Case Report

Solitary Cerebellar Metastasis from a non-muscle Invasive Transitional Cell Carcinoma of Bladder

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Abstract

Brain metastasis from non muscle invasive transitional cell carcinoma of the urinary bladder occurs very rarely. Herein, a patient who underwent transurethral resection of bladder tumor and received intravesical bacillus Calmette-Guérin for pT1, G3 bladder carcinoma accompanied by carcinoma in situ, and who subsequently developed solitary cerebellar metastasis following 18 months cystoscopic follow-up period with normal findings was reported. To our knowledge, only two cases of solitary cerebellar metastasis from pT1 bladder cancer was reported in the English literature.

Keywords: Transitional cell carcinoma of bladder, Solitary cerebellar metastasis

INTRODUCTION

Hematogenous metastasis from bladder cancer normally occurs in the liver (38%), lung (36%), bone (27%), adrenal gland (21%) and intestines (13%), and rarely occurs in the brain (0.3–8.0%)¹. Intracranial metastasis is seen especially in patients having advanced cancer undergoing systemic chemotherapy or total cystectomy and with other systemic metastases as well. However, solitary cerebellar metastasis from non-muscle invasive bladder carcinoma (NMIBC) is very rare⁸. In the present case, a solitary cerebellar metastasis was developed after...
resection and immunotherapy of organ-confined high grade pT1 transition cell carcinoma, although cytologic and cystoscopic follow-up revealed no evidence of carcinoma recurrence. Review of the literature concerning this issue disclosed only two reported cases\(^{(1,2)}\).

**CASE PRESENTATION**

The patient was a 75-year-old man, admitted to the department of urology in our center with a main complaint of gross hematuria for a while. Abdominal Magnetic Resonance Imaging (MRI) displayed diffuse thickening of the bladder. The patient was evaluated with cystoscopic examination which demonstrated a papillary tumor on the bladder posterior wall extending to left lateral wall, 30x30 mm in size. After urine example for cytologic examination was obtained, transurethral resection of the bladder tumor (TUR-Bt) and the underlying bladder wall with the detrusor muscle and the edges of the resection area and random biopsies from bladder and prostatic urethra were carried out on 26th December 2012. The tumor had an irregular fragmented macroscopic consistency and, histopathological examination revealed malignant papillary structures with transitional epithelial morphology formed by large pleomorphic hyperchromatic nuclei (Fig. 1). There was no tumor in surgical margins and the random biopsies. The case was reported as a high grade pT1a tumour with carcinoma in situ, without muscle involvement. The patient then underwent six cycles of Bacille Calmette Guerin (BCG) installation. Postoperative 3, 9, 12 and 15 months control cystoscopies demonstrated no tumoral or suspicious lesions with negative cytology results. A few weeks after the last cystoscopy control, the patient was admitted to the department of neurosurgery due to confusion, dizziness, vomiting and slurring of speech. MRI scans of the head revealed a mass lesion, in 28x19 mm diameter, within the posterior fossa extending to vermis in the midline and to left cerebellar hemisphere. The mass lesion was hypointense in T1 and iso-hyperintense in T2 and FLAIR weighted sequences with irregular borders. Postcontrast T1 and T2 weighted sequences showed marked edema at the periphery of the lesion which obliterated 4th ventricle, narrowed quadrigeminal system and shrunken cerebellar folia (Fig. 2). Initially, grade 3 glial tumor or solitary metastatic tumor was suspected. The patient was operated, histopathological examination of the mass excised revealed a gray-white lesion with soft consistency showed cerebellar neuroglial tissue infiltrated by malignant epithelial neoplasia (Fig. 3). In the immunohistochemistry panel to determine tumoral origin, strong membranous staining with cytokeratin 7 (CK 7) was observed with positive CK 20 and 34 be12 (Figure 4A, B and C). For synaptophysin and chromogranin markers were negative, primary cerebellar neoplasia were ruled out and, metastatic lesion of high grade urothelial carcinoma metastasis was reported. The patient was discharged as his acute symptoms subsided on 5th day postoperatively and sent to oncology department for further treatment. He rejected receiving chemotherapy. He underwent cranial radiotherapy. Two months later he died.
**Figure 1:** High grade transitional cell carcinoma with papillary structure at bladder dome H&E x 100

**Figure 2:** Mass demonstrated in cerebellum on magnetic resonance imaging (MR).
**Figure 3:** Cerebellar parenchyma at right lower quadrant continuing with infiltrative epithelial malignant tumor

**Figure 4A:** Strong membranous staining with cytokeratin 7 (CK 7) in tumoral cells (x400) **Figure 4B:** Strong membranous staining with cytokeratin 20 (CK 20) in tumoral cells (x100) **Figure 4C:** Membranous 34 beta12 staining in tumoral cells (x100)
DISCUSSION

Solitary metastasis of NMIBC to the brain and especially to cerebellum is very rarely seen. In contrast to muscle invasive bladder cancers, most of the superficial cancers can be treated with transurethral resection and intravesical BCG therapy, monitored regularly with cystoscopy and urinary cytology. In spite of these measures, %5-20 of NMIBC may become muscle invasive. Furthermore, high grade superficial tumors are known to metastasize to regional lymph nodes before becoming muscle invasive\(^4\). Although extremely seldom, distant metastasis of NMIBC were reported\(^6\). The incidence of intracranial metasteses from NMIBC is rare, as liver and lungs function as a filter which is probably responsible for the lower incidence in brain metastases\(^9\). Brain metastases occur on the last stage of systemic disease as the study of Dhote et al. showed that patients having controled systemic metastases under chemotherapy developed frequently brain metastasis in the long term as systemic chemotherapeutic agents did not cross blood-brain barrier whereas bladder tumor cells could find a way with an unknown mechanism to gain access into the brain for metastasis\(^9\). In their report where they have presented a solitary brain metastasis from pT1, G3 bladder cancer, Zennami et al generated three hypothesis concerning this access route; i) Micrometastasis may occur just before or after TUR-Bt. ii) Prostatic interstitium may be invaded by high grade tumor or carcinoma insitu through prostatic channels. iii) Residual tumor may remain after TUR-Bt but any abnormality is observed during follow up cystoscopies and/or cytologies\(^10\). The first two of the above mentioned hypotheses seem to be probable for our case.

There are controversial reports concerning solitary brain metastasis of the bladder tumor in the literature. In a series, localized solitary brain metastasis was studied and, authors found out that primary tumors from pelvic or gastrointestinal region metastasize % 50 to subventorial location. Furthermore, the study suggested that higher incidence of pelvic or gastrointestinal metasteses to this area could be explained with neither arterial embolization nor Batson plexus\(^5\). However, another study stated that venous network surrounding spinal cord and vertebrae that generates Batson plexus might lead tumor cells to propagate from pelvis to the brain\(^7\).

In our patient, thorough radiological examination of urinary system up to the kidneys did not support any recurrent disease. Histopathological examination after TUR revealed high grade urothelial carcinoma without muscularis propria invasion (stage pT1a+carcinoma insitu). After removal of the cerebellar mass, immunohistochemical panel to identify tumoral origin cytkeratin 7(CK 7) strong membranous staining with positive CK 20 and 34 ße12 was observed. The case was detected as high grade urothelial carcinoma metastasis since primary cerebellar neoplasia were ruled out with negative synaptophysin and chromogranin markers. In this context, our case is the third cerebellar and forth intracranial solitary metastasis of a non invasive superficial bladder carcinoma according to literature review.

CONCLUSION

In conclusion, although rare, pT1 high grade NMIBC may metastasize to cerebellum as a solitary mass. The mechanism or route of this kind of metastases may be elucidated with increasing number of advanced examination methods in the future.

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REFERENCES


