

Vision Disturbances in Pituitary Prolactinomas: A Clinical Case Study

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ABSTRACT

A pituitary prolactinoma is a benign tumour of the pituitary gland that causes excess production of prolactin, the hormone normally responsible for the formation of milk during pregnancy. It is the commonest type of pituitary tumour and is most prevalent in females under the age of 40.

Considering the close proximity of the optic nerves to the pituitary gland, it is imperative that patients diagnosed with this condition undergo regular ophthalmologic examinations, including perimetry, to monitor any potential changes. The visual field defect commonly seen in patients with pituitary tumours is a superotemporal quadrantanopia as the inferonasal fibres are affected. Bitemporal hemianopias are also commonly seen. Aside from the visual disturbances

associated with pituitary prolactinomas, affected individuals can also experience infertility, low bone density and hypopituitarism.

A case study of an 18 year old woman diagnosed with a pituitary prolactinoma who interestingly also became pregnant will be presented. It is well documented that women with prolactin-secreting tumours can experience further pituitary enlargement than what is expected in a healthy pregnant woman. The progress of this case was closely examined with MRI scans and perimetry, all of which will be presented.

Keywords: pituitary gland, prolactinoma, pregnancy, quadrantanopia, Bromocriptine.

INTRODUCTION

The pituitary gland is a small, bean-shaped gland that is situated at the base of the brain, sitting inside the sella turcica. As part of the endocrine system, its role as the '*master gland*' involves the regulation of growth, development, reproduction and metabolism¹. A pituitary prolactinoma is the most common type of hormone-secreting pituitary tumour that occurs mostly in women under the age of 40. It is a benign tumour that produces the hormone prolactin². They are clinically classified according to their size: microadenomas do not exceed 10mm in diameter whereas macroadenomas measure greater than or equal to 11mm in diameter². The association between a pituitary prolactinoma and ophthalmology lies in the proximity of the pituitary gland to the optic nerves. The optic nerves, chiasm and optic tracts sit directly above the pituitary gland and therefore suprasellar extension of the gland can cause compression leading to visual disturbances³. When the tumour size reaches 10mm or

more, it can impinge on the optic chiasm, located 8-13mm above the pituitary gland. The chiasm can either lie directly above the sella (80% of cases)⁴, or alternatively, it can be pre fixed, where the chiasm is anterior over the tuberculum sellae (10% of cases). Alternatively, a post-fixed chiasm is situated posteriorly over the dorsum sellae (10% of cases)⁵, thus causing altered positioning of the tracts and nerves. The chiasmatic impingement causes the hallmark superior bitemporal quadrantanopia or hemianopia, and in the case of a hemianopia, with increased superior density, as the infero-nasal fibres are primarily damaged. These infero-nasal fibres are most susceptible to damage from growing tumours, as they cross low and anteriorly⁵. The tumour growth is normally asymmetrical, so the field loss between the two eyes is also asymmetrical⁶. The retinal topography at the anterior of the chiasm involves the separation of crossed and uncrossed retinal fibres. Inferior crossed fibres decussate and move anteriorly into the opposite optic nerve, then move posteriorly into the optic tract⁵, superior crossing fibres decussate and enter the contralateral optic tract via the superomedial ipsilateral optic tract, whereas uncrossed temporal fibres remain lateral in the chiasm. Nasal macular

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fibres, on the other hand, cross the chiasm mainly central and posteriorly⁵.

Several different visual field defects can arise due to compression of the optic chiasm (Table 1). These include nasal loss, where the temporal retinal fibres are compressed, and temporal field defects due to medial compression of the nasal retinal fibres⁵. Arcuate defects are due to vascular changes in the optic nerve⁷. A unilateral hemianopic defect manifests due to a lesion occurring at the junction of the optic nerve and chiasm, where the crossed and uncrossed retinal nerve fibres separate. Therefore, a lesion at the location of the crossed and uncrossed fibres would cause such a defect⁸. A junctional scotoma is a rarely documented field defect, and is described as an early-stage feature of compression of the chiasm⁵, and finally, a paracentral scotoma located superior and temporally, may be a very early indicator of a tumour that involves the nasal retinal fibres, which just extends to the chiasm⁵. Vascular compromise can also occur at the diaphragmatic sellae, causing tumour ischemia. This ischaemia can then result in necrosis and haemorrhage. This vascular compromise may lead to a quickly expanding sellar mass which in turn causes optic nerve compression, headaches, and meningeal irritation on occasion⁴.

The signs and symptoms that manifest with a prolactinoma arise due to hyperprolactinaemia (excess prolactin levels in the blood) or from compression, if the tumour is large¹⁷. The elevated prolactin levels affect the reproductive system; hence the symptoms may vary between genders. Females can experience irregular or lack of menstrual cycle and possible galactorrhoea, whereas males can experience impotence and loss of body hair. Both genders can experience headaches, infertility, low bone density and visual disturbances. Whilst prolactinomas can cause an increase in pituitary volume and increased secretion of prolactin, pregnancy can further exacerbate a prolactinoma. During pregnancy, prolactin-secreting lactographs that normally constitute 20% of all pituitary cells in nulliparous women (and in men), increase to 50% of all pituitary cells at the end of pregnancy. Radiologically, the pituitary gland develops an upward convexity of the superior surface^{2, 12}. Consequently, the pituitary gland increases in weight and size by 35% and 50-70% respectively, owing to the increased number of lactographs². Hence, if a woman presents to her doctor

with unexplained galactorrhoea, irregular menstrual cycle or infertility, prolactin levels in the blood must be tested. A case study, exhibiting some of these characteristics will be presented.

CASE STUDY

An 18 year old woman presented to her doctor with galactorrhoea. Her blood test indicated prolactin levels of 2927ug/mL; normal prolactin levels range from 60-480ug/mL¹³. High prolactin levels are expected in pregnant women; however the patient was not pregnant. These levels were therefore considered suspicious and thought indicative of a pituitary prolactinoma. The patient underwent a cranial Magnetic Resonance Imaging (MRI) as the diagnosis of a prolactinoma is confirmed by the presence of hyperprolactinaemia and a positive MRI scan². The radiology report of the most recent MRI scan (Figure 1) read as follows:

'The lesion is again identified in the dorsum sella on the left side. It measures 1x1x1cm in size. On measuring the adenoma on the previous scan 6 months earlier, the dimensions of the lesion are entirely unchanged. The chiasm is just contacted by the upper surface of the gland but there is no evidence to suggest compression. The cavernous sinuses are clear bilaterally.'

This patient's prolactinoma was classified as a microprolactinoma as it measured 1cm in size. Her complete diagnosis was a Left Pituitary Microprolactinoma producing galactorrhoea with hyperprolactinaemia. Bromocriptine was prescribed as part of treatment.

Soon after being prescribed Bromocriptine, the patient returned to her endocrinologist as she had since become pregnant. She was advised to discontinue Bromocriptine therapy and attend for regular check-ups and visual field testing. Her ophthalmologic testing revealed normal visual acuities of 6/5 and 6/4 of the right and left eye respectively, normal pupil reactions and intraocular pressures of 16mmHg in both eyes. Her cup to disc ratios were normal and she did not exhibit any pallor or swelling. Her initial visual fields, as measured on the Humphrey Visual Field Analyser, using

Field Defect	Cause
Nasal defect	Temporal retinal fibres are compressed
Temporal defect	Medial compression of the nasal retinal fibres
Arcuate scotoma	Vascular changes in the optic nerve
Unilateral hemianopia	Lesion at the junction of the optic nerve and chiasm
Junctional scotoma	Early-stage feature of compression of the chiasm
Paracentral scotoma located superior and temporally	Early indicator of a tumour involving the nasal retinal fibres, which just extends to the chiasm.

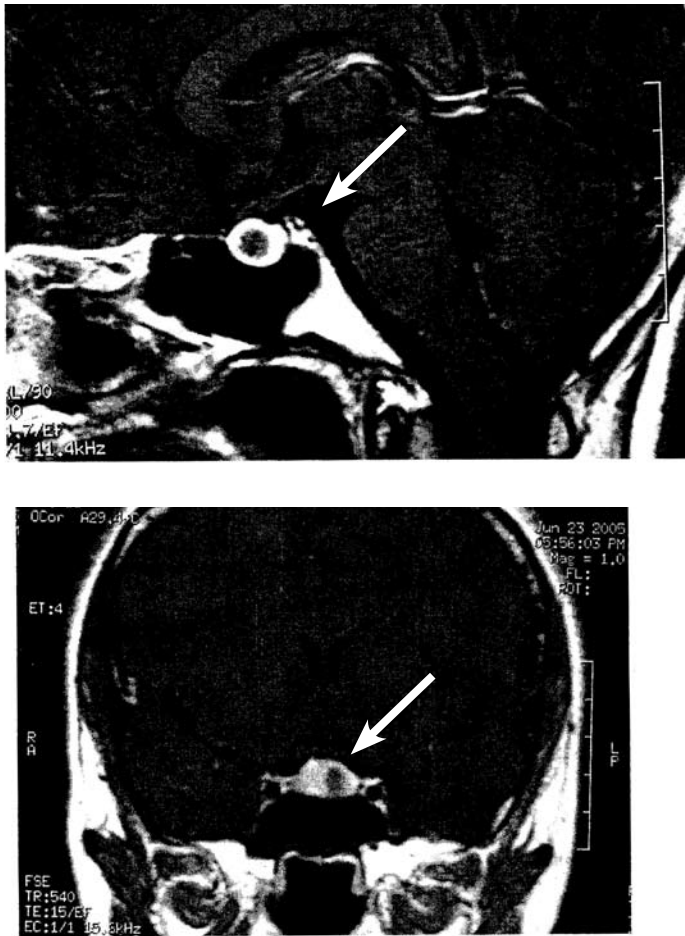


Figure 1. MRI scans depicting this patient's 1x1x1cm microprolactinoma.

a central 24-2 threshold test, were unremarkable and both were within normal limits (Figure 2). However, 6 weeks later some changes were detected in both eyes using a central 30-2 threshold test (Figure 3). Each eye exhibited an additional 6 defects as noted on the pattern deviation, which adjusts for increases or decreases in the patient's hill of vision. All field changes were localized to the superior temporal quadrant of each eye. While there were changes evident on the visual fields, her vision remained unchanged. As there were visual field changes, it was essential to monitor this patient throughout her pregnancy to observe the tumour size and her visual fields. However, this patient was lost to follow-up as she failed to attend her follow-up appointments.

DISCUSSION

Given the stimulatory effects of pregnancy on the lactographs, symptomatic enlargement of the pituitary gland can be expected. However, the number of tumours that actually do expand is very small. The risk of clinically significant enlargement for pregnant women with microprolactinomas is 1.3%¹². The risk of enlargement

for women with untreated macroprolactinomas is 23.2%, whereas a treated macroprolactinoma has a 2.8% risk of clinically significant enlargement¹². Similarly, Randeve et al.² reported the risk of clinically significant enlargement for women with macroprolactinomas during pregnancy as being between 15.5-35.7%.

Chiasmatal compression can also be linked with other visual symptoms, including cranial nerve palsies, post fixational blindness, hemifield slide and see saw nystagmus⁵. Cranial nerve palsies can include the third, fourth or sixth cranial nerves and can result in involvement of the extraocular muscles, hence causing a strabismus and possible diplopic symptoms⁵. These type of palsies occur when there is involvement of the 'cavernous sinus by lateral extension of a pituitary tumour'¹⁴. The hemifield slide phenomenon may be responsible for horizontal or vertical diplopia in cases where there is no obvious muscle palsy or cranial nerve paresis⁵. This phenomenon may result in problems relating to fusion¹⁵ due to the development of a bitemporal hemianopia. Post-fixational blindness is another symptom relating to chiasmatal compression. When a patient with a bitemporal hemianopia fixates a near object, a totally blind area is produced because the two blind temporal fields cross over⁵. See-saw nystagmus occurs due to the close proximity of the structures responsible for see-saw nystagmus to the chiasm⁵.

The aims of treatment for prolactinomas encompass 4 areas: to reduce the tumour size, to restore prolactin levels in the blood to normal, to correct any visual problems and to restore normal pituitary functioning¹⁷. A dopamine agonist, Bromocriptine, can be used to treat the prolactinoma, as it is the chemical that normally inhibits prolactin secretion. Bromocriptine can shrink the tumour and restore prolactin levels in 90% of cases¹². The discontinuation of Bromocriptine in this case was because of two key issues that must be addressed when a woman with a prolactinoma becomes pregnant: the negative effects of dopamine agonists on early foetal development before a pregnancy is diagnosed, and the effects of a pregnancy on the size of the prolactinoma. After pregnancy has been confirmed, the dopamine agonist should be withdrawn and the patient must be closely monitored for tumour expansion¹⁶. In over 6000 pregnancies, Bromocriptine has not been shown to increase the number of spontaneous abortions or congenital malformations^{2, 12}. However, while the above evidence suggests that Bromocriptine is safe during pregnancy, it is advised that exposure of the foetus to such a dopamine agonist should be limited¹². If there is suspicion of tumour expansion, this can be investigated through an MRI scan after four months gestation and visual field testing¹⁶. Visual field testing is hence an integral part of monitoring change. Randeve et al.² has also commented that with microprolactinomas, most endocrinologists recommend visual field assessment in each trimester of pregnancy and expectant patients are urged to report any visual symptoms or headaches.

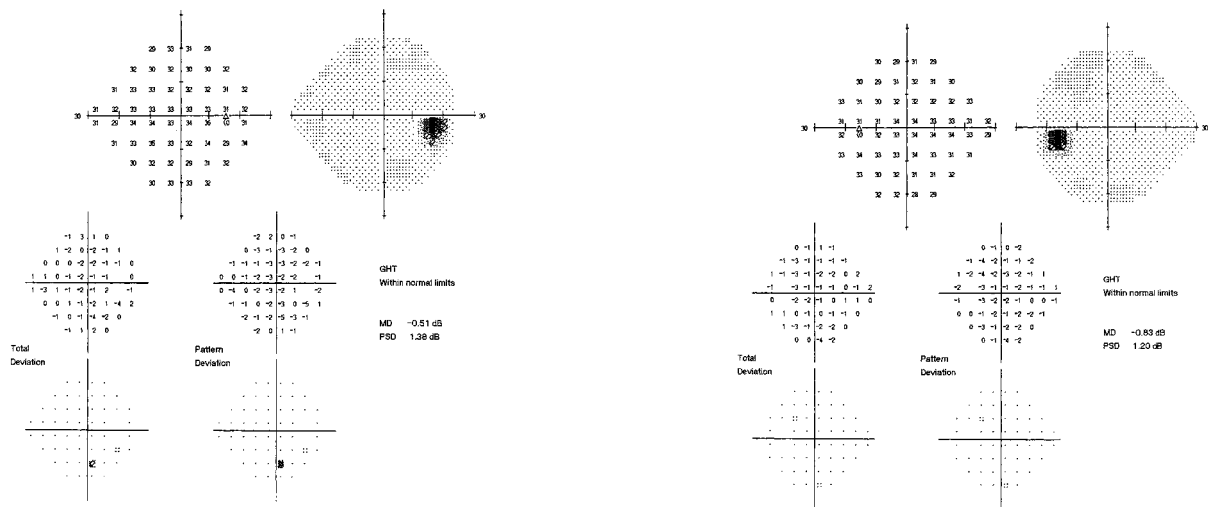


Figure 2. Humphrey Visual Field assessment (24-2) on the first visit.

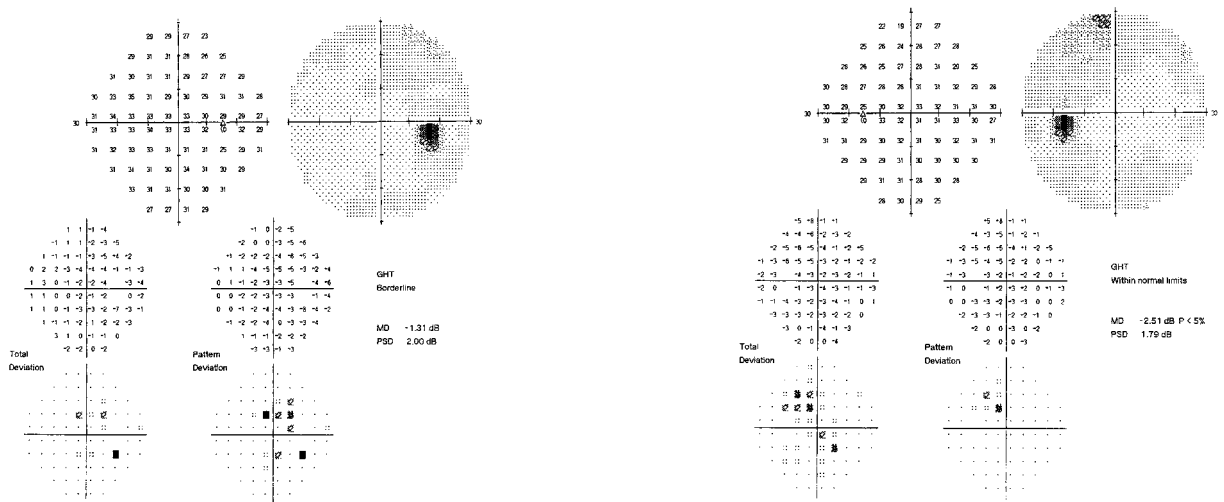


Figure 3. Humphrey Visual Field assessment (30-2) performed 6 weeks later.

Due to the increase in prolactin levels during pregnancy, regular monitoring of prolactin levels in the blood is of no use². A study investigating prolactinomas and optic nerve compression found that a participant with a prolactinoma, who had been experiencing visual disturbances for 8 months, underwent Bromocriptine treatment, and within two weeks had complete recovery of their visual fields and an acute fall in their prolactin levels. Additionally, on CT scans, the suprasellar extension had disappeared. On the other hand, the same study reported another participant who had a two year history with no visual improvement after one year of treatment. However, the CT scan revealed no suprasellar extension when repeated after three months¹⁷. Hence, the researchers concluded that Bromocriptine is capable of tumour shrinkage and can replace surgical intervention in certain patients.

A study by Kupersmith, Rosenberg, & Kleinberg¹⁸ examined the potential risk for developing visual loss during pregnancy in women with pituitary adenomas. The researchers recruited 65 women with pituitary adenomas who had not been treated with surgery. They were all monitored during their pregnancies and all had their prolactin levels measured. Sixty of 65 women had elevated prolactin levels. In measuring tumour size, 57 patients had tumours of greater than 0.3cm. The remaining eight patients had macroadenomas greater than 1.1cm. Visual loss was experienced by six out of these eight participants. In eight eyes of these six patients, there were incomplete superior temporal quadrantanopias. In three eyes of three patients there were complete superior temporal quadrantanopias. Therefore, these results indicate that those patients with pituitary adenomas of 1.2cm or greater are at a greater risk of developing visual loss during

pregnancy than those patients who had microadenomas. It is important to note that all of the women in this study with visual field loss had adenomas of 1.2cm or more. A study by Gemzell & Wang¹⁹ also reviewed tumour size and symptoms in 217 pregnancies in 187 women with prolactinomas. Microprolactinomas without surgical intervention were seen in 91 pregnancies in 85 women. Systematic tumour enlargement was seen in 5 pregnancies (5.5%), and these manifested as headaches or visual disturbances. Untreated macroprolactinomas were seen in 56 pregnancies of 46 women, and 20 of these pregnancies (35.7%) had severe headaches or vision impairment.

CONCLUSION

The clinical history presented in this paper indicates that whilst the patient was diagnosed with a microprolactinoma, she was asymptomatic to any visual disturbances during her pregnancy. However, she constitutes the small minority of women with microprolactinomas that do demonstrate visual field changes. Unfortunately, her visual progress could not be followed-up as she had not undergone any additional visual field tests because of failure to attend subsequent appointments. However, this case study demonstrates the need to adhere to strict visual field monitoring of pregnant women with pituitary prolactinomas.

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