MYELOID SARCOMA OF THE BLADDER IN A PATIENT WITH CHRONIC MYELOMONOCYTIC LEUKAEMIA: A CASE REPORT AND LITERATURE REVIEW
Rebecca Smith, Bashir Mohamed, Jeremy Nettleton
Cheltenham General Hospital, Gloucestershire Hospitals NHS Foundation Trust, UK

Correspondence author: rebecca.smith64@nhs.net

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. 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). 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.
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. 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%).

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) 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...
Myeloid Sarcoma of the Bladder in a Patient with Chronic Myelomonocytic Leukaemia

(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 marrow4), 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 haematological 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.5 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

J Endolum Endourol Vol 4(3):e36–e43; December 21, 2021
This article is distributed under the terms of the Creative Commons Attribution-Non Commercial 4.0 International License. © Smith R et al.
<table>
<thead>
<tr>
<th>Case</th>
<th>Age/Sex</th>
<th>Location</th>
<th>Presentation</th>
<th>Underlying diagnosis</th>
<th>Interval</th>
<th>Diagnosis</th>
<th>Tumour description</th>
<th>Treatment</th>
<th>Status</th>
<th>Time from diagnosis to last follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>John et al 2013</td>
<td>39F</td>
<td>Bladder, mesentery</td>
<td>Abdominal pain, frequency, bilateral hydronephrosis</td>
<td>None</td>
<td>NR</td>
<td>Isolated MS</td>
<td>NR</td>
<td>Cytarabine, idarubicin, consolidation</td>
<td>Complete remission</td>
<td>8 months</td>
</tr>
<tr>
<td>Chin et al 2011</td>
<td>70F</td>
<td>Bladder</td>
<td>Abdominal pain, haematuria</td>
<td>MDS (RAEB)</td>
<td>15 months</td>
<td>MDS → AML</td>
<td>19×17×11 mm both lateral walls, base, superior wall</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Goh et al 2009</td>
<td>72F</td>
<td>Bladder</td>
<td>Haematuria, suprapubic pain</td>
<td>MDS (RAEB)</td>
<td>NR</td>
<td>MDS → AML</td>
<td>Base of bladder 25 mm</td>
<td>Cytarabine</td>
<td>NR</td>
<td>Lost to follow up</td>
</tr>
<tr>
<td>Sonmez et al 2009</td>
<td>71M</td>
<td>Bladder</td>
<td>Haematuria</td>
<td>MDS/MPN (unspecified)</td>
<td>2 months</td>
<td>MDS → AML</td>
<td>Patchy areas of mucosal swelling with hyperaemia</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Al-Quran et al 2006</td>
<td>47M</td>
<td>Bladder and right epididymis</td>
<td>Haematuria, right testicular swelling</td>
<td>None</td>
<td>NR</td>
<td>De novo AML</td>
<td>4×3×2 cm mass in right posterior wall</td>
<td>Cytarabine, idarubicin</td>
<td>Complete remission</td>
<td>32 months</td>
</tr>
<tr>
<td>Uner et al 2004</td>
<td>57F</td>
<td>Bladder</td>
<td>Urinary incontinence, fatigue</td>
<td>None</td>
<td>NR</td>
<td>Isolated MS</td>
<td>Trigone 74×21 mm</td>
<td>Cytarabine, idarubicin, radiotherapy</td>
<td>Remission</td>
<td>1 month</td>
</tr>
<tr>
<td>Aki et al 2002</td>
<td>36M</td>
<td>Bladder</td>
<td>Haematuria, abdominal pain</td>
<td>None</td>
<td>NR</td>
<td>Misdiagnosed as Grade 3 TCC, then isolated MS</td>
<td>76×67×36 mm left anterolateral wall</td>
<td>Cytarabine, idarubicin</td>
<td>Death- day 16 of treatment (sepsis)</td>
<td>NR</td>
</tr>
<tr>
<td>Kerr et al 2002</td>
<td>80F</td>
<td>Bladder</td>
<td>Haematuria, dysuria</td>
<td>MDS (RAEB)</td>
<td>NR</td>
<td>MDS → AML</td>
<td>Left anterolateral wall 2×2 cm</td>
<td>Radiotherapy</td>
<td>Recurrence</td>
<td>NR</td>
</tr>
<tr>
<td>Chaitin et al 1984</td>
<td>29F</td>
<td>Bladder</td>
<td>Haematuria, dysuria</td>
<td>None</td>
<td>NR</td>
<td>Isolated MS</td>
<td>Trigone 8×7×6 cm</td>
<td>Doxorubicin, vincristine, cytarabine, prednisolone</td>
<td>Complete remission</td>
<td>13 months</td>
</tr>
<tr>
<td>Liu et al 1973</td>
<td>NR</td>
<td>Bladder</td>
<td>NR</td>
<td>AML</td>
<td>NR</td>
<td>Relapsed AML</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

NR = not recorded.
<table>
<thead>
<tr>
<th>Case</th>
<th>Age/ Sex</th>
<th>Location</th>
<th>Presentation</th>
<th>Initial diagnosis</th>
<th>Interval</th>
<th>Diagnosis</th>
<th>Tumour description</th>
<th>Treatment</th>
<th>Status</th>
<th>Time from diagnosis to last follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matanes et al 2019&lt;sup&gt;17&lt;/sup&gt;</td>
<td>46F</td>
<td>Generalised lymphadenopathy</td>
<td>Fatigue and dyspnoea</td>
<td>None</td>
<td>NR</td>
<td>CMML, MS</td>
<td>NR</td>
<td>Cytarabine, idarubicin, alloHCT, fludarabine, mephalan</td>
<td>No evidence of recurrence</td>
<td>230 days</td>
</tr>
<tr>
<td>Nagra et al 2015&lt;sup&gt;18&lt;/sup&gt;</td>
<td>51M</td>
<td>Anal sphincter</td>
<td>Tender perianal lesion and associated abscess</td>
<td>None</td>
<td>NR</td>
<td>CMML→AML</td>
<td>NR</td>
<td>Cytarabine, daunorubicin</td>
<td>No evidence of recurrence</td>
<td>NR</td>
</tr>
<tr>
<td>Fukushima et al 2014&lt;sup&gt;19&lt;/sup&gt;</td>
<td>77M</td>
<td>Jejunum</td>
<td>Haematochezia</td>
<td>None</td>
<td>NR</td>
<td>CMML, MS</td>
<td>Multiple smooth ulcers with clear edges in the jejunum, elevated around their circumference</td>
<td>Endoscopic mucosal resection of ulcer</td>
<td>No evidence of recurrence</td>
<td>2 years</td>
</tr>
<tr>
<td>Craig et al 2013&lt;sup&gt;20&lt;/sup&gt;</td>
<td>52M</td>
<td>Testis</td>
<td>Painless testicular enlargement, chest pain, myalgia, arthralgia</td>
<td>None</td>
<td>NR</td>
<td>CMML, MS</td>
<td>5.8cm vascular hypoechoic mass right testicle</td>
<td>Radical orchidectomy, decitabine, methotrexate</td>
<td>Death 6 months – sepsis</td>
<td>6 months</td>
</tr>
<tr>
<td>Corcoran et al 2005&lt;sup&gt;21&lt;/sup&gt;</td>
<td>NR</td>
<td>Testis</td>
<td>NR</td>
<td>CMML</td>
<td>NR</td>
<td>CMML, MS</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Akiyama et al 2002&lt;sup&gt;22&lt;/sup&gt;</td>
<td>59M</td>
<td>Transverse colon</td>
<td>NR</td>
<td>CMML</td>
<td>6 months</td>
<td>RAEB → AML</td>
<td>NR</td>
<td>Cytarabine, aclarubicin</td>
<td>Death – pneumonia and intestinal obstruction</td>
<td>NR</td>
</tr>
</tbody>
</table>
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.
**Funding**

None to declare.

**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.

**Acknowledgements**

None.

**REFERENCES**