Urology Case Reports 33 (2020) 101394

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: http://www.elsevier.com/locate/eucr

Oncology

A rare case of pancreatic adenocarcinoma metastasized to the bladder

James Frederick W. Pike [a,*], William F. Abel [a], Jordan M. Eldersveld [b], Charles G. Marguet [a,c], Ryan P. Werntz [a,c]

[a] University of South Carolina School of Medicine Greenville, 607 Grove Rd., Greenville, SC, 29605, USA
[b] Pathology Associates of Greenville, 701 Grove Rd., Greenville, SC, 29605, USA
[c] Department of Surgery, Division of Urology, PRISMA Health Upstate, 701 Grove Rd., Greenville, SC, 29605, USA

ARTICLE INFO

Keywords:
Pancreatic adenocarcinoma
Metastasis
Bladder cancer
Pancreatic cancer metastasis

ABSTRACT

Pancreatic cancer is usually detected in late stages due to lack of identifiable symptoms and rapid progression. It commonly metastasizes to the liver, lung, and peritoneum, but only rarely to the bladder. We present a 41-year-old female with a history of pancreatic adenocarcinoma, asthma, gastroesophageal reflux disease, uterine fibroids, and tobacco use who presented with hematuria, polyuria, and abdominal pain. The CT showed bilateral hydroureteronephrosis with a hyperdense region in the posterior wall of the bladder. Pathology revealed metastatic pancreatic adenocarcinoma to the bladder. This is the fourth reported case of pancreatic adenocarcinoma metastasizing to the bladder since 1953.

Introduction

Pancreatic adenocarcinoma is the fourth most common cause of cancer death in the United States and is diagnosed in late stages over half of the time. Treatment for pancreatic adenocarcinoma that has already metastasized includes FOLFIRINOX (folinic acid, 5-fluorouracil, irinotecan and oxaliplatin) and gemcitabine/nab-paclitaxel as part of palliative chemotherapy. The most common sites of distant metastasis include the liver, lung, and peritoneum.[1] In rare instances, pancreatic adenocarcinoma has been documented to metastasize to the bladder, with three known cases reported in literature since 1953.[2] Here we present a case of pancreatic adenocarcinoma with distant bladder metastasis.

Case presentation

Our patient is a 41-year-old female with Stage IV pancreatic cancer status post palliative chemotherapeutic treatment. Past medical history includes asthma, gastroesophageal reflux disease, uterine fibroids, and tobacco use. She presented to the emergency department with a chief complaint of hematuria and abdominal pain. These symptoms had been present for three to four weeks and she decided to go to the emergency department when she passed several blood clots on the day of her presentation. She reported suprapubic pain and a feeling of being "plugged up" with relief after passing a clot. She acknowledged polyuria, fever, chills, nausea, and shortness of breath, but denied chest pain, vomiting, constipation, and diarrhea.

Physical examination revealed suprapubic tenderness and fullness, but no costovertebral angle tenderness. Serum creatinine was 3, blood urea nitrogen 22, calcium 7.5, albumin 3.1, estimated glomerular filtration rate 21, and hemoglobin 7.1. An abdominal computed tomography (CT) scan was ordered, revealing a distended bladder with bilateral hydroureteronephrosis and dilated ureters extending to the level of the bladder. There was also a hyperdense region in the posterior wall of the bladder revealed by CT suggesting a possible hematoma or mass (Fig. 1). The patient received 2 units of packed red blood cells due to her hemoglobin level and Urology was consulted. Urology hand irrigated at bedside with minimal clot return and planned for cystoscopy with possible fulguration. The bilateral hydroureteronephrosis was thought to be secondary to obstruction from dependent clot. During cystoscopy with transurethral resection of the bladder tumor (TURBT), the mass was found to involve the trigone of the bladder and was blocking both ureteral orifices. A large consolidated bladder dome clot was also removed, and bilateral percutaneous nephrostomy tubes were placed by interventional radiology. Foley was removed post-operative day one and patient was discharged post-operative day two with hemoglobin stable and creatinine improved. The mass was determined to be metastatic adenocarcinoma from the pancreas (Fig. 2, Fig. 3). Future urologic management included long-term stent exchanges, but unfortunately the patient's cancer spread to other sites leading to multiple

* Corresponding author.
E-mail address: pikejw@email.sc.edu (J.F.W. Pike).

https://doi.org/10.1016/j.eucr.2020.101394
Received 5 August 2020; Received in revised form 20 August 2020; Accepted 22 August 2020
Available online 26 August 2020

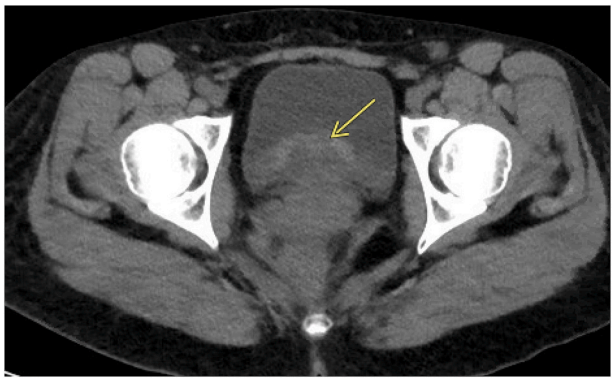

Fig. 1. Abdominal/pelvic CT revealing a mass on the posterior wall of the bladder (arrow) with close proximity to the distal ureters.

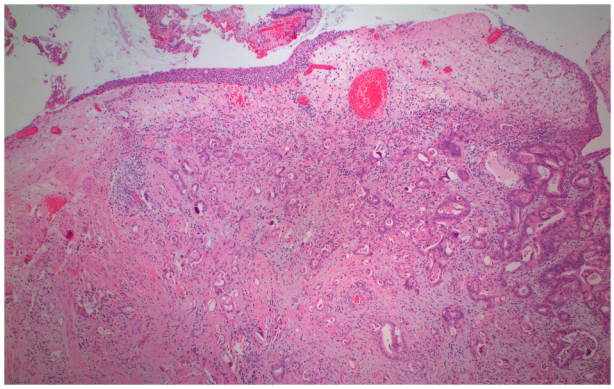

Fig. 2. Moderately differentiated adenocarcinoma extensively invading the bladder lamina propria. Overlying urothelium is benign without evidence of urothelial carcinoma in situ or papillary urothelial carcinoma. (H&E, 40x magnification).

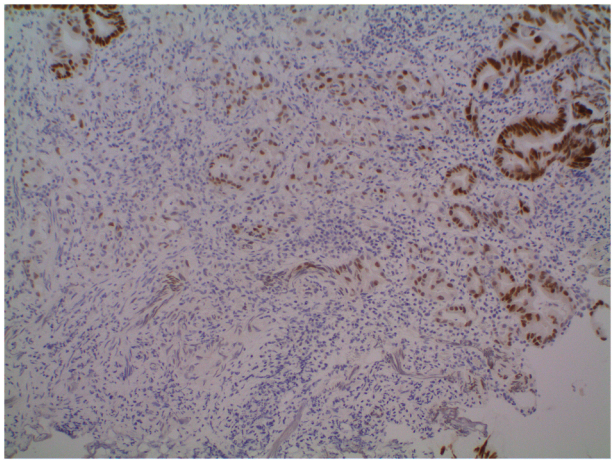

Fig. 3. Neoplastic glands showing positive nuclear staining for CDX2, a marker of gastrointestinal and pancreaticobiliary differentiation. GATA3, a marker of urothelial differentiation, was negative. (100x magnification).

bowel obstructions, and she was placed on palliative care.

Discussion

This case represents the fourth documented presentation of pancreatic adenocarcinoma metastasis to the bladder. There is only one other case where bladder cancer presented after existing pancreatic cancer, which also included an initial presentation of gross hematuria. That case is also is the only other reported case where the primary site of cancer was the pancreatic tail. Another case involved a patient presenting with hematuria and polyuria leading to an initial diagnosis of bladder cancer. The pancreatic origin was not found until 2 years later after the patient died of saddle embolus, where on autopsy the diagnosis was determined pancreatic cancer with metastases to the bladder, peritoneum, omentum, and retroperitoneal lymph nodes. In the latest reported case in 2018, the patient did not present with urinary symptoms or microscopic hematuria, but rather with abdominal discomfort and weight loss. The pancreatic head origin and bladder metastasis were found simultaneously on CT scan.[2] The symptoms and presentation in our case compared to the other reported cases further contribute to its unique diagnosis of pancreatic cancer metastasis.

Both a passive and active mechanism of tumor metastasis have been postulated, with the two not being considered mutually exclusive in any case of metastasis. The passive theoretical mechanism involves tumor cells coming into contact with damaged blood vessels and intravasating as a result of unattenuated growth of the tumor and diminished mechanisms to prevent cell detachment. The active theoretical mechanism involves chemotactic migration of tumor cells up chemokine gradients leading to eventual intravasation when blood vessels that are a source of chemokines are encountered. Further, changes in lymphatics and vasculature within tumors lead to disorganized vessels that are more permeable than their non-pathologic counterparts.[3] While it is difficult to determine the exact mechanism that was employed by the patient's cancer cells, there are a number of genes including those for cellular adhesion molecules, integrins, cadherins, and matrix metalloproteinases that are often aberrantly expressed in pancreatic adenocarcinoma. The absence of E-cadherin has also been associated with pancreatic adenocarcinoma that are more aggressive and less cohesive.[4] It is likely that a combination of the active and passive mechanisms for metastasis combined with inappropriate expression of various cellular molecules led to metastasis in our patient.

When a solid pancreatic mass is identified, endoscopic ultrasound with fine needle aspiration (EUS-FNA) is the standard for diagnosing its etiology. In addition to the histological diagnosis, there are other biomarkers associated with pancreatic cancer with CA 19-9 showing the best results. Sensitivity of the CA 19–9 assay was found to be 83.7% and specificity was 90.4%, and a high CA 19-9 level was typical of advanced inoperable pancreatic cancer.[5] In this case, bladder imaging (Fig. 1) prior to diagnosis suggested a hematoma while reporting a mass as less likely. The diagnosis of this patient could not be confirmed prior to the pathology report, which emphasizes the relevance of biopsy in cancer diagnosis in order to determine the right treatment.

Conclusion

This case shows the importance of considering distant metastasis when new masses are discovered on imaging, especially in patients with pre-existing cancer. Often with cancer metastasis to the bladder, the patient does not present with urinary symptoms. However, when patients are symptomatic with preexisting malignant disease, metastasis to the bladder should exist on the differential.

Consent

Written informed consent was obtained from the patients for publication of this case report and any accompanying images.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

Acknowledgements

None.

References

1. Hidalgo M, Cascinu S, Kleeff J, et al. Addressing the challenges of pancreatic cancer: future directions for improving outcomes. *Pancreatology*. 2015;15(1):8–18. https://doi.org/10.1016/j.pan.2014.10.001.
2. Velcheti V, Govindan R. Metastatic cancer involving bladder: a review. *Can J Urol.* 2007;14(1):3443–3448.
3. Bockhorn M, Jain RK, Munn LL. Active versus passive mechanisms in metastasis: do cancer cells crawl into vessels, or are they pushed? *Lancet Oncol*. 2007;8(5):444–448. https://doi.org/10.1016/S1470-2045(07)70140-7.
4. Keleg S, Büchler P, Ludwig R, et al. Invasion and metastasis in pancreatic cancer. *Mol Canc*. 2003;2(14). https://doi.org/10.1186/1476-4598-2-14.
5. Cwik G, Wallner G, Skoczylas T, et al. Elevated tumor marker CA 19-9 in the differential diagnosis of pancreatic mass lesions. *Ann Univ Mariae Curie Sklodowska Med.* 2004;59(2):213–218.