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A blind spot in urology: Prostate cancer associated retinopathy

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ABSTRACT

Paraneoplastic syndromes associated with prostate cancer that cause visual disturbances are rare. We present the case of a 71 year old man with a history of adenocarcinoma of the prostate who developed cancer associated retinopathy concomitant with small cell transformation. This represents an unusual paraneoplastic syndrome that may be progressive and irreversible, requiring prompt diagnosis and treatment to preserve visual function and guide further oncological care.

Introduction

Paraneoplastic syndromes affecting the visual and nervous systems are rare, and occur in approximately 0.01% of patients with cancer.[1] Paraneoplastic syndromes may be the cause of the initial presentation (70%) or may indicate disease progression (20%) and are usually associated with aggressive tumours or occur in the late stages. Prostate cancer is the most common urological malignancy, and is the second most common urological malignancy to be associated with a paraneoplastic syndrome after renal cell carcinoma.[2] Cancer associated retinopathy is a rare paraneoplastic syndrome causing visual loss due to the molecular mimicry of retinal cells by homologous tumour cells. Over expression of retinal proteins such as recoverin, alpha–enolase and heat shock proteins on tumour cells leads to exposure of these proteins to antigen presenting cells. This leads to a production of auto-antibodies that bind to retinal cells, leading to apoptosis. This causes a variable progressive visual loss.[3]

Case presentation

A 71-year-old man diagnosed with Gleason 3 + 4(40%) = 7 prostate adenocarcinoma in June 2016 after investigation of an elevated PSA of 22 and a PIRADS 5 lesion on pre-biopsy magnetic resonance imaging (MRI). Initial treatment with androgen deprivation therapy (ADT) and external beam radiation therapy yielded a good response, with a PSA nadir of 0.96. The patient had no significant ocular history. Fifteen months later, over the course of six months, he noticed progressive visual loss in both eyes and difficulty adapting from light to dark. He was seen by an optometrist who diagnosed cataracts and was referred to an ophthalmologist (EZ). Ocular examination revealed best corrected visual acuity of 6/9 in each eye. Colour vision was impaired in both eyes. Pupil responses were normal. The anterior segments showed +1 anterior chamber cells and trace nuclear cataracts. There were +1 vitreous cells and the fundus appeared normal. An optical coherence tomography examination of the macula revealed widespread loss of outer retinal layers (Fig. 1) and a computerized visual field test showed bilaterally and severely constricted fields to a central 10° "tunnel" (Fig. 2). A full field electroretinogram showed bilateral severe reduction in both rod and cone responses. A diagnosis of carcinoma-associated retinopathy was suspected and a PSA test was ordered, showing a level of 10.9.

Re-biopsy of his prostate demonstrated small cell transformation. Treatment of the retinopathy with prednisolone 75mg was started, combined with Docetaxel. The latter was aborted following significant treatment-related toxicity events of febrile neutropenia and pulmonary embolus associated with the first cycle. However, significant subjective improvement of vision was demonstrated by a modest expansion of the visual field (Fig. 3). No changes were seen on the structural studies of the retina (optical coherence tomography). Prednisolone was weaned to 2.5mg and has been maintained at that level.

Discussion

Small cell prostate carcinoma (SCPC) is a rare subtype of prostate

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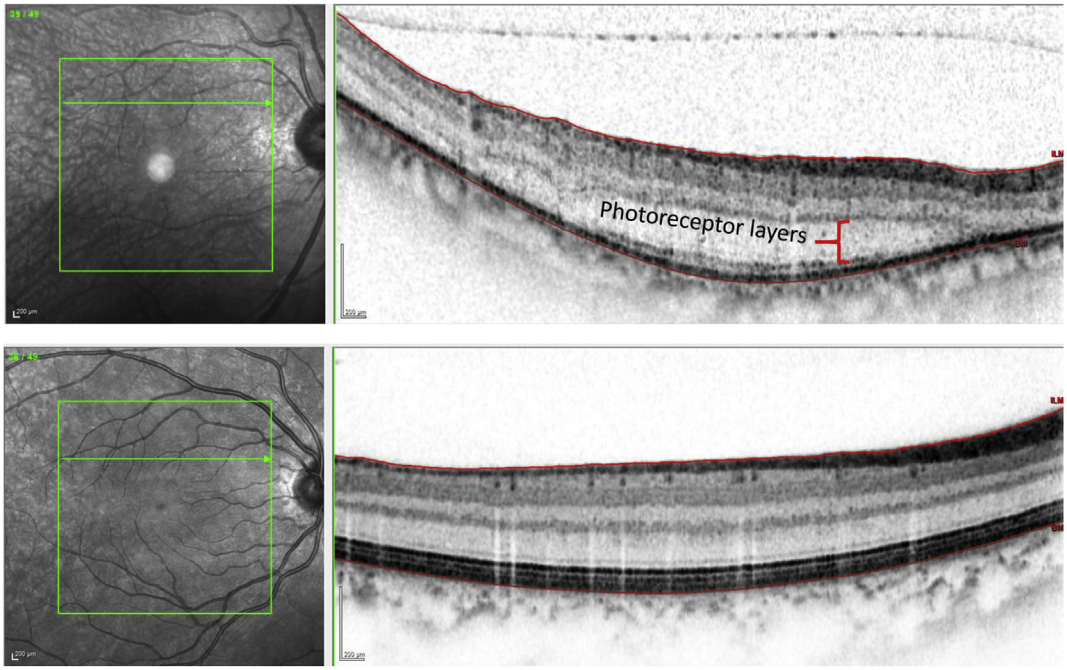

Fig. 1. Spectral domain optical coherence tomography (SD-OCT) cross sectional scan of the superior macula of the right retina on presentation. Top image is the patient's retinal scan. Bottom image is a corresponding cross section through a normal macula of a healthy person. Note relative preservation of the retinal photoreceptor layers centrally, but loss of these layers on both right and left sides of the cross section, also manifesting as thinning of the retina.

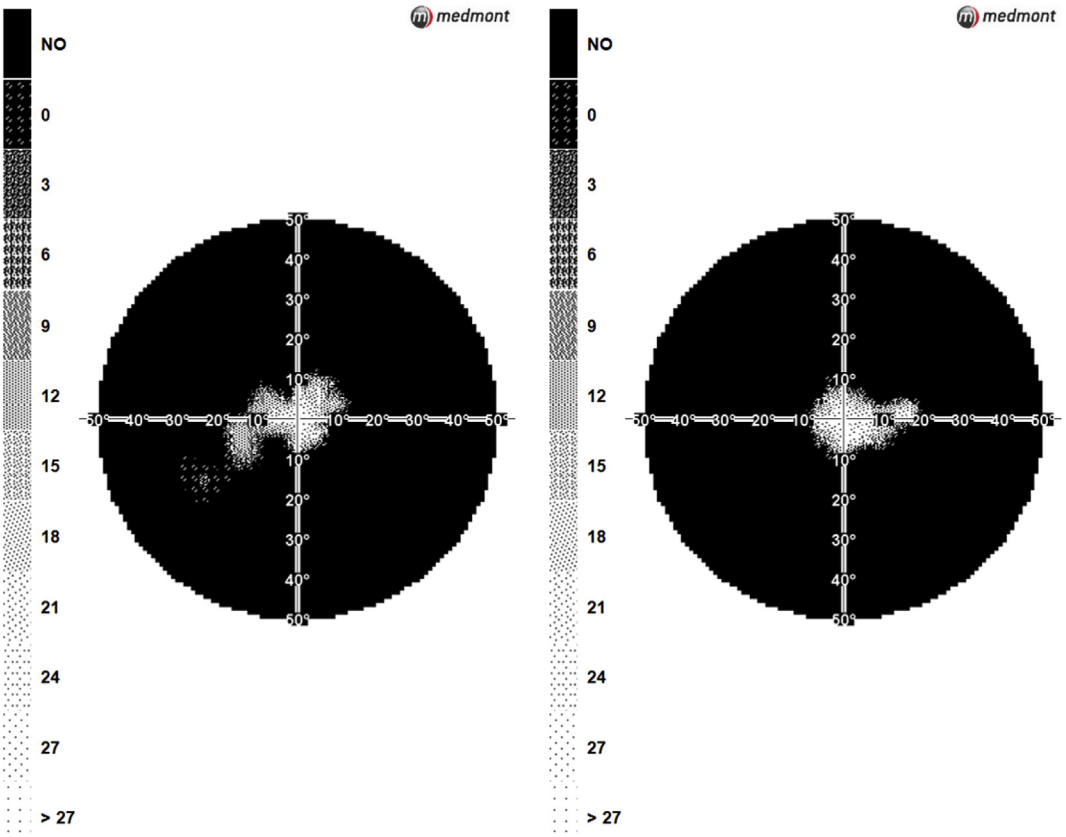

Fig. 2. Threshold computerized visual field test of each eye at presentation. Demonstrates severe constriction of the visual field to the central 10–20° approximately.

cancer occurring in < 2% of cases, with more than half associated with additional prostatic malignancies. A review by Ro et al.[4] demonstrated that diagnosis of SCPC may follow the diagnosis of adenocarcinoma in a large proportion of patients (45%) with a variable time course (median 18 months, range 7–96 months) though there was no difference in survival in between the groups that presented with SCPC and those who presented with adenocarcinoma initially, with a median survival of 10 months following diagnosis at this time. Metastatic disease is common

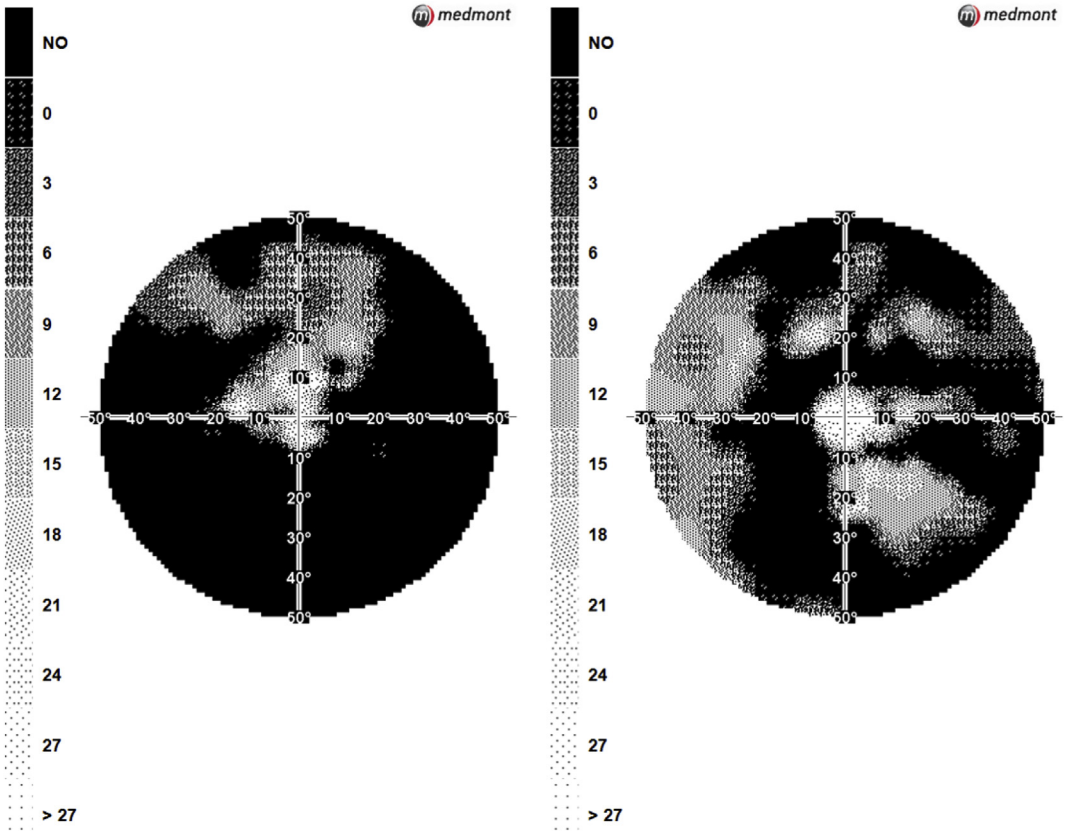

Fig. 3. Threshold computerized visual field test of each eye a month after commencing treatment Demonstrates significant improvement and expansion of the central "tube" of vision.

and occurs early and is associated with a poor prognosis. Moreover, Palmgren et al. suggested that the presence of paraneoplastic syndromes may be a poor prognostic factor[5]

SCPC is more likely to be associated with symptoms at the time of presentation than adenocarcinoma of the prostate, often voiding and obstructive symptoms.[5] Paraneoplastic syndromes occur more commonly with SCPC than with other types of prostate cancer. With adenocarcinoma of the prostate, however, paraneoplastic cancer-associated retinopathy remains very rare, with less than 10 cases reported in the literature.[2,3]

Furthermore, though rare, development of a paraneoplastic syndrome may be the earliest signal that disease progression or transformation has occurred, as was the case in our patient. A level of suspicion is required for early detection of seemingly unrelated symptom which may be easily missed by the urologist in context of routine surveillance.

Unlike many other paraneoplastic syndromes, cancer-associated retinopathy and associated conditions involving the optic nerve and retina may not resolve with treatment of the underlying malignancy, and irreversible or progressive visual loss may persist. The nature of prostate cancer treatment with ongoing review and surveillance of PSA in all treatment groups means the urologist is often seeing these patients more regularly than other physicians. As such, urologists are well positioned to be the first opportunity to detect the development of these rare syndromes.

Conclusion

This case adds to the small number of reported cases in the literature of visual paraneoplastic syndrome associated with prostate cancer. Auto-antibody mediated cancer associated retinopathy is a rare, but potentially irreversible. Early detection, diagnosis and treatment are crucial in reducing visual loss. In addition, development of paraneoplastic syndromes may indicate significant progression of disease and must not be ignored.

Conflicts of interest

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

Informed consent

This case report has been described with the full and complete informed consent of the patient.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eucr.2019.100872.

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