CASE REPORT

A perianal presentation of myeloid sarcoma

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SUMMARY

Myeloid sarcoma is a rare tumour associated with acute myeloid leukaemia (AML). Infrequently, it can occur in myelodysplastic/myeloproliferative overlap syndrome conditions such as chronic monomyelocytic leukaemia (CMML), where it often heralds the transformation towards an AML. We discuss a rare presentation of myeloid sarcoma in the perianal region of a 51-year-old man, who was seen by various clinicians and treated for haemorrhoids and perianal abscess. There were no gross abnormalities in initial haematological investigations and the patient was systemically well. A histological biopsy demonstrated myeloid sarcoma and bone marrow aspirate, and trephine confirmed CMML transforming to AML. Treatment of myeloid sarcoma is dependent on whether there is associated AML in the bone marrow. Dual chemotherapy with cytarabine and daunorubicin remains the gold standard treatment in these patients. Sending histology samples of atypical lesions when performing incision and drainage procedures is extremely important, as it contributes to early detection of rare and malignant tissue diagnoses.

BACKGROUND

Myeloid sarcoma is a rare tumour occurring in patients with myelodysplastic conditions. Its presence is associated more closely with acute leukaemias, particularly acute myeloid leukaemia (AML), and can indicate transformation from chronic to acute leukaemia. Myeloid sarcoma can also occur in isolation as a primary, non-leukaemic tumour (incidence of less than 2 in 1 000 000). These tumours were first described in 1811, however, they were not classified as 'chloromas' (due to the interaction of their myeloperoxidase content with air resulting in a greenish histological tinge) by King *et al* until 1853.^{1,2} Owing to the scarcity of cases and the frequency of misdiagnosis as large cell lymphoma (up to 75% in one case series),³ patient demographic data are limited, but it has been described in a wide age-range of patients (from 2 to 81 years in one series, mean 48 years).⁴

Clinical and histological diagnosis remains challenging. The presentation is typically with a solitary nodule with surrounding pain and symptoms related to the size and location of the tumour. Histological diagnosis is relatively complex, requiring a high index of suspicion and an understanding that some AML immunohistochemical markers may be negative. If myeloid sarcoma is suspected, a confirmatory bone marrow biopsy is indicated to investigate whether there is concurrent leukaemia.

Myeloid sarcomas most commonly occur in the soft tissues, peritoneum, lymphatic system and gastrointestinal tract. The literature reports only

one case, by Sen *et al*,⁵ of myeloid sarcoma presenting in the perianal region in a woman in the Indian subcontinent.

We report a case of myeloid sarcoma in an unusual anatomical location, which highlights the need for histological diagnosis and a high index of clinical suspicion when physicians examine perianal lesions and when surgeons perform incision and drainage of abscesses.

CASE PRESENTATION

A 51-year-old man of South East Asian descent presented to our emergency department with a 7-day history of a tender, perianal lesion and associated abscess. The lesion was first noticed by the patient 2 months earlier and was initially diagnosed as haemorrhoids. The lesion was located intimately related to the anal sphincter towards the left buttock, immediately inferolateral to the natal cleft. It was over 5 cm in diameter and ovoid in shape with an erythematous, inflammatory appearance (figure 1). The lesion was well defined and it was exquisitely tender on palpation. A combination of blood and pus could be expressed from the site. There was no associated lymphadenopathy in the inguinal region. The patient had no significant medical history, but carried a maternally inherited thalassaemia trait. He had no further family history, took no regular medications and was a non-smoker.

The patient was referred to a general surgeon who diagnosed a perianal abscess, and underwent an elective examination under anaesthetic (EUA) with proctosigmoidoscopy and drainage of his perianal lesion. The material was sent for bacterial and fungal cultures and histology. Two days later the patient became progressively unwell, with decreased appetite, fevers, painful discharge from the lesion, tachycardia, tachypnoea and hypotension.

Figure 1 A photograph showing the perianal lesion post-incision and drainage.

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Figure 2 MRI of the pelvis showing a fistula across the anal sphincter inferiorly and a horseshoe abscess extending into the left natal cleft.

A further diagnosis of infected perianal abscess was made and a second EUA was performed, with incision and drainage of the abscess.

INVESTIGATIONS

At presentation, the patient's blood count was grossly normal, except for normocytic anaemia (haemoglobin 97 g/L, nucleated red blood cells 0.0 g/L) and a slightly raised white cell count ($11.2 \times 10^9/L$, reflecting a monocytosis of $2.5 \times 10^9/L$). Intraoperative cultures for aerobic/anaerobic bacteria and yeast/fungal spores failed to isolate any causative organism. MRI of the pelvis revealed a fistula crossing the anal sphincter at 6 o'clock (inferiorly) and a horseshoe abscess, which extended inferiorly into the left natal cleft (figure 2).

Histological sections obtained from the surgical drainage showed ulcerated skin with dermal perivascular infiltration by heterogeneous blast-like cells that were myeloperoxidase+ and CD68+, but glycophorin C- and CD61-, as well as being negative for the blast cell markers c-kit (CD117) and CD34 (figure 3).

A definitive diagnosis of myeloid sarcoma was made and the subtype regarded as being either CMML or AML (with

myelomonocytic differentiation). This is a difficult distinction on morphological and on immunohistochemical grounds, because the blast cell markers c-kit (CD117) and CD34 are frequently negative in myelomonocytic blast cells and the morphology of myelomonocytic blast cells is difficult to distinguish histologically from more mature myelomonocytic cells. This distinction therefore required detailed correlation between all available clinical and pathological parameters.⁶ Consequently, a bone marrow aspirate and trephine were performed. The bone marrow aspirate showed markedly hypercellular marrow with very few megakaryocytes and marked expansion of the myeloid series with maturation arrest. The majority of cells observed were myelocytes and medium-sized blasts, with no obvious dysplasia or Auer rods. The cell differential count was: neutrophils 1%, lymphocytes 6%, monocytes 0%, myelocytes 68%, nucleated RBCs 24% and blasts 6%. Trephine showed hypercellular (90%) bone marrow, in which all lineages were represented, but there was severe tri-lineage dysplasia with a very significant increase in the number of megakaryocytes. Approximately 15–20% of the total cells were c-kit+ myeloid blasts, most of which also expressed CD34, lysozyme and CD68. The appearances were those of CMML with at least an excess of blasts, but, as discussed above, not all myelomonocytic blasts expressed the blast cell markers, c-kit and CD34, meaning that it was not possible to determine with any certainty whether acute myelomonocytic leukaemia had supervened.⁶

A specific myeloid panel-targeted resequencing assay, a research test not yet validated for routine clinical use, detected the DNMT3A mutation.

The presence of myelomonocytic differentiation in the bone marrow mirrored that in the perianal lesion. Given the difficulties in determining when CMML has transformed to AML, detailed review of all available clinical and pathological parameters was undertaken and the diagnosis was felt to be most consistent with AML arising in CMML.

DIFFERENTIAL DIAGNOSIS

We have discussed a rare presentation of a perianal lesion due to a myeloid sarcoma. The common differentials to exclude are

Figure 3 Histological sections from the perianal region showed ulcerated skin, with the dermal perivascular infiltration by heterogeneous blast-like cells (H&E, A) that were myeloperoxidase+ (stained brown, B) and CD68+ (stained brown, C), but glycophorin C- and CD61-, as well as being negative for the blast cell markers c-kit (CD117) and CD34. Histological sections from the trephine showed hypercellular (90%) bone marrow, with severe tri-lineage dysplasia (stained brown, D). The majority of the cells were of myelomonocytic lineage and coexpressed myeloperoxidase (stained brown, E) lysozyme (stained brown, F) and CD68 (not shown); some of these expressed the blast markers c-kit (CD117) and CD34 (not shown). Scale bar (A) is 50 μ m.

abscesses of the anorectum/perianus, anal fistulae, manifestations of inflammatory bowel disease and infections.

In patients with recurrent abscesses, fistulas or non-healing wounds after surgical treatment, the differential diagnosis should be expanded to consider underlying disease such as primary anal and colorectal carcinomas, Crohn's disease should be reconsidered and, rarely, tuberculosis and sexually transmitted infections such as syphilis.

OUTCOME AND FOLLOW-UP

The patient was enrolled in the AML17 trial, which involved treatment with cytarabine and daunorubicin-based chemotherapy and showed a good response.

DISCUSSION

Perianal lesions are a commonly presented symptom to primary care physicians and general surgeons. Myeloid sarcoma presenting as perianal abscess is well documented in pre-existing leukaemia affecting around 7% of patients.⁷ However, there are few documented cases of perianal abscesses being a presenting feature of leukaemia. Myeloid sarcoma, a rare differential for a perianal lesion, occurs in patients with AML, but there has been only one reported case of perianal myeloid sarcoma as a presenting feature of AML.⁵ Myeloid sarcoma can be associated with myeloproliferative neoplasms (eg, chronic myeloid leukaemia), myelodysplastic syndromes and overlap syndromes between these two (eg, CMML), but can also occur in isolation.⁸

We conducted a literature search (February 2015) using the search string “myeloid sarcoma OR chloroma OR granulocytic sarcoma OR extramedullary myeloid tumour AND perianal” in the MEDLINE/PubMed database, with no date restrictions. Of the four papers our search returned, one was of a similar case to the one discussed here. The patient in this case was also from South-East Asia. The presentation was comparable, with a perianal lesion causing the patient discomfort, despite normal haematological tests, including a normal monocyte level of $1.0 \times 10^9/L$. In our case, the diagnosis of perianal abscess was made and, only after persistence of the lesion, was a wedge biopsy taken, which showed myeloid sarcoma histologically. AML was subsequently diagnosed.⁵

This is the first reported case of a perianal abscess due to myeloid sarcoma, in which the patient was shown to have CMML transforming to AML. Furthermore, the specific mutation noted, DNMT3A, has been shown to occur in 10% of patients with CMML and is associated with poor outcomes.⁹

This case demonstrates that all atypical perianal lesions should be biopsied. Although benefits of early management are not clear in patients with primary myeloid sarcoma, patients with myeloid sarcoma in the context of AML achieve complete remission in 65% of cases, with a median survival time of 20 months, if treated with various chemotherapy regimens,¹⁰ for example, idarubicin/fludarabine/daunorubicin and cytarabine or idarubicin/cyclophosphamide, cytarabine, topotecan and granulocyte colony-stimulating factor with or without additional radiotherapy. Early systemic chemotherapy decreases the rate of progression to acute leukaemia (41% vs 71% $p=0.001$) while increasing survival rates (>50% alive at 25-month median follow-up in treated groups vs 13-month survival for untreated group).¹¹ Progression to acute leukaemia is significantly longer in patients receiving chemotherapy compared with patients who received local excision surgery/radiotherapy.¹² Therefore,

accurate diagnosis and timely implementation of therapy are both key determinants of outcome.

Learning points

- ▶ It is important to be aware of the wide differential when considering anal lesions and imperative to think of small-print diagnoses in recurrent presentations in primary care.
- ▶ Histology is important when performing incision and drainage procedures, as it can reveal atypical presentations of potential malignant conditions.
- ▶ Myeloid sarcomas are a rare presentation of myelodysplastic/acute leukaemic disorders. They occur in almost every tissue type, but predominantly present in the skin as solid tumours composed of leukaemic cells.
- ▶ Myeloid sarcomas often hail the transformation of a chronic monomyelocytic leukaemia to an acute myeloid leukaemia, or the beginning of a ‘blast crisis’.
- ▶ Management of myeloid sarcomas should be under a multidisciplinary team, requiring close liaison between haematological and surgical teams, with chemotherapy rather than surgical intervention, as an initial treatment.

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Contributors PM was involved in the operative management of the patient and coauthored the case report.

Competing interests None declared.

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REFERENCES

- 1 Yilmaz AF, Saydam G, Sahin F, *et al.* Granulocytic sarcoma: a systematic review. *Am J Blood Res* 2013;3:265–70.
- 2 King A. A case of chloroma. *Mon J Med* 1853;17:97.
- 3 Meis JM, Butler JJ, Osborne BM, *et al.* Granulocytic sarcoma in nonleukemic patients. *Cancer* 1986;58:2697–709.
- 4 Neiman RS, Barcos M, Berard C, *et al.* Granulocytic sarcoma: a clinicopathologic study of 61 biopsied cases. *Cancer* 1981;48:1426–37.
- 5 Sen R, Singh S, Qury MS, *et al.* Chloroma of perianal region masquerading as perianal abscess. *Indian J Dermatol* 2013;58:85.
- 6 Swerdlow S, Campo E, Harris N, *et al.* *WHO classification of tumours of haematopoietic and lymphoid tissues*. 4th edn. Lyon, France: IARC Press, 2008.
- 7 Büyükaşık Y, Özcebe OI, Sayinalp N, *et al.* Perianal infections in patients with leukemia: importance of the course of neutrophil count. *Dis Colon Rectum* 1998;41:81–5.
- 8 Bakst RL, Tallman MS, Douer D, *et al.* How I treat extramedullary acute myeloid leukemia. *Blood* 2011;118:3785–93.
- 9 Jankowska AM, Makishima H, Tiu RV, *et al.* Mutational spectrum analysis of chronic myelomonocytic leukemia includes genes associated with epigenetic regulation: UTX, EZH2, and DNMT3A. *Blood* 2011;118:3932–41.
- 10 Tsimberidou AM, Kantarjian HM, Wen S, *et al.* Myeloid sarcoma is associated with superior event-free survival and overall survival compared with acute myeloid leukemia. *Cancer* 2008;113:1370–8.
- 11 Imrie KR, Kovacs MJ, Selby D, *et al.* Isolated chloroma: the effect of early antileukemic therapy. *Ann Intern Med* 1995;123:351–3.
- 12 Yamauchi K, Yasuda M. Comparison in treatments of nonleukemic granulocytic sarcoma: report of two cases and a review of 72 cases in the literature. *Cancer* 2002;94:1739–46.

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