

Light up the Future – a New Paradigm: Photobiomodulation as a Non-Surgical Cancer Treatment Modality: a Case Report

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Abstract

Non Functioning Pituitary Macroadenoma (NFPA) comprise about 80% of all pituitary macroadenomas. NFPA are frequently found incidentally during imaging studies performed for unrelated reasons. Photobiomodulation (PBM) is a non-invasive technique that uses certain wavelengths of light to restore, repair, and protect tissue that is either injured, degenerating, or at risk of dying. It has the ability to promote the body's own immune responses and are able to penetrate into the cells, tissues, blood, nerves, the brain, and into the bones. Perhaps besides radical surgical approach, we could explore adjuvant methods of treatments to complement this. In conclusion, PBM might be introduced as an adjunct treatment option for patients with brain tumour, non-operable brain lesions or those who declined radical surgery and opted for active surveillance. This case report highlights photobiomodulation antitumorigenesis effects in reduction of pituitary tumour volume.

Keywords: Non-functioning Pituitary Macroadenoma (NFPA), Prolactin, Transsphenoidal Surgery, Photobiomodulation

Background

Non Functioning Pituitary Macroadenoma (NFPA) comprises about 80 % of all pituitary macroadenomas. It is likely there are many in the population with undetected macro adenomas [1]. NFPA are frequently found incidentally during imaging studies performed for unrelated reasons [2]. Photobiomodulation (PBM), also known as Red Light Therapy is a natural, non-invasive technique that uses certain wavelengths of light to restore, repair, and protect tissue that is either injured, degenerating, or at risk of dying. It has the ability to promote the body's own immune responses. It is a safe and effective procedure that uses red light-emitting diodes (LED's) which diffuse wavelengths through a person's skin [3].

Red light and near-infrared light are able to reach deep into the human body (several centimeters, and close to 2 inches, in some cases) and are able to penetrate into the cells, tissues, blood, nerves, the brain, and into the bones [3]. This case report highlighted a procedure that initially meant for whitening and skin rejuvenation treatments through photobiomodulation, turned out to have a beneficial effect in reduction of pituitary tumour volume.

Case Presentation

A 44-year-old lady who visited the hospital with a head injury after motorvehicle accident in May 2017, was referred to the neurosurgical department because of an abnormality incidentally detected by magnetic resonance imaging (MRI). The patient reported chronic intermittent headache. No visual loss or double vision. General

examination was found to be normal. No thyroid enlargement was found. Ocular examination revealed that visual acuity in both eye was 6/6 respectively. Extraocular movements were of full range. Fundus examination was within normal limits. There was no mass palpable in the orbit or no bruit. She denied taking any medications and supplements, no history of trauma, no loss of weight or weight gain, normal menstrual period and normal sleep pattern.

An initial MRI Brain (14/5/17) detected a pituitary mass measuring 1.6 cm x 1.9 cm x 2.0 cm (volume ~25.5 cm³, $V = (4/3)\pi r^3$). Hormonal assay was carried out. Initial blood test (14/5/17) revealed Prolactin 41.9 ng/mL (~ 891.48 mIU/L), FT4 11.3 pmol/L, TSH 0.58 uIU/mL, Cortisol 14.2 ug/dL. On the basis of clinical examination and investigations, a clinical diagnosis of pituitary macroadenoma was made. Neurosurgical department was consulted, she was suggested for transsphenoidal surgery with adenoma removal since its advantages are being less invasive and no visible scarring, but the patient is not keen and she felt her intermittent headache is bearable. She opted for active surveillance instead. Repeated MRI brain and pituitary gland was performed 6 months later (7/11/17) showed enhancing rounded midline pituitary tumour, no significant interval changes seen measuring 1.6 cm x 1.9 cm x 2.0 cm compared to previous MRI. The mass is seen abutting on the adjacent right internal carotid artery. No sellar floor erosion. The pituitary tumour impinges on the optic chiasma. She was advised for close ophthalmological and radiographic monitoring with repeated MRI 6 months later.

MRI brain and pituitary gland imaging was repeated on 9/7/18 and showed a reduction in the size of the pituitary macroadenoma measuring 1.5 cm x 1.2 cm x 1.8 cm (volume ~ 13.6 cm³, $V = (4/3)\pi r^3$). Lesion is

isotense to grey matter in T1/T2 and does not contain any significant area of cystic transformation, haemorrhage or necrosis. Possibility of meningioma, craniopharyngioma, or metastasis is unlikely. Repeated Prolactin level (20/8/18) revealed 782.3 mIU/L, creatinine 0.071 mmol/L, Potassium 4.5 mmol/L, Sodium 143 mmol/L. Both doctor and patient herself were surprised of repeated MRI results. Patient recalled that on April 2018, she underwent a trial program of photobiomodulation application lasted for 3 months, thrice a week, with each session lasting 25 minutes, with wavelength 660-670 nm, and intensity is 40 Joule/cm². During those time period she followed usual diet, normal activities, and did not take any medications. As there are no others reason could explain the reduction of pituitary volume, possibility of photobiomodulation application beneficial effect was considered. Currently patient is well, asymptomatic and under ophthalmological and radiographic monitoring 6 monthly.

Discussion

Pituitary tumours can be classified by size or by function. The best current diagnostic imaging method for evaluating pituitary adenomas is MRI. Size, as determined by MRI, less than 1 cm in diameter is considered a microadenoma and those tumours greater than 1 cm in diameter are considered a macroadenoma. Function is described by the detectable increase of a pituitary hormone through blood tests. Therefore, if no hormones were manufactured, the tumour is defined nonfunctioning. Non Functioning Pituitary Macroadenoma (NFPA) comprise about 80 % of all pituitary macroadenomas. It is likely there are many in the population with undetected macroadenomas [1]. NFPA are frequently found incidentally during imaging studies performed for unrelated reasons [2].

In this case, patient was middle age women who was incidentally found out to have pituitary macroadenoma on her MRI Brain measuring 1.6 cm x 1.9 cm x 2.0 cm (6.08 cm³). She denied any visual loss or double vision. Visual acuity in both eye was 6/6 respectively. She denied taking any medications and supplements. A clinical diagnosis of pituitary macroadenoma was made. Hyperprolactinemia at level less than 150 ng/ml does not indicate tumoral prolactin production. Instead it may be the result of stalk section effect. Macroadenomas often produce stalk effect, in which mild to moderate elevations of prolactin (PRL) hormone result from stalk compression caused by growing tumor mass. This mass blocks the transport of dopamine and thus releases the anterior pituitary from the inhibitory control by the hypothalamus [4]. In this case, initial prolactin level 41.9 ng/mL (~ 891.48 mIU/L) was mildly increased, but it is most likely due to the tumour stalk effect. FT4, TSH, Cortisol level was within normal limits. Other hormonal assay were not tested as patient did not showed any symptoms. Since patient does not produce a hormonal hypersecretion syndrome, she was considered Non Functioning Pituitary Macroadenoma (NFPA).

NFPAs that touch the optic apparatus, without visual dysfunction, may be followed with close ophthalmological and radiographic monitoring, pending tumour and imaging characteristics. Pharmacological treatment of the NFPA tumour itself is typically unsuccessful. Surgery should be contemplated for those patients with concerning tumour growth, loss of endocrinological function, a lesion close to the optic chiasm, a desire to become pregnant, or unremitting unspecified headaches. For those adenomas larger than 1 cm (the majority), after excluding hormone deficiencies, it is common to proceed to surgical management. These macroadenomas more commonly exert pressure effects [1].

As the tumour enlarges it pushes up on the chiasm and stretches it upward. Four to six millimetres of chiasmal elevation is needed to produce visual field defects. A more detailed study found that 6.3 mm of chiasmal elevation was required to induce visual field defects in 50 per cent of patients and an additional 5.0 mm is needed to increase the frequency to 90 per cent [5]. In this case, although the MRI showed the pituitary tumour impinges on the optic chiasma, but patient did not show any visual defects. Patient was suggested for transsphenoidal surgery with adenoma removal, due to concern of tumour growth and a lesion impinges on the optic chiasma, but she refused. Ophthalmological and radiographic monitoring were then carried out.

Spontaneous regression of pituitary adenoma is frequently reported; however, the mechanism underlying this phenomenon is unclear. Many of these reports describe cases of functional pituitary adenoma. In contrast, spontaneous regression is rare in cases of nonfunctioning pituitary adenoma [6]. Dekker et al. reported spontaneous regression of tumor volume in 34 out of 304 patients (11%). Seven cases of spontaneous regression of nonfunctioning adenoma have been previously reported. The average age of these patients was 48 years. Four of the patients were female. In 4 cases (57.1%), tumor regression was caused by pituitary apoplexy (PA). In one case of asymptomatic nonfunctioning adenoma, spontaneous intratumoral haemorrhage resulted in tumor regression [6].

In this case, the first MRI done in May 2017 and second MRI done 6 month later in November 2017 showed no significant interval changes seen measuring 1.6 cm x 1.9 cm x 2.0 cm (volume ~25.5 cm³). But repeated MRI in August 2018 showed a significant reduction in the size of the pituitary macro adenoma measuring 1.5 cm x 1.2 cm x 1.8 cm (volume ~ 13.6 cm³), lesion is isotense to grey matter in T1/T2 and does not contain any significant area of cystic transformation, haemorrhage or necrosis. Instead of worsening tumour growth, last MRI showed reduction in size. Patient recalled that last 3 months, she joined a trial program for whitening and skin rejuvenation treatments through photobiomodulation application, thrice a week, with each session lasting 15 minute, with wavelength 660-670 nm, and intensity is 40 Joule/cm². During those time period, she followed usual diet, normal activities, and did not take any medications. Patient did not show any symptoms and MRI did not show any haemorrhage or necrosis, therefore pituitary apoplexy and intratumoral haemorrhage were unlikely. As there are no others reason could explain the reduction of pituitary volume, possibility of photobiomodulation application beneficial effect was considered.

This case report highlighted a procedure that initially meant for whitening and skin rejuvenation treatments through photobiomodulation, turned out to have a beneficial effect in reduction pituitary tumour volume.

Conclusions

NFPAs without any visual dysfunction, need close ophthalmological and radiographic monitoring. Pharmacological treatment of the NFPA tumour itself is typically unsuccessful. Surgery should be contemplated for those patients with concerning tumour growth, loss of endocrinological function, a lesion close to the optic chiasm, a desire to become pregnant or unremitting headaches. Spontaneous regression of pituitary adenoma is frequently reported; however, the mechanism underlying this phenomenon is unclear.

Photobiomodulation (PBM), also known as Red Light Therapy is a non-invasive technique that uses certain wavelengths of light to restore, repair, and protect tissue that is injured, degenerating, or at risk of dying and are able to penetrate into the cells, tissues, blood, nerves, the brain, and the bones. Photobiomodulation application may be an adjuvant application modality which may be considered in patient with pituitary macroadenoma who refuse or is not suitable for transsphenoidal surgery and opted for active surveillance [7-22].

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