than 20 ng/mL for women, and less than 450 mIU/L for men. A prolactinoma is a benign tumor (adenoma) of the pituitary gland that produces a hormone called prolactin. It is the most common type of pituitary tumor. Hyperprolactinemia is a cause for infertility which is reversible with treatment with dopamine agonists.[1]

KEY WORDS: Hyperprolactinemia – Prolactinoma – Infertility



DR.T.VIDHYA LOGINI

Department of Biochemistry, Sree Balaji Medical College
And Hospital, Chrompet , Chennai

CASE REPORT

A 46 years old female patient married at the age of 16 years. At the age of 22years, she developed galactorrhoea [1] for which she went to the hospital for the first time. She gave a history of infertility. Prolactin levels were checked and found to be higher. MRI was done and diagnosed as a case of prolactinoma. Medical management was started at the age of 22years in the form of Oral Bromocryptine. At the age of 30, she conceived for the first time. She was advised to continue Bromocryptine during pregnancy. At 8 months pregnancy was terminated due to congenital anomalies. The patient again conceived at the age of 32 and gave birth to a female child. The child is now 14 years old. Now the patient presented with 3 months of amenorrhea. Pregnancy test is negative now. Prolactin levels checked and found to be high.

Investigations

Prolactin level :At the age of 22years it was found to be 379 ng/ml, at six months after treatment with bromocryptine it was 88ng/ml, at the time of first conception it was 33ng/ml , at six months after conception it was 58ng/ml, at term it was 74ng/ml. At the age of 42 ---- 189ng/ml (after voluntary discontinuation of dopamine agonist)

DISCUSSION

prolactin

Prolactin being secreted by the lacto trope cells of anterior pituitary is encoded by the PRL gene in chromosome 6. It acts like cytokines through prolactin receptors. Secretion is regulated by hypothalamus through dopamine which inhibits the secretion [2,3]

Chemical structure of prolactin[2,3]

Prolactin is Composed of 199 amino acids , the molecular wt being 24000 daltons . It has a single chain of polypeptide with 4 major helices, 2 minor helices and 2 loops .The 3 disulphide bonds are responsible for its tertiary structure. Cleavage of disulphide bonds leads to loss of biological activity

Reference ranges [2,3]

General guidelines for diagnosing prolactin excess (hyperprolactinemia) define the upper threshold of normal prolactin at 25 µg/L for women, and 20 µg/L for men. Similarly, guidelines for diagnosing prolactin deficiency (hypoprolactinemia) are defined as the prolactin levels below 3 µg/L in women and 5 µg/L in men.

Cases

Physiological: Lactation, Sleep, Stress, Coitus, Exercise

Pharmacological [4]

Antipsychotics

Typical Haloperidol Chlorpromazine, Thioridazine, Thiothixene
Atypical Risperidone, Amisulpride Molindone, Zotepine

Antidepressants

Tricyclics Amitriptyline, Desipramine
Clomipramine Amoxapine
SSRI Sertraline, Fluoxetine, Paroxetine
MAO-I Pargyline, Clorgyline

Other Psychotropics

Buspirone Alprazolam Prokinetics
Metoclopramide, Domperidone

Antihypertensive

Alpha-methyldopa, Reserpine, Verapamil

Opiates, Morphine

H2 Antagonists Cimetidine, Ranitidine Others
Fenfluramine, Physostigmine Chemotherapeutics

Pathological: [6,7,8]

Hypothalamic pituitary stalk Damage,
Granulomas, Infiltrations, Irradiation,
Rathke's cyst, Trauma, pituitary stalk
resection, suprasellar surgery, Tumors,
Craniopharyngioma, Germinoma
Hypothalamic metastases, Meningioma,
Suprasellar pituitary mass extension

Clinical manifestation

Males: Loss of libido, Infertility

Females: Oligomenorrhea, Amenorrhea, Infertility, Galactorrea In both sexes, headache and visual field defects due to mass effect and Osteoporosis due to hypogonadism

Investigations for all patients

Complete blood count, ESR, Urea and electrolytes, LFT, Bone profile Fasting glucose and lipids, Baseline pituitary function, MRI pituitary

For selected cases [9]

CXR, ECG, ECHO, Visualperimetry and acuity Insulin stress test, Glucagontest, Arginine GHRH test, Bone densitometry scan

Investigations done for this patient: basic blood investigations, ECG, serum prolactin and MRI brain, which revealed prolactinoma of <10mm size.

Medical treatment:

Bromocryptine, Cabergoline

Bromocryptine [10,11]

It is an ergot alkaloid and D2 receptor agonist. The initial dose being 1.25-2.5 mg day, may be increased by 2.5 mg/day q2 for 7 Days. Usual therapeutic dosage is 5-7.5 mg/day, ranging from 2.5-15 mg/day. Adverse effects are nausea, vomiting, postural hypotension, delusion, auditory hallucination, arrhythmias, pericarditis and rarely seizures.

Carbегoline [5,10,11]

Longer acting, Costlier, Side effects is less, Data on the safety use during pregnancy is limited

Surgery [6]

Gold standard treatment in 1970s. Presently medical management is the gold standard.

Indications for surgery

1. Size of the tumor not decreasing with medical therapy.
2. The patients not withstanding adverse effects of medical therapy.

Hyperprolactinemia and pregnancy

Studies show there is no proven teratogenic effects of dopamine agonists [12] But still dopamine agonists should be stopped during pregnancy if possible Periodical follow up should be done by visual field testing If more symptomatic, dopamine agonists can be used at a lower dose.

CONCLUSION

In our case, the patient was clinically diagnosed as having hyperprolactinemia, which is a treatable cause of infertility and requires long term treatment. [13].

REFERENCES

1. Wilson, J.D., 1998. Endocrine Disorders of the Breast. In: Braunwald E, Isselbacher KJ, Wilson J, *et al.* Harrison's Principles of Internal Medicine. 14thed. New York, NY: McGraw-Hill; 2116-2117.
2. Melmed S, Kleinberg D. Anterior pituitary. In: Kronenberg HM, Melmed S, Polonsky KS, Larsen PR, eds. Williams Textbook of Endocrinology. 11th ed. Philadelphia, PA: Saunders Elsevier; 2008.
3. Molitch ME. Anterior pituitary. In: Goldman L, Schafer AI, eds. Cecil Medicine. 24th ed. Philadelphia, Pa: Saunders Elsevier; 2011.
4. Davies, P.H., 1997. Drug-related hyperprolactinaemia. Adverse Drug React Toxicol Rev. Jun 16(2):83-94. [Medline].
5. Oh, M.C., S.Kunwar, L. Blevins and M.K. Aghi, 2012. Medical versus surgical management of prolactinomas. Neurosurg Clin N Am. Oct 23(4):669-78. [Medline].
6. Asa SL, Ezzat S. The pathogenesis of pituitary tumours. Nat Rev Cancer 2002; 2: 836-49. CrossRefMedline.
7. Vallette-Kasic S, Morange-Ramos I, Selim A, Gunz G, Morange S, Enjalbert A, *et al.* Macroprolactinemia revisited: a study on 106 patients. J Clin Endocrinol Metab 2002; 87:581-8. CrossRefMedline.
8. Thodou E, Asa SL, Kontogeorgos G, Kovacs K, Horvath E, Ezzat S. Clinical case seminar: lymphocytic hypophysitis: clinicopathological findings. J Clin Endocrinol Metab 1995; 80:2302-11. CrossRefMedline.
9. Melmed S, Casanueva FF, Hoffman AR, *et al.* Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. J ClinEndocrinolMetab. Feb 2011; 96(2):273-88. [Medline]
10. Di Sarno A, Landi ML, Cappabianca P, Di Salle F, Rossi FW, Pivonello R, *et al.* Resistance to cabergoline as compared with bromocriptine in hyperprolactinemia: prevalence, clinical definition and therapeutic strategy. J Clin Endocrinol

- Metab 2001; 86:5256-61.CrossRefMedline.
11. Webster J, Piscitelli G, Polli A, Ferrari CI, Ismail I, Scanlon MF, for the Cabergoline Comparative Study Group. A comparison of cabergoline and bromocriptine in the treatment of hyperprolactinemic amenorrhea. N Engl J Med 1994;331:904-909
 12. Molitch ME. Management of prolactinomas during pregnancy. J Reprod Med 1999; 44:1121-6.Medline.
 13. Passos VQ, Souza JJ, Musolino NR, Bronstein MD. Long-term follow-up of prolactinomas: normoprolactinemia after bromocriptine withdrawal. J Clin Endocrinol Metab 2002; 87:3578-82.CrossRefMedline.