Luteinizing Hormone-Releasing Hormone Analogue-Induced Cataract in a Patient with Prostate Cancer

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Key Words

Prostate cancer • Luteinizing hormone-releasing hormone analogue • Cataract

Abstract

Objective: To report a case of right posterior subcapsular cataract induced by 3-monthly depot luteinizing hormone-releasing hormone (LHRH) analogue therapy in a patient with early prostate cancer. **Case Presentation:** A 52-year-old male with static myopia of several years' duration was given a 3-month depot LHRH analogue (goserelin 10.8 mg) as part of neoadjuvant treatment for early prostate cancer. Four weeks after the treatment, the patient developed right posterior subcapsular cataract commonly associated with steroid treatment. The patient had right eye cataract extraction followed by insertion of a new lens. **Conclusion:** This report shows a case of a posterior subcapsular cataract as an adverse reaction to depot goserelin acetate. This is a feature commonly seen in steroid-induced cataract. Patients with prostate cancer and poor vision if due to cataract may not be ideal patients for depot preparations of LHRH analogues.

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Introduction

Luteinizing hormone-releasing hormone (LHRH) analogues have been the mainstay of advanced and metastatic prostate cancer therapy. These classes of drugs are also used as part of neoadjuvant treatment of early prostate cancer and effective for treating breast cancer in premenopausal women [1–3]. Early therapies consisted of daily injections of synthetic LHRH analogues (e.g. leuprolide, goserelin, etc.). In recent years depot formulations which are given as 1-, 3-, 4- or 12-monthly injections have been developed [3]. Complications associated with LHRH analogue are mild and include hot flushes in both sexes, amenorrhoea and vaginal dryness in women, osteoporosis and testicular atrophy in men [1, 2]. Serious complications have rarely been reported particularly with the longer depot preparations. We report a 52-year-old cytopathologist who had no ocular complications while on the monthly depot LHRH analogue injections but developed disabling cataract when he was given the 3-monthly depot preparation.

Case Report

A 52-year-old cytopathologist presented with low back and right hip pain of 6 months' duration. The pain was associated with bilateral lower limb paraesthesia. Apart from mild reduction in urinary stream, he had no other urinary symptoms. The patient is an asthmatic and had previously been treated for bacterial prostatitis. He has a history of allergic reaction to sea food. He also has history of long-term myopia affecting both eyes for which he wears corrective glasses. This short-sightedness has remained static for several years. The patient has a family history of prostate cancer, his father having been diagnosed with the disease at the age of 80 years. There was also a history of myopia affecting several members of his family. Rectal examination revealed a 30-gram firm to hard prostate gland.

Haematological and biochemical investigations were all normal. Initially his serum total prostate-specific antigen (PSA) was 16 ng/ml (normal 1–4 ng/ml), but increased to 31.9 ng/ml after 3 months. Transrectal ultrasound (TRUS) of the prostate and needle biopsy were performed. TRUS demonstrated a prostate volume of 12 ml with focal calcification and mixed echogenicity in the peripheral zone of the left lobe. The capsule was intact. Histopathology revealed well-differentiated adenocarcinoma of the prostate with a Gleason score of 3.

Following a thorough discussion of different treatment modalities with the patient, he opted for radiotherapy and neoadjuvant hormone manipulation. He was commenced on flutamide 250 mg 3 times a day followed 2 weeks later by a single-dose subcutaneous (s.c.) injection of Zoladex 3.6 mg monthly. He was also commenced on conformal external beam radiotherapy to the prostate gland. He had a total of 6 weeks of radiotherapy. The patient had no substantial side effects during the treatment apart from gynaecomastia with a troublesome dysuria and occasional haematuria which eventually subsided. Serum PSA fell to 1.1 ng/ml within 3 months of commencing treatment. He was maintained on monthly injections of Zoladex (3.6 mg/month s.c.) and remained in good health. This was changed to a 3-month depot long-acting Zoladex 10.8 mg s.c. injection to allow him to take a 3-month vacation abroad. Four weeks after administration of depot Zoladex, he noticed poor vision in the right eye in the form of complete white-out appearance and haziness. He was seen urgently by an ophthalmologist and slit lamp examination revealed right posterior subcapsular cataract resembling a steroid-induced cataract. The left eye was normal on slit lamp examination. He underwent cataract surgery on the right eye in the form of phacoemulsification under local anaesthesia. A new lens was inserted into the right eye. The postoperative course was uneventful. He has regained almost total vision in the right eye 3 years after the cataract surgery. The patient is under regular follow-up. The disease remains in remission 4 years after the start of treatment with PSA of 1.1 ng/ml. The patient remains in good health and still works as a cytopathologist.

Discussion

LHRH analogues have been used in the treatment of prostate cancer for many years. Adverse reactions with LHRH analogues include hypo-oestrogenic side effects

such as hot flushes and bone loss along with reported cases of recurrent anaphylactic reaction following the use of leuprolide acetate (Lupron). In the United States clinical trials using goserelin acetate have been specifically associated with hot flushes and sweats in 98% of patients in one study [1], bone loss and bone pain, headaches, nausea, breast pain or swelling (especially in men being treated for prostate cancer), weight gain, muscle cramps, mild rash, local reaction at injection site, acne, oily hair and skin, emotional lability, depression, and reduction in libido [2–5]. There have also been reports of systemic hypersensitivity reaction to goserelin acetate [6].

Our patient developed cataract 4 weeks following the depot s.c. injection of (10.8 mg) LHRH analogue (Zoladex). Posterior subcapsular cataract is one of the most visually disabling types of cataract and accounts for a significant proportion of cataract extractions [7]. This form is commonly seen in steroid-induced cataract [7–9]. Limited evidence suggests that cataract regression may occur if therapy is stopped or the dose reduced. In our patient depot Zoladex was stopped, cataract surgery performed and the patient regained almost total vision in the right eye. Hence it is plausible to suggest that the 3-month depot Zoladex administration or the vehicle caused the right posterior subcapsular cataract. Therefore, we suggest that patients with poor vision should be informed about the possible cataractogenic effect of LHRH analogue especially when the use of the depot 3- to 12-monthly injection is being considered. Alternatively, since most men with advanced cancer are elderly, cataract should be excluded prior to the use of depot LHRH preparations. The reason for the link between steroid therapy or the use of depot LHRH analogue (as in our patient) and the formation of posterior subcapsular cataract deserves further elucidation.

Some of the side effects produced by LHRH analogues are secondary to the mechanism of action of the drug and/or its metabolites [4]. In humans, the administration of LHRH analogues results in an initial increase in circulating levels of luteinizing hormone and follicle-stimulating hormone, leading to a transient increase in the levels of gonadal steroids (testosterone and dihydrotestosterone in males and oestrone and oestradiol in premenopausal females) [4]. However, continuous administration of the drug results in decreased levels of luteinizing hormone and follicle-stimulating hormone. This results in reduction of testosterone levels to castrate levels in men. Reduction of testosterone to castrate level results in inhibition of growth of hormone-dependent tumours like prostate cancer. Fraunfelder et al. [9] were the first to doc-

ument that patients given the 4-weekly depot injection of leu-prolide acetate, an LHRH analogue, developed ocular side effects like blurred vision. This side effect was observed in some patients within 1–2 h of drug administration while it occurred in about 6 months in other patients [9]. It is possible that the patients who developed blurred vision about 6 months after commencing the 4-weekly injection of leuprolide acetate might have developed cataracts like our patient. Depot steroid therapy has also been associated with a higher incidence of ocular complications compared to non-depot preparations [10, 11]. Drug vehicle used in depot preparation has been implicated in the aetiology of ocular complications [10]. As our patient developed significant cataract within 4 weeks of being on the depot goserelin, it is possible that it was the vehicle used in the depot formulation of goserelin that produced the complication rather than the actual drug

itself. Lastly, there is a genetic predisposition to the development of steroid-induced cataract [11]. As our patient has a strong family history of diseases of the eyes, his genetic make might also have contributed to the development of this complication. The mechanisms involved in the ocular complications of LHRH analogues warrant further study to make this class of drugs safer.

Conclusion

This report shows a case of a posterior subcapsular cataract as an adverse reaction to depot goserelin acetate. This is a feature commonly seen in steroid-induced cataract. Patients with prostate cancer and poor vision if due to cataract may not be ideal patients for depot preparations of LHRH analogues.

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