Osteoclast like Giant cell Urothelial Carcinoma of Urinary Bladder

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Citation

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Abstract

Extra osseous manifestations of osteoclast-like giant cell tumors (OGCTs) in soft tissue are very unusual, especially in the urinary bladder. Terminology, histogenesis, biologic behavior and optimum treatment of these tumors remain controversial till date. Here, we present a case of 71 year old male who presented with painless hematuria. Trans urethral resection was done and the histomorphology and immunoperoxidase profile was compatible with urothelial carcinoma with osteoclast-like giant cells so called Osteoclast-rich undifferentiated urothelial carcinoma .patient developed local recurrence within few weeks of TURBT. Patient was placed in palliative care program and lived for a year .

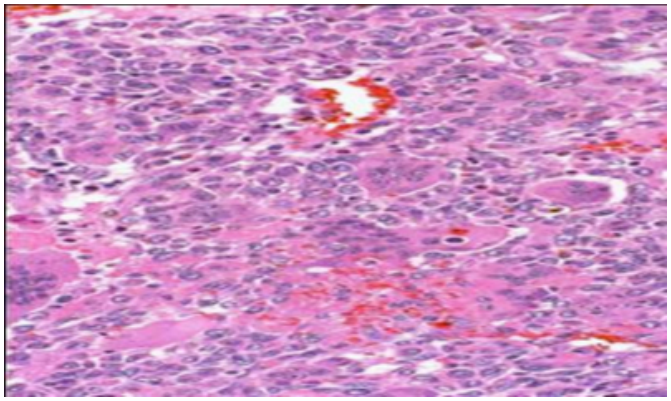
INTRODUCTION

90% of bladder cancers are transitional cell carcinoma and 8- 9% are squamous cell carcinoma, adenocarcinoma, sarcomas, small cell carcinoma and secondary deposits from cancers elsewhere in the body. Primary non urothelial malignancies of bladder are rare and account for less than 1% of all bladder cancers. To date very few cases have been reported so far in English literature. We report a rare case with osteoclast like giant cell urothelial carcinoma of the urinary bladder.

CASE REPORT

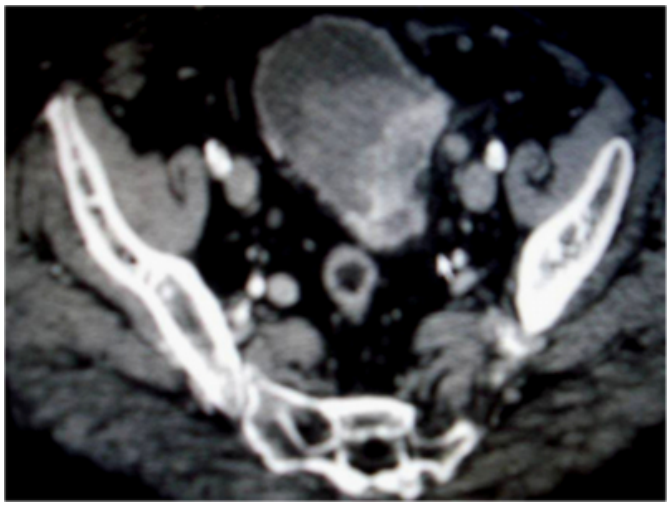
A 71year old pleasant gentleman known to have a coronary artery disease presented to local hospital emergency room with complaint of chest pains suggestive of unstable angina pectoris. Electrocardiogram showed an acute inferior wall myocardial infarction. He was given TNK (tenecteplase) and started on warfarin based therapy. After few days he developed subcutaneous hematoma on both arms and hemoglobin dropped to 60 gram necessitating blood transfusions. He developed massive painless hematuria and on interviewing it seemed that he has had issues with hematuria for the past few months. He completed treatment related to his heart attach and was sent home Few days later he reported back to ER with retention of urine. Catheter was passed which drained blood stained urine and big blood clots. This was attributed to warfarin based anti coagulant therapy so was stopped. Unfortunately his urinary symptoms did not settle but got aggravated and catheter got plugged with clots leading to urinary retention. Urine cytology was negative for cancer cells. His INR was normal. Office bladder ultrasound showed a large mass in the bladder which was recorded as a possible large clot. He underwent cystoscopy which unfortunately got complicated as urologist had hard time in evacuating large clot. Beneath the large clot there was a tumor on a stalk which was completely removed by transurethral bladder resection (TURBT). The pathology revealed extensive geographic necrosis and hemorrhage in most fragments. The viable fragments had osteoclast-like multinucleated giant cells in a sea of oval plump mononuclear cells exhibiting mild nuclear atypia. The tumor had sheets of large pleomorphic cells with high mitotic rate, pathologic mitosis and large areas of necrosis. Spindle cell morphology was present in several areas. Other areas showed large number of osteoclast-like giant cells and focal areas showing invasion of smooth muscle. Lymphatic and vascular invasion was not evident. Some areas showed low grade urothelial carcinoma. CD 68 outlined the cytoplasm membrane of osteoclast like giant cells. The mononuclear cells were reactive for S100.LCA and stained the cytoplasm of giant cells and mononuclear cells. No actin expression was seen. The histomorphology and immunoperoxidase profile was compatible with urothelial carcinoma with osteoclast-like giant cells so called Osteoclast-rich undifferentiated urothelial carcinoma (Figure1).

Figure 1



Case was discussed in multidisciplinary rounds and consensus was to offer him radical cystectomy if staging work was negative. Because of the cardiovascular related co-morbid condition such a coronary artery disease, recent heart attack, COPD, atrial fibrillation patient was deemed not a viable candidate for aggressive surgery such as radical cystectomy. Staging CT scan done in two weeks after TURBT showed massive disease with fungating component that extended into bladder lumen. An enhancing mass was seen at the superior aspect of the bladder wall immediately right of midline and associated metastatic adenopathy in the pelvis (Figure 2).

Figure 2



CT scan of the chest showed pulmonary metastasis. Bone scan was negative for any bony abnormality. Patient was admitted for severe perineal discomfort and difficulty in urination. Due to severe pelvic discomfort he received palliative radiation. After 3 weeks his symptoms subsided and patient was feeling better. Gemcytabine based chemotherapy was offered as system treatment but patient declined. He was enrolled in palliative care program and succumbed to disease in 6 months time since diagnosis.

DISCUSSION

Osteoclastic giant-cell tumors are rarely seen involving the urothelial tract; the first case was described by Kimura et al[1]. He described various giant-cell morphologies within urothelial tumors: (1) pleomorphic giant-cell carcinomas; (2) sarcomatoid carcinomas with sarcomatous spindle cell giant cells; (3) syncytiotrophoblastic giant cells in high-grade infiltrating urothelial carcinoma; (4) scattered reactive stromal giant cells; (5) choriocarcinoma of the bladder; (6) carcinomas containing osteoclast-like cells; and (7) lesions with the classical morphology of osteoclastic giant-cell tumors. Out of these, giant cell carcinomas traditionally occur within bones. These entities are very aggressive in nature and despite radical surgery and tend to recur. Extra osseous manifestations of osteoclast-like giant cell tumors (OGCTs) in soft tissue are very unusual, especially in the urinary bladder[2]. However, multinucleated osteoclast-like giant cells have been described in association with epithelial malignancy of breast, gall bladder and pancreatic carcinoma. In urinary tract less than 10 cases have been reported so far in English literature. Due to this diversity there is lot of disagreement regarding the origin of this neoplasm. Dr Molberg and et al in their study indicated that OGCTs may arise from the fusion of mononuclear histiocytes and macrophages which are attracted to the main tumor site by various growth and chemo tactic factors released by neoplastic epithelial cells[3]. Terminology, histogenesis, and biologic behavior of these tumors remain controversial till date.

Pathologically most of these tumors are positive for vimentin, CD68, CD45 (cell surface proteins) and negative for cytokeratin and epithelial membrane antigen. Vimentin usually identifies mesenchymal tissue. CD68 (cluster of differentiation) is a glycoprotein which identifies macrophages and giant cells.CD45 is a protein tyrosine phosphates an enzyme known to be a signaling molecules that regulate a variety of cellular processes including cell growth, differentiation, mitotic cycle, and oncogenic transformation[4]. So pathologists play an important role by making a careful morphologic assessment of the primary tumor and its relation to adjacent structures. The immunohistochemical profile supports an epithelial origin for the mononuclear cells and non-neoplastic reactive histiocytes lineage for the osteoclast-like giant cells[5]. There is genetic evidence based data to support origin from duct epithelium as K-ras oncogenic mutations have been detected

in osteoclast giant cell tumors[6]. Ideally, evaluation of the primary site will segregate patients into groups with distinct clinical features, biologic behavior, and response to therapy. Traditionally, to accomplish this goal, pathologists have relied on factors such as histological tumor type, grade, invasion of muscle, and presence or absence of lympho-vascular invasion. Recently, in an effort to enhance the ability to sub classify these patients, new modalities, such as flow cytometry, monoclonal antibodies, proliferative rate, cytogenetic and molecular genetic testing's are being used[7]. Under cystoscopy it looks like any other TCC but difference is seen only under microscope in pathology. In situ hybridization shows messenger RNA (mRNA) for transforming growth factor 1 (TGF-1) and transforming growth factor 2 (TGF-2) in neoplastic stromal cells and osteoclast-like giant cells within the recurrent and primary extra osseous tumors as well as in active osteoblasts on the surfaces of recently formed spicules of metaplastic bone. In situ hybridization also revealed mRNA for TGF-1 and TGF-2 in primary intra osseous tumors from these cases and from four cases in which neither extra osseous recurrence nor osseous metaplasia was identified. In the microenvironment of the extra osseous soft tissue, production of these osteoinductive growth factors by GCT may have a paracrine effect on mesenchymal progenitor cells, thereby stimulating the osteoblastic differentiation and metaplastic bone formation associated with these lesions[8].

Clinically these tumors' in bones are aggressive; we anticipate they are aggressive at other sites too similar to their counter part in bones. Most of the bladder cases with OGC variant in literature were treated with transurethral resection without evidence of recurrence. One patient had radical cystoprostatectomy with partial ureterectomy and transureteroureterostomy and was recurrence free at 5 months follow up. In English literature very few case reports of this kind are available so to formulate a optimum treatment is very difficult. However it seems the trend is if tumor becomes invasive then more aggressive approach is adopted probably extrapolated from the experience in muscle invasive transitional bladder carcinomas. In recurrent osteoclast like giant cell tumors in the bladder, the optimal treatment is unknown but a case was reported where anterior pelvic exenteration, vaginectomy and urinary diversion was performed and patient was recurrence free for at least 6 months period6. Role of radiation and chemotherapy is undecided[9]. Logically radiation should be helpful as giant cell tumors are radiosensitive in nature and that may be reason why our patient had quick symptom relief after palliative radiation. Because of the rarity of this entity the prognosis is controversial. As per few pathology articles it carries dismal prognosis. Some reports have quoted median survival less than 24 months[10]. At this point we think aggressive surgical approach should be adopted for primary and recurrent neoplasms.

CONCLUSION

In summary, despite close morphological similarities between osteoclastic giant-cell tumors of the bones and the urinary tract, these lesions diverge in many aspects such as age at presentation, strong male predominance, immunohistochemical expression of epithelial markers and association with urothelial carcinoma. Most importantly, osteoclast-rich undifferentiated carcinoma of the urinary tract exhibit aggressive behavior and have a dismal prognosis.

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