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MYELOID SARCOMA OF THE BLADDER IN A PATIENT WITH CHRONIC MYELOMONOCYTIC LEUKAEMIA: A CASE REPORT AND LITERATURE REVIEW

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Abstract

Background

Myeloid sarcoma is a rare extramedullary tumour of immature granulocytes, most commonly involving the skin, bone, lymph nodes, and soft tissue. It is usually associated with a diagnosis of relapsed or de novo acute myeloid leukaemia, acute lymphoblastic transformation of a myelodysplastic/myeloproliferative neoplasm, or can occur as isolated myeloid sarcoma.

Case report

A 66-year-old female with a 7-year history of stable chronic myelomonocytic leukaemia presents with urgency, frequency, dysuria symptoms, and without new constitutional symptoms. She is found to have atypical, multifocal lesions on the right posterolateral wall of the bladder with associated hydronephrosis. Pathology reveals the diagnosis as myeloid sarcoma; surprisingly, bone marrow evaluation does not show evidence of acute leukaemic transformation.

Conclusions

Myeloid sarcoma occurring in patients with chronic myelomonocytic leukaemia is extremely rare, and there are no cases reported in the English literature of these patients developing lesions in the bladder. The urological manifestations of an underlying haematological malignancy are best managed with a combination of systemic chemotherapy and allogeneic stem cell transplant, and in this case, the only surgical intervention required was ureteric stenting and tissue biopsy. Although rare, it is essential to consider alternative diagnoses when confronted with an atypical bladder tumour; failure to do so may result in patient harm by exposure to unnecessary intervention and delay to potentially curative treatment.

Keywords: *Myeloid sarcoma, chronic myelomonocytic leukaemia, bladder, urinary tract, case report*

BACKGROUND

Myeloid sarcoma (MS), or granulocytic sarcoma, is a rare extramedullary tumour of immature granulocytes. It most commonly involves the skin, bone, lymph nodes, and soft tissue.[1,2] Several cases of myeloid sarcoma of the bladder have been reported in the literature, although this is typically associated with relapsed or de novo acute myeloid leukaemia (AML).[3]

Chronic myelomonocytic leukaemia (CMML) is a myelodysplastic (MDS)/myeloproliferative neoplasm (MPN) characterized by a sustained absolute (>1 × 10^9/L) and relative (>10%) peripheral blood monocytosis and dysplastic bone marrow features.[1,4]

There is an approximately 15% risk over 3-5 years of patients with CMML transforming to AML, which can be described as acute blastic/leukaemic transformation.[5] The incidence of MS occurring in patients with CMML without evidence of acute leukaemic transformation is extremely low: a study conducted by the Mayo Clinic of 452 patients with CMML found that only 2 patients had myeloid sarcoma (0.5%).[6]

The discovery of an atypical bladder tumour in a patient with CMML should raise suspicions of acute leukaemic transformation; however, as presented in this case, there are rare occurrences where extramedullary tumours arise without evidence of acute transformation. To our knowledge, this is the first case report of myeloid sarcoma of the bladder in a patient with CMML.

CASE REPORT

Presentation

A 66-year-old female non-smoker presented to her general practitioner with a several-week history of frequency, urgency, and dysuria. She otherwise felt fit and well, apart from some discomfort in the left side of her neck associated with an enlarging lump, for which she has been referred to the ear, nose, and throat team for further investigation. Her only past medical history is a diagnosis of type 0 chronic myelomonocytic leukaemia (CMML-0: <2% blasts in peripheral blood, <5% blasts in bone marrow[4]) in 2014, since which she has been under active surveillance with a performance status of 0.

Investigations

Preliminary investigations in the community were fairly unremarkable: blood results showed satisfactory renal function and a full blood count in keeping with stable CMML-0; urine cultures were positive for Escherichia coli infection, which was fully sensitive to standard antibiotics therapy. However, despite treatment with appropriate antibiotics, her lower urinary tract symptoms persisted; thus an ultrasound of her kidneys, ureters, and bladder (USKUB) was performed. This revealed right-sided hydronephrosis with right lateral wall bladder thickening and prompted an urgent urology referral.

Flexible cystoscopy showed significant atypical, multifocal lesions on the posterior wall of the bladder. Subsequently, the patient underwent incomplete loop resection of the lesion, and tissue was sent for histopathological and immunohistochemical analysis. A right-sided ureteric stent was inserted to treat hydronephrosis.

A staging contrast-enhanced computed tomography (CT) confirmed an irregular thickening of the right lateral wall of the bladder involving the right vesico-ureteric junction with moderate right hydronephrosis and hydroureter, with possible nodal involvement in the abdomen and pelvis. Positron emission tomography (PET) confirmed avid retroperitoneal lymphadenopathy, as well as cervical lymphadenopathy and a pleural based lesion in the left hemithorax. In addition to urological investigations, biopsies of the bone marrow and left cervical level II lymph nodes were performed.

Pathology

Three separate specimens were analysed:

1. Bladder tumour biopsy: features consistent with myeloid sarcoma (positive: CD33, MPO, CD68, CD117, CD14) (negative: CD34, CD20, CD3, S100, MNF116, CD21, CD23)
2. Left cervical level II node biopsy: features consistent with myeloid sarcoma, with the same histology and immunophenotype of cervical node biopsy.
3. Bone marrow biopsy: 2% blasts. Features in keeping with CMML-0 and no evidence of transformation to AML

This ultimately confirmed a diagnosis of MS on a background of CMML-0.

Management

The patient received one cycle of a liposomal formulation of daunorubicin and cytarabine

(CPX-351). This was tolerated well, apart from one episode of uncomplicated neutropenic fever, which responded to first-line antibiotics. Two months after initial diagnosis, she then underwent a repeat PET-CT, which demonstrated overall disease progression, albeit with less pronounced bladder wall thickening. Repeat bone marrow aspirate at three months after initial diagnosis confirmed progression to CMML-2 (5–19% blasts in peripheral blood, 10–19% blasts in bone marrow[4]), but still no evidence of AML.

She then underwent salvage chemotherapy with a combination of fludarabine, cytarabine, idarubicin, and granulocyte-colony stimulating factor (FLAG-Ida). This was complicated by Klebsiella oxytoca sepsis, but she recovered following treatment with second-line antibiotics. Repeat PET-CT and bone marrow aspirate, now four months after initial diagnosis showed complete response to treatment in keeping with remission, and so she was referred for allogeneic haematopoietic stem cell transplantation with curative intent. From a urological point of view, repeat flexible cystoscopy and periodic ultrasonography were planned to resolve her hematological malignancy's urological manifestations.

Seven months following initial diagnosis, due to donor-related delays in receiving stem cell transplantation, she received a single dose of bridging chemotherapy; following this, she became acutely unwell and was admitted to the intensive care unit to treat tumour lysis syndrome. Unfortunately, she died two days later.

LITERATURE REVIEW: METHODOLOGY AND RESULTS

A literature search was conducted on PubMed in July 2021 using the following search terms:

"myeloid sarcoma bladder"
"granulocytic sarcoma bladder"
"chronic myelomonocytic leukaemia bladder"
"chronic myelomonocytic leukaemia myeloid sarcoma"
"chronic myelomonocytic leukaemia granulocytic sarcoma"

Papers not in the English language or those reporting paediatric cases were excluded. Our search returned 10 cases of MS occurring in the bladder. Of these, 4 were reported as isolated MS, 1 was related to de novo AML, 1 was occurring as relapsed AML, and 4 occurred as a result of blastic transformation of MDS/MPN. No cases were identified relating to a diagnosis of CMML (Table 1).

There are 6 cases of MS occurring in patients with CMML reported in the literature: 2 cases eventually developed acute blastic transformation, and 4 cases remained as CMML without evidence of transformation. These cases involved anatomical sites, including the testis and the gastrointestinal tract, but none involved the bladder (Table 2).

LITERATURE REVIEW: DISCUSSION

MS is a haematological malignancy characterised by extramedullary tumours of immature granulocytes. It is most commonly associated with a diagnosis of AML (either de novo or relapsed) but can also occur as isolated MS or in patients with established MDS/MPN, indicating acute blastic transformation.[4] It occurs more commonly in the skin, lymph nodes, and soft tissues; however, MS of the urinary bladder is extremely rare.[2,3]

The literature identifies haematuria as the most common presenting complaint, as well as frequency, dysuria, suprapubic pain, and constitutional symptoms such as fatigue. Patients may also present with other unexplained tumours or lymphadenopathy, or have a past medical history of haematological malignancy.

Descriptions of cystoscopic examination findings are non-specific: MS tumours may be atypical, large (>2 cm), and both unifocal and multifocal. Additional investigations which should be performed as part of the initial workup include:

- Full blood count – to assess for haematological abnormality, such as cytopenia

TABLE 1 MS Occurring in the Bladder

Case	Age/ Sex	Location	Presentation	Underlying diagnosis	Interval	Diagnosis	Tumour description	Treatment	Status	Time from diagnosis to last follow up
John et al 2013[7]	39F	Bladder mesentery	Abdominal pain, frequency, bilateral hydronephrosis	None	NR	Isolated MS	NR	Cytarabine, idarubicin, and consolidation	Complete remission	8 months
Chin et al 2011[8]	70F	Bladder	Abdominal pain, haematuria	MDS (RAEB)	15 months	MDS → AML	19×17×11 mm both lateral walls, base, superior wall	NR	NR	NR
Goh et al 2009[9]	72F	Bladder	Haematuria, suprapubic pain	MDS (RAEB)	NR	MDS → AML	Base of bladder 25 mm	Cytarabine	NR	Lost to follow up
Sonmez et al 2009[10]	71M	Bladder	Haematuria	MDS/MPN (unspecified)	2 months	MDS → AML	Patchy areas of mucosal swelling with hyperaemia	NR	NR	NR
Al-Quran et al 2006[11]	47M	Bladder and right epididymis	Haematuria, right testicular swelling	None	NR	De novo AML	4×3×2 cm mass in right posterior wall	Cytarabine, idarubicin	Complete remission	32 months
Uner et al 2004[12]	57F	Bladder	Urinary incontinence, fatigue	None	NR	Isolated MS	Trigone 74×21 mm	Cytarabine, idarubicin, radiotherapy	Remission	1 month
Aki et al 2002[13]	36M	Bladder	Haematuria, abdominal pain	None	NR	Misdiagnosed as Grade 3 TCC, then isolated MS	76×67×36 mm left anterolateral wall	Cytarabine, idarubicin	Death- day 16 of treatment (sepsis)	NR
Kerr et al 2002[14]	80F	Bladder	Haematuria, dysuria	MDS (RAEB)	NR	MDS → AML	Left anterolateral wall 2×2 cm	Radiotherapy	Recurrence	NR
Chaitin et al 1984[15]	29F	Bladder	Haematuria, dysuria	None	NR	Isolated MS	Trigone 8×7×6 cm	Doxorubicin, vincristine, cytarabine, prednisolone	Complete remission	13 months
Liu et al 1973[16]	NR	Bladder	NR	AML	NR	Relapsed AML	NR	NR	NR	NR

NR = not recorded.

TABLE 2 MS in Patients with CMML

Case	Age/ Sex	Location	Presentation	Initial diagnosis	Interval	Diagnosis	Tumour description	Treatment	Status	Time from diagnosis to last follow up
Matanes et al 2019[17]	46F	Generalised lymphaden-opathy	Fatigue and dyspnoea	None	NR	CMML, MS	NR	Cytarabine, idarubicin, alloHCT, fludarabine, mephalan	No evidence of recurrence	230 days
Nagra et al 2015[18]	51M	Anal sphincter	Tender perianal lesion and associated abscess	None	NR	CMML→AML	NR	Cyatarabine, daunorubicin	No evidence of recurrence	NR
Fukushima et al 2014[19]	77M	Jejunum	Haematochezia	None	NR	CMML, MS	Multiple smooth ulcers with clear edges in the jejunum, elevated around their circumference	Endoscopic mucosal resection of ulcer	No evidence of recurrence	2 years
Craig et al 2013[20]	52M	Testis	Painless testicular enlargement, chest pain, myalgia, arthralgia	None	NR	CMML, MS	5.8cm vascular hypoechoic mass right testicle	Radical orchidectomy, decitabine, methotrexate	Death 6 months – sepsis	6 months
Corcoran et al 2005[21]	NR	Testis	NR	CMML	NR	CMML, MS	NR	NR	NR	NR
Akiyama et al 2002[22]	59M	Transverse colon	NR	CMML	6 months	RAEB → AML	NR	Cytarabine, aclarubicin	Death – pneumonia and intestinal obstruction	NR

- Renal function – to assess for renal failure
- Urinalysis – to assess for haematuria or concurrent infection
- USKUB/CT – to demonstrate possible hydroureter/hydronephrosis

From a urologist's point of view, diagnosis relies on taking tissue biopsies during cystoscopy of the atypical lesion to send for histopathological analysis. Histological confirmation of MS should raise a high index of suspicion for underlying AML or blastic transformation of MDS/MPN. Therefore, the patient should be urgently referred to a haematologist for further investigations such as bone marrow biopsy, immunophenotyping, molecular analyses, and PET-CT to confirm the diagnosis [23]. MS occurring in a patient with CMML without evidence of blastic transformation is extremely rare. Anatomical locations described in the literature include the testis and gastrointestinal tract; there are no cases involving the bladder.

Initial treatment for MS is with early intensive chemotherapy with AML induction therapy, possibly with allogeneic stem cell transplantation.[2,24] If treatment is successful, urological manifestations of the disease should improve. Thus, complete resection of the bladder tumour is not indicated as it may cause unnecessary harm and delay potentially curative treatment. Surgical management, such as tumour debulking, cystodiathermy, bladder washout, ureteric stent, or nephrostomy insertion, may only be indicated if the tumour is bleeding or causing significant urinary obstruction.

Due to the rarity of the disease, there is limited published literature regarding treatment outcomes and prognosis. However, a recent multi-centre survey of 48 patients receiving treatment for MS described a median overall survival of 16.7 months.[2] Factors that significantly improve overall survival include younger age, achieving complete remission after intensive chemotherapy, and undergoing allogeneic stem cell transplant. The need for urological follow-up should be assessed on a patient-by-patient basis and could include surveillance cystoscopy or radiology to confirm the resolution of any urological phenomena.

CONCLUSION

Patients are commonly referred to urologists for suspected bladder tumours, most of which are transitional cell carcinomas. These have classical features and are easy to diagnose. Although haematological malignancy presenting as a bladder tumour is rare, it should be considered in light of any suspicious features in the patient's history and atypical lesions found on cystoscopic examination. An atypical lesion may represent MS, indicating new haematological disease or acute leukaemic transformation of existing haematological disease. In this case, MS was detected in the bladder in a patient with CMML without evidence of transformation to AML: to our knowledge, this is the first of its kind described in literature.

Inclusion of MS in the differential diagnosis for a new, atypical bladder tumour may avoid unnecessary surgical intervention. Treatment of MS primarily relies on systemic chemotherapy and allogeneic stem cell transplant; surgical procedures and subsequent complications may lead to patient harm and a delay to potentially curative treatment. It is expected that successful treatment of any underlying haematological malignancy will lead to full resolution of any urological manifestations of the disease.

DECLARATIONS

Ethics approval and consent to participate:

Not applicable.

Consent for publication

Verbal informed consent for publication of their clinical details was obtained from the patient, and written informed consent for publication of their clinical details was obtained from the patient‘s next of kin.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

RS was the primary author of the manuscript, including contributions to the concept, data acquisition, and interpretation. BM and JN critically revised the article for intellectual content. All authors gave final approval of the version to be published.

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