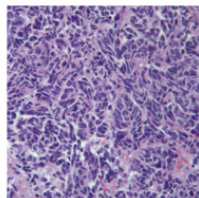


Introduction

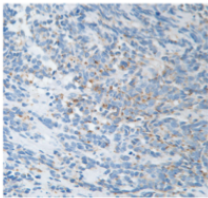
Bladder cancer in America is the fifth most common cancer diagnosis with greater than 76,000 new cases and over 16,000 deaths per year [1]. While most bladder cancers are diagnosed as transitional cell carcinoma, which some may call urothelial carcinoma, other cancers such as squamous cell carcinoma, adenocarcinoma, various types of sarcomas, and neuroendocrine carcinoma such as small cell carcinoma and large cell carcinoma are also present [2,3]. Small cell carcinoma (SCC) makes up less than 1% of all bladder tumors. Prognosis is usually very poor due to the high metastatic rate. Patients are usually diagnosed once metastasis has already occurred [4]. Due to the limited number of cases of SCC in the bladder, consensus on specific protocols for treatment has not been established nor one treatment having a greater outcome over another.

Case Report

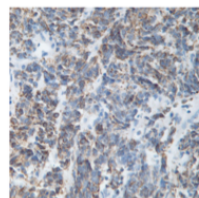
A 69-year-old white male was referred to us for a bladder biopsy positive for SCC. Patient had a past medical history significant for transitional cell carcinoma (TCC) of the bladder, elevated PSA, hypertension, COPD, coronary artery disease, diabetes, and a 45-year tobacco use history. Surgical history is significant for transurethral bladder tumor excision with fulguration, prostate biopsy, and coronary artery stents. Patient had been complaining of hematuria on and off for almost a year along with recurrent UTIs treated with fluoroquinolones. On most recent cystoscopy, a 5 cm tumor was spotted on the posterior wall of the bladder. Biopsy results came back showing SCC of the bladder with involvement of the lamina propria and muscularis propria of the detrusor muscle. Patient had a CT scan as well as a bone scan which were negative. A treatment plan consisting of cisplatin along with etoposide was prescribed along with a referral to surgery to determine if the patient was a good surgical candidate, otherwise radiation therapy may be used in lieu of cystectomy



H&E
Figure 1.



Chromogranin
Figure 2.



AE1/AE3
Figure 3

Discussion

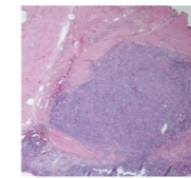
Due to the aggressive nature of SCC, it is not surprising that more than 60% of patients reported to have SCC had metastatic lesions at the time of diagnosis [4]. It is also not uncommon to have a diagnosis of TCC along with SCC, as it is thought that the small-cell phenotype can reflect differentiation of multipotent malignant urothelial cells [5]. Due to the relative similarities seen with SCC and TCC on gross examination, they must be differentiated using histopathological analysis. Figure 1 and 4 shows the small cell characteristics of increased nuclear to cytoplasmic ratio. The key immunohistochemical stains used to diagnose SCC are cytoplasmic chromogranin A (figure 2), synaptophysin (figure 5), and "dot like" cyokeratin (CK20) (figure 2) [6].

For our patient, immunohistochemical stains came back positive for CK20, CK7, TTF-1, AE1/AE3 (figure 3), SYN, chromogranin A, and CD-56. Thyroid transcription factor-1 (TTF-1), seen in figure 6, was initially thought of as a specific marker for adenocarcinoma of the lungs and small cell carcinoma of the lungs, but it has been seen that around 25-39% of patients with SCC of the bladder will also display a positive TTF-1, like in our patient [6]. CT scan, bone scan and PET scans are used after diagnosing SCC of the bladder to check for metastasis due to the high metastatic rates with this cancer. CT scan and bone scan of our patient were negative for metastasis. Even with negative scans, the probability of metastasis is still quite high even after treatment with micrometastases being commonly not picked up by scans. Monitoring patients long term, DNA methylation is one of the methods used as a way to follow up with SCC of the bladder [7].

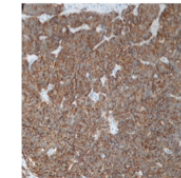
Treatment for SCC has not been thoroughly investigated due to the lack in the number of cases seen. Typically for early stage SCC, transurethral resection or radical cystectomy is the first line treatment. When the cancer is more invasive involving the muscle or lymph nodes, a combination therapy is warranted which can include adjuvant chemotherapy, radiation therapy, or both. Even though cystectomy is usually a first line treatment option, the research Cheng gathered from his 64-patient study found that 1-year and 5-year survival rate for patients who underwent cystectomy were 57% and 16%, while the 1-year and 5-year survival rate of patients who did not undergo cystectomy was 55% and 18%. Even though this study is limited in sample size, from what is presented, cystectomy does not provide an increased survival time for patients. It was noted that when comparing patients who had adjuvant chemotherapy, usually cisplatin, along with cystectomy, their disease-specific survival was 66% compared to 45% with cystectomy alone [8]. This is why it is important that once diagnosis has been established, chemotherapy be added as soon as possible for a longer survival time.

Conclusion

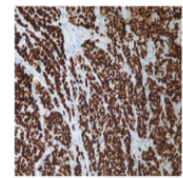
SCC of the bladder is a very rare form of bladder cancer with not a lot of data to go by. Medical literature has not provided much in terms of specific protocols for treatment that can be used universally for SCC. The best course of action to go by from the limited retrospective cases seen shows that cystectomy along with chemotherapy is a good way to start treating the cancer aggressively as long as the patient is a good surgical candidate. Radiation therapy can be used in place of cystectomy, but research has not shown if this is an inferior or superior approach compared to surgery. Further investigation needs to take place for other chemotherapeutic treatment options or immunotherapeutic treatments for SCC. With high rates of micrometastases in SCC, which tends to be the biggest factor in the cancer spreading even after treatment, developing a method to slow down the micrometastases would be ideal in increasing the 1 year and 5-year survival rates.



H&E
Figure 4.



Synaptophysin
Figure 5



TTF1
Figure 6

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