Bladder Metastasis: An Unusual Presentation of Stomach Cancer

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Abstract

Linitus plastica of the stomach is a type of gastric carcinoma usually diagnosed at a late stage due to a lack of early pathognomonic symptoms. A diagnosis is usually by endoscopy and biopsy, however, lack of mucosal involvement leads to false negative reports. Over 50% of patients present with distant metastasis. Metastasis to bladder is rare and synchronous detection of bladder metastasis along with the primary tumor has only been reported in 5 cases in English literature. We present a case where clinical suspicion of a gastric malignancy was made in retrospect after biopsy of bladder tumor confirmed metastasis from a gastrointestinal primary.

Keywords: Adenocarcinoma bladder, Signet-ring cell adenocarcinoma, Synchronous bladder metastasis

INTRODUCTION

Cancer of the stomach is a common occurrence in the developing world with adenocarcinoma being the most common histological type. Diffuse adenocarcinoma of the stomach also called linitis plastica accounts for about 3-19% of gastric adenocarcinomas.¹ They are usually diagnosed at a late stage due to the lack of pathognomonic symptoms. Endoscopy is the most sensitive and specific diagnostic method for the diagnosis of patients with suspected gastric cancer.² The negativity of an endoscopic biopsy in a case of linitis plastica is up to 30% especially if there are no mucosal lesions³ and repeat endoscopic biopsy or even endoscopic ultrasound guided biopsies are recommended for diagnosis and further treatment. Biopsy of the metastatic lesion is not commonly done and may only indicate the advanced stage of the disease and need for palliation. A synchronous detection of metastasis to the bladder is rare⁴ but primary diagnosis from bladder metastasis has not been reported. We present a case where a clinical suspicion led to the discovery of a bladder tumor which on immunohistochemistry pointed to the stomach as the most likely primary source.

CASE REPORT

A 58-year-old female presented with a lower abdominal discomfort in the left lumbar and suprapubic region for the past 6 years. She had decreased appetite and occasional upper abdominal pain and vomiting for the past 3 months. The patient also had a history of dysuria for the past 2 months with no symptoms of hematuria. She had attained menopause 6 years ago and had undergone a lower segment caesarean section 20 years ago. She underwent an oesophagastroduodenoscopy for the above complaints, which revealed a non-distensible stomach with suspicion of linitis plastica. Multiple gastric biopsies were taken which showed chronic inflammation, non-specific gastritis with no evidence of malignancy. Clinical suspicion of stomach cancer led to a computed tomography (CT) scan of the abdomen and pelvis being done. The findings revealed circumferential wall thickening of the stomach of 13 mm and a 10 mm × 7 mm irregular hypodense sub-capsular lesion in segment 6 of the liver (Figure 1). Bilateral moderate hydronephrosis with multiple calculi in the right kidney, mild circumferential
wall thickening at right pelvi-ureteric junction and proximal ureter, dilated left ureter. There was an enhancing mass of the superior and right lateral wall of bladder 6.4 cm × 4.6 cm × 1.7 cm, serosa of the bladder over the mass was irregular. Mild ascites. Small anterior uterine intramural fibroid (Figures 2 and 3). Bilateral moderate pleural effusion with passive atelectasis of the lung.

In view of the bladder tumor, the patient was taken up for a cystoscopy and resection of the bladder tumor. On cystoscopy, there was meatal stenosis of 12 Fr. which was dilated up to 28/32 Fr. Urethra, trigone and both ureteric orifices were normal, a polypoidal thickening of bladder mucosa was seen in the right postero-lateral wall of around 2 cm × 3 cm from which multiple biopsies were taken.

The specimen was sent for histopathology and it revealed poorly differentiated adenocarcinoma of signet ring cell morphology present in the lamina propria (Figure 4). To differentiate whether the adenocarcinoma was primary of the bladder or metastatic, immunohistochemistry was done. The markers done were CK7, CK20, CEA, and CDX2. The cells were positive for CK7 (Figure 5), CDX2 and CEA and negative for CK20 (Figure 6) indicating a gastrointestinal (GI) origin of the neoplasm.

In view of the neoplasm being metastatic, the patient has been referred for palliative chemotherapy.

**DISCUSSION**

Gastric linitis plastic is a diffuse type of cancer of the stomach which is characterized by thickening and rigidity of the stomach wall, most often presents clinically in the advanced stage. The symptoms associated with the disease too vary from dyspepsia, dysphagia, vomiting and weight loss, all of which are non-specific to the disease. Linitis plastica arises from the lower third of the mucosa and the architecture of the stomach wall is preserved. Endoscopy is the most sensitive and specific diagnostic tool

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**Figure 1:** Contrast CT scan of the abdomen axial view showing circumferential thickening of the stomach wall

**Figure 2:** Contrast CT scan of the abdomen and pelvis, coronal view showing stomach thickening and bladder tumour.

**Figure 3:** Contrast CT scan of the abdomen and pelvis, sagittal view showing bladder tumour.

**Figure 4:** Hematoxylin and eosin (40x objective) of bladder mucosa showing signet ring adenocarcinoma.
in patients suspected to have gastric cancer.\textsuperscript{2} The sparing of the mucosa by malignant infiltration makes endoscopic diagnosis difficult. Endoscopic biopsy specimens usually contain only mucosa, and thus, result in a negative yield. In patients where there is endoscopic suspicion a diathermic snare or multiple forceps biopsies from the same site can be tried, however, they have an increased risk of perforation. When combined with radiologic modalities like endoscopic ultrasound it may be easier to establish a diagnosis and also stage the tumour and assess the extent of perigastric lymph node involvement.

CT is usually the next step in the investigation ladder to check for local infiltration, nodal, and distant metastasis. Kuntz and Herfarth\textsuperscript{5} suggested that CT has a sensitivity of 88\% for tumor detection.

Greater than 50\% of patients present with unresectable locally advanced or metastatic gastric adenocarcinoma.\textsuperscript{6} The majority of patients, including those with early-stage disease, develop metastases at some point during the course of their illness.

Only about 1\% of bladder tumors are metastatic and the mechanism of spread to the bladder may be by direct extension of the primary focus, implant from exfoliated cells, hematogenous or lymphatic spread from a distant primary. When it comes to the bladder as a site for a distant secondary, the most common site from which metastasis occurs happens to be melanoma and breast followed by stomach.\textsuperscript{7} Macroscopically and radiologically, the metastatic bladder cancer can be either protuberant or diffuse type. In the protuberant type, there is usually gross hematuria and in the diffuse type an irritable bladder without gross hematuria.\textsuperscript{8} In our case, the patient had neither of the two symptoms and the tumor was picked up by CT.

The pattern of metastasis of gastric cancer usually is to the lymph nodes, peritoneum, and liver. In gastric signet ring carcinomas the pattern of metastasis seems to differ and peritoneal, pulmonary, ovarian and atypical metastases seem to be more common.\textsuperscript{9}

Metastasis from gastric primary to the bladder behave differently in males and females. In females, bladder tumors are most often associated with the presence of Krukenberg's tumor (ovarian secondaries from GI tumors). Therefore, the ovaries were hypothesized to direct metastasis from the stomach and other GI organs to the urinary bladder.\textsuperscript{9}

Adenocarcinoma of the signet-ring variant is a rare entity, and when diagnosed in the bladder, is most likely a primary. However, a metastatic spread from a GI primary should be excluded by an appropriate workup to locate any other primary as the treatment of the primary type differs from that of the metastatic type.\textsuperscript{10} The treatment of primary signet-ring cell adenocarcinoma is primarily surgical while that of the metastatic type is with chemotherapy.

There are only 16 cases reported in English literature of bladder metastasis secondary to gastric cancer.\textsuperscript{4,7,8,10-19} In 11 cases, bladder metastasis was noted anywhere from 7 to 120 months after the initial diagnosis of the primary gastric tumor and only 5 cases noted synchronous bladder metastasis. 9 cases had isolated bladder metastasis and 7 had multiple metastasis. 10 of the cases had signet-ring cell adenocarcinoma as the histopathology and six of them presented as metastatic disease. This shows consistency with the fact that signet-ring cell gastric cancers have an aggressive course. In our patient, the histopathology report of the gastric biopsy was inconclusive as to the origin of the signet-ring adenocarcinoma and hence immuno-histochemistry had to be done to confirm the diagnosis. It was a clinical suspicion on endoscopy that led to the further workup of the patient.

Primary signet ring carcinomas of the bladder have a long-term survival with radical cystectomy.\textsuperscript{20} Hence, it is
important to distinguish between primary and secondary signet-ring carcinomas and immuno-histochemistry may be helpful.

In metastatic disease, systemic chemotherapy is the only treatment modality that has demonstrated a significant improvement in survival. There are no standard chemotherapeutic regimens for metastatic gastric carcinoma, but the best survival rates are seen with a three-drug regimen containing 5-flourouracil, anthracycline, and a platinum-based compound.

However, median survival rate rarely surpasses 10 months.

**CONCLUSION**

The diagnosis of signet ring cell adenocarcinoma of the diffuse type (linitis plastica) can be difficult due to lack of symptoms and lack of representative tissue on endoscopic biopsy. Tissue diagnosis is a must for further treatment and often diagnostic laparoscopy and biopsy is needed. Bladder metastasis originating from a signet ring cell linitis plastica is a rare occurrence in clinical practice and carries a poor prognosis. Bladder metastasis usually present with symptoms and are rarely asymptomatic. In cases where cancer is detected synchronously or when the primary is not apparent, immunohistochemistry should be done to locate the primary origin of cancer as treatment approaches and outcomes are different. In our case instead of subjecting the patient to repeated endoscopies, or even a diagnostic laparoscopy, a cystoscopic biopsy, and immunohistochemistry done led us to a diagnosis.

**REFERENCES**