Oncology

Robotic radical prostatectomy in a patient with prostate cancer and MERRF syndrome, a rare mitochondrial disorder affecting muscle fibers

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Introduction

Myoclonus epilepsy ragged-red fiber (MERRF) syndrome is a very rare mitochondrial encephalomyopathy characterized by varying degrees of muscle twitching and weakness, progressive spasticity, and exercise intolerance. Although the syndrome is not accompanied by bowel or bladder symptoms, in many patients it may be characterized by peripheral neuropathy and muscle weakness which worsens during the day.

In the event a patient with MERRF syndrome would be diagnosed with prostate cancer, the choice of treatment could be difficult since theoretically its associated myopathy might impact the recovery of continence if radical prostatectomy is undertaken and radiotherapy may be associated with muscle atrophy and demyelination. Herein we report the first case of a patient with MERRF syndrome and prostate cancer treated with a robotic radical prostatectomy with satisfactory functional outcomes.

Case presentation

A 50-year-old male with a history of MERRF syndrome was found to have serum prostate specific antigen of 9.45 ng per milliliter on routine screening. His urological history was significant for mild to moderate voiding dysfunction consisting of hesitancy and nocturia, with an International Prostate Symptom Score of 14/35. There was no erectile dysfunction with a normal International Index of Erectile Function score (24/25). His urinalysis was negative for pyuria or microscopic hematuria.

The patient had been diagnosed with a sporadic form of MERRF as an adult after developing symmetric lipomas in his cervical region along with exercise intolerance and mild muscle atrophy. Despite having the common MERRF mitochondrial DNA mutation (A8344G) in his blood with multiple symmetric lipomas, his variant of MERRF did not include cognitive impairment nor seizures.

His past medical history was significant for a history of hypertension and hypercholesterolemia and his medications included levocarnitine, losartan, hydrochlorothiazide, and metoprolol. His surgical history included a tonsillectomy as a child and plastic surgery to remove neck lipomas. His family history was positive for lung and liver cancer in his mother.

His physical examination showed normal vital signs and a body mass index of 25 (height: 1.65 m, weight: 68 kg). Relevant findings included large, painless, symmetrical cervical lipomas (Fig. 1A and B), normal external genitalia, and a digital rectal examination revealing a soft prostate with good lateral definition bilaterally and an estimated volume of 30 cubic centimeters (cc.). A neurological examination was normal except for mild muscle weakness at the end of the day.

The patient underwent a 12-core ultrasound-guided transrectal prostate biopsy revealing grade group 2 adenocarcinoma (Gleason score 3 + 4 = 7) at the left mid for 9 mm (mm.) and right base for 5.5 mm., and grade group 1 (Gleason score 3 + 3 = 6) at the left base for 9 mm. Perineural invasion was present. His transrectal prostate ultrasound showed a prostate volume of 28.9 cc but no hypoechoic nodules. His calculated PSA density was 0.32 ng/ml/cc.

After discussing all the treatment options, the patient chose a radical prostatectomy given his young age, high PSA density, moderate voiding dysfunction, and grade group 2 with significant involvement (9 mm. 5.5 mm., 9 mm.). Since proceeding with surgery was contingent upon neurology clearance, the patient was evaluated by his neurologist with a specialty in mitochondrial disorders. Given that his MERRF variant was only associated with mild myopathy, the patient was cleared for surgery with a willingness to accept a potentially higher risk of complications during intubation given his neck lipomas, as well as a theoretically higher risk of urinary incontinence or erectile dysfunction given the associated myopathy which characterizes the MERRF syndrome.

The patient underwent a transperitoneal bilateral nerve-sparing robotic radical prostatectomy and pelvic lymphadenectomy without complications. There were no intubation-related complications; operative time was 150 minutes with an estimated blood loss 50 cc. The patient was discharged on postoperative day 1 without complications nor transfusions and his catheter was removed on postoperative day 7. His prostatectomy pathology was grade group 2, pathologic stage T2 with negative margins and lymph nodes. Based on the EPIC short form...
A questionnaire administered four months after surgery the patient was free of pads and his PSA was less than 0.1 ng/ml. After 6 months, the patient could achieve intercourse with the aid of vardenafil on-demand with an International Index of Erectile function of 20/25. At last follow-up 52 months after surgery, the patient continues to be continent, has satisfactory sexual function using daily tadalafil, and his PSA remains less than 0.1 ng/ml.

Discussion

Myoclonus epilepsy ragged-red fiber (MERRF) syndrome is a rare mitochondrial encephalomyopathy with a prevalence of 1 in 400,000 characterized by varying degrees of muscle twitching and myoclonus, myopathy-related weakness, progressive spasticity, and multiple symmetric lipomatosis. The disease typically begins in childhood and may also be characterized by short stature, peripheral neuropathy, decreased night vision, dementia, hearing loss, and exercise intolerance. While the syndrome is highly variable in the manifestation of symptoms, it typically does not involve bowel or bladder function. In over 80% of cases, it is caused by a maternally-inherited mutation in position 8344 of the mitochondrial genome which changes a highly conserved adenine to a guanine. This transfer RNA mutation results in decreased translation of key proteins necessary for oxidative phosphorylation, particularly respiratory chain complexes I and IV.

While associations to other conditions have been difficult to establish given its rarity, several studies have suggested that mitochondrial disorders may be associated with a higher risk for developing malignancies, with reported rates being 3–4 fold higher than the prevalence in the general population. Altered intracellular metabolism, mitochondrial DNA mutations, and direct effects of excess reactive oxygen species due to impaired mitochondrial function have all been linked to prostatic malignant cell proliferation. Although in some retrospective studies prostate cancer has been reported in patients with mitochondrial disease, we report the first case of a patient with prostate cancer and MERRF syndrome with satisfactory functional results after a radical prostatectomy. We underscore the fact that this patient exhibited a milder form of the syndrome and presented favorable characteristics for surgery. It is imperative that before proceeding with surgery in patients with MERRF syndrome they undergo a thorough evaluation by a mitochondrial diseases specialist to ascertain his specific risk of muscle atrophy progression.

Consent

The patient provided informed consent for the information and photographs presented here to be shared.

Conflicts of interest

None.

Funding

None.

Appendix A. Supplementary data

Supplementary data related to this article can be found at [https://doi.org/10.1016/j.eucr.2018.10.006](https://doi.org/10.1016/j.eucr.2018.10.006).

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