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Case Report

Isolated Myeloid Sarcoma Masquerading as Scattered Abscesses in a Septic Patient: A Case Report and Literature Review

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Keywords
Myeloid sarcoma · Soft tissue lesions · Sepsis of unknown origin

Abstract
Introduction: Myeloid sarcoma (MS) is also known as chloroma, extramedullary acute myeloid leukemia (AML), or granulocytic sarcoma. MS is a rare extramedullary infiltration of myeloid cells, most commonly collecting in the skin and causing a small number of localized lesions. It is strongly associated with AML; however, MS more commonly occurs after diagnosis of AML is previously established or after previous treatment of AML. ***Case Presentation:*** This case describes a patient with an atypical presentation of MS with no known history of AML and up to 18 lesions identified on CT scan that were previously being monitored for months by her primary care physician. She presented with sepsis attributed to choledocholithiasis versus bacteremia from scattered abscesses versus osteomyelitis of her left knee; nonetheless, lactic acid failed to improve after common bile duct stent with biliary sphincterotomy/dilation or with incision and drainage and empiric antibiotics. Core needle biopsy of her left abdominal sidewall was eventually positive for MS, but she unfortunately developed multiorgan failure with symptomatic hypercalcemia refractory to treatment and ultimately decided to go to comfort care rather than pursue further workup and treatment. Although bone marrow biopsy was ultimately not performed to rule out synchronous AML, this is likely a case of isolated MS due to her scattered skin lesions being present for months prior to hospitalization and acute illness. ***Conclusion:*** This case highlights the importance of maintaining MS in the differential diagnosis and the importance of early diagnostic core needle biopsy for patients with persistent skin lesions of unknown origin.

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Introduction

Myeloid sarcoma (MS) was initially named chloroma due to the green color of tumor secondary to high myeloperoxidase (MPO) expression; however, around 30% of cases do not show MPO positivity [1]. In 80–90% of MS patients, the disease develops in conjunction with acute myeloid leukemia (AML) either at diagnosis or later in the disease course [2]. Isolated MS (presence of a soft tissue mass in the absence of the diagnosis of AML) is rare with an incidence of 2 in 1,000,000 adults [3] and accounts for only 0.7% of AML cases [4], while 2–8% of newly diagnosed AML cases have synchronous MS [2]. If left untreated without anti-leukemic chemotherapy, it was shown that 71% of isolated MS develops into AML within 9 months compared to 41% who received treatment [5]. Isolated MS may also signal initial relapse for patients previously treated for AML with hematopoietic stem cell transplant in up to 15% of patients [2]. The median time from transplant to isolated MS relapse for patients in first complete remission is 6–12 months and relapses that occur 10 years after transplant are commonly isolated MS [2]. Here we present a case of isolated MS which was complicated by a septic presentation that was originally attributed to choledocholithiasis versus skin abscesses versus osteomyelitis of her left knee.

Case Report

A 76-year-old female with a past medical history of bilateral knee osteoarthritis, previous tobacco use, cirrhosis, esophageal varices, and hypothyroidism presented to an outside hospital emergency department for increasing fatigue, weakness, intolerance to cold, and 60–90 pounds of weight loss over the past year. She also had a painful mass in her right lateral abdominal wall and "bumps" in multiple parts of her body that her PCP previously had recommended observation for. These "bumps" involved both sides of her abdomen, right axilla, and right knee area. On presentation to the emergency department, she was tachycardic with a heart rate of 115 along with the following labs included in Tables 1 and 2.

CT abdomen/pelvis with contrast (Fig. 1) showed distension of the gallbladder as well as intrahepatic and extrahepatic biliary ductal dilation and luminal filling defects in the common bile duct related to 1.5 cm masses versus stones in both the mid-common bile duct and near the ampulla. CT demonstrated more than 18 subcutaneous soft tissue masses ranging from 0.5 to 5.5 cm in diameter, scattered circumferentially around the abdomen and extending to the proximal lower extremities. Additional findings included a 1.7 cm left lower lobe pulmonary nodule and small right pulmonary nodules, endometrial thickening, and moderate ascites. The patient received a sepsis bolus, was started on vancomycin and piperacillin/tazobactam, and was transferred for GI evaluation with possible endoscopic ultrasound/endoscopic retrograde cholangiopancreatography.

Lactic acid continued to be elevated at 6.5 after 18 h. Persistent lactic acidosis was then attributed to Type B lactic acidosis in setting of hepatic dysfunction/hepatitis after an additional 2 L bolus failed to reduce lactic acid. Endoscopic ultrasound/endoscopic retrograde cholangiopancreatography was performed, finding esophageal varices and 2 large common bile duct stones that were unable to be removed. Common bile duct stent was placed, and biliary sphincterotomy/dilation was performed. She became hypotensive requiring phenylephrine pushes postoperatively and was briefly transferred to the ICU. Right hip mass aspiration at bedside was unsuccessful. Incision and drainage was initially deferred due to worsening anemia with a hemoglobin level of 10 and thrombocytopenia with platelets around 50. Incision and drainage of the right lower abdomen were performed a few days later with culture studies, and the right axillary eschar was excised. Additional maintenance fluids failed

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Table 1. CBC on admission

WBC	**3.8 L**
RBC	3.58
Hemoglobin	**10.6 L**
Hematocrit	**31.8 L**
MCV	89
MCH	29.6
MCHC	33.3
RDW	**18.8 H**
MPV	10.6
Platelet count	**74 L**
RBC morphology	Normal
Segs relative	41
Segs absolute	1.6
Bands absolute	0.8
Lymphocytes Abs	1.0
Monocytes %	2
Monocytes Abs	0.3
Eosinophils %	2
Eosinophils Abs	0.1
Reactive lymphocytes	**1+**
Myelocytes %	2
Metamyelocytes Abs	0.0
Neutrophil Abs	2.4

Bolded values in the tables indicate abnormal lab values, with L representing low values and H representing high values.

to reduce lactic acid levels with lactic acid remaining elevated around 6. INR increased to 1.9 and the patient received IV vitamin K to allow for CT-guided right abdominal sidewall mass biopsy along with CT-guided paracentesis. Peritoneal fluid showed atypical cells with scattered mitotic features, not definitively diagnostic of malignancy as well as a total nucleated cell count of 56 with 0% neutrophils and few gram-negative rods that did not grow on culture. Initial biopsy of the right abdominal sidewall mass was indeterminate due to diffuse necrotic tissue, prompting biopsy at the left abdominal sidewall. Patient was found to be positive for *Staphylococcus capitis* in 2 out of 2 blood culture samples with positive Hep B surface antigen as well. On the second day of hospitalization, piperacillin/tazobactam was changed to ceftriaxone and metronidazole for erythema and weeping nodules present in the right groin and axilla.

Repeat CT chest re-demonstrated the 2 cm nodule in the left lower lobe of the lung and resolution of prior right lung nodules. MRI of the left knee to rule out left knee abscess/septic arthritis versus Baker's cyst was performed (Fig. 2). This showed concern for possible septic arthritis with superimposed osteomyelitis of the left medial and lateral tibial plateaus in addition to an anteromedial enhancing fluid collection concerning an abscess. The left knee was aspirated with findings of a monocyte predominance; aspirated fluid was negative for crystals or bacteria. Antibodies for Chlamydia psittaci were negative, and the patient was

Table 2. CMP and lactic acid on admission

Sodium	145
Potassium	3.9
Chloride	**111 H**
CO_2	27
BUN	22
Creatinine	0.88
Glucose	84
Calcium	5
Alkaline phosphatase	**714 H**
Albumin	**1.7 L**
Total protein	**4.7 L**
Globulin	3.0
AST	**147 H**
ALT	55
Bilirubin, total	1.5
eGFR	**68 L**
Lactic acid	**3.4 H**

Bolded values in the tables indicate abnormal lab values, with L representing low values and H representing high values.

changed from vancomycin to doxycycline. Fluconazole was started for vaginal candidiasis. Rheumatology was consulted for possible polyarteritis nodosa versus pyoderma gangrenosum; however, ANCA testing was negative.

The patient developed an acute kidney injury with creatinine 1.3 likely secondary to cardiorenal versus hepatorenal syndrome and was started on a continuous IV infusion of furosemide without response. Since admission, her cumulative net fluid balance has increased to 14 L with borderline blood pressures. Low urine sodium <5 ruled out acute tubular necrosis. Labs suggested against tumor lysis syndrome with elevated calcium, low phosphorus, and normal uric acid. Acute interstitial nephritis was considered secondary to antibiotics received during hospitalization. Albumin 25% 12 g every 8 h was started in addition to the continuous IV infusion of furosemide, which improved urine output. She received pamidronate without robust response for hypercalcemia that was persistently elevated >12, likely due to malignancy with low parathyroid hormone, a normal Vit D-25-OH level, and a chloride-to-phosphorous ratio of 39, suggestive of parathyroid hormone-mediated process. She was trialed on calcitonin without improvement of hypercalcemia. The patient developed hypoglycemia and remained hypoglycemic despite dextrose at 10% in water infusion. She was transitioned to dextrose 50% in water at 75 cc/h. Palliative care was consulted, and the patient wished to remain full code. She was started on gabapentin and dronabinol 2.5 mg twice daily with only mild improvement in appetite.

After 2 weeks into the hospitalization, the core biopsy preliminary pathology report of the left abdominal sidewall resulted with high-grade hematolymphoid neoplasm with differential including MS and blastic plasmacytoid dendritic cell neoplasm. The patient demonstrated difficulty maintaining alertness and was unable to make decisions (thought to be due to refractory hypercalcemia). Bone marrow biopsy and aggressive anti-cancer therapy were deferred until goals of care discussion with family and correction of hypercalcemia. Antibiotics

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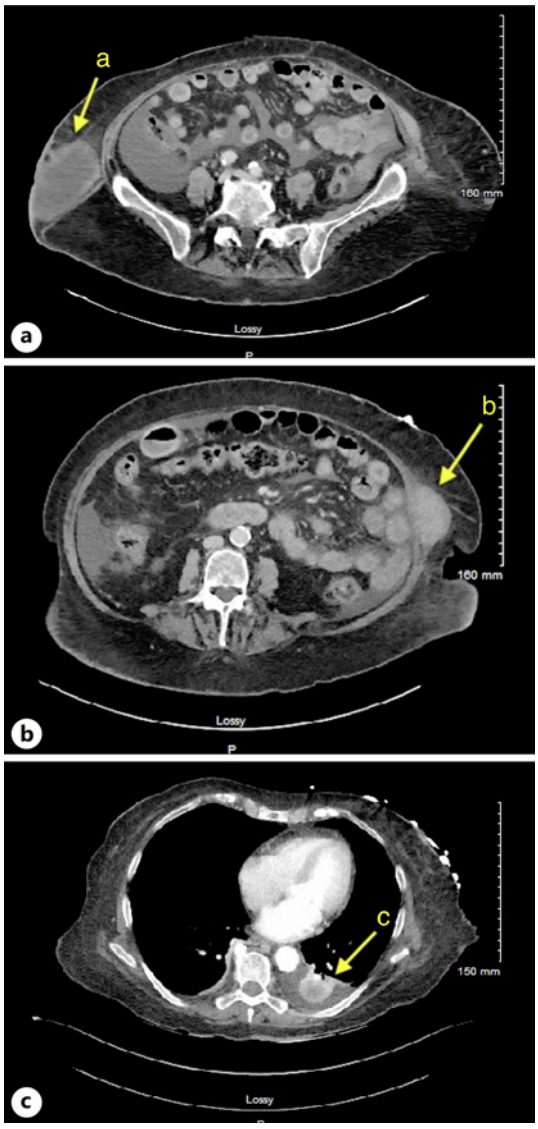

Fig. 1. CT findings. **a** Right abdominal wall 6.3 × 5.5 × 5.5 cm peripherally enhancing mass with central low-attenuation. **b** Left abdominal wall 5.6 × 3.4 × 12.2 cm enhancing mass. **c** Left lower lobe 2 cm pulmonary nodule.

and continuous IV infusion of furosemide were discontinued. The patient declined recommended Dobhoff nutrition. Lactic acid continued to worsen up to 21 despite ½ normal saline with 3 ampoules of sodium bicarbonate at 150 mL/h. Palliative care had discussion with family and decided to transition to comfort care when additional family arrived. The final pathology report from the left abdominal sidewall, core biopsy resulted in a positive for MS rather than blastic plasmacytoid dendritic cell neoplasm. The immunohistochemistry was positive for lysozyme and MPO while negative for CD56 and TdT, and only rarely positive for TCL1 (Fig. 3, 4). The patient's additional family arrived, all IV's were turned off, and the patient unfortunately passed away. The clinical course timeline summary can be seen in Figure 5.

Discussion

This patient had a complex presentation, and it has been reported that, historically, up to 75% of isolated MS cases have been misdiagnosed [6]. With recent advancements in flow cytometry, immunohistochemistry, and FISH, the misdiagnosis rate is now around 25–47%

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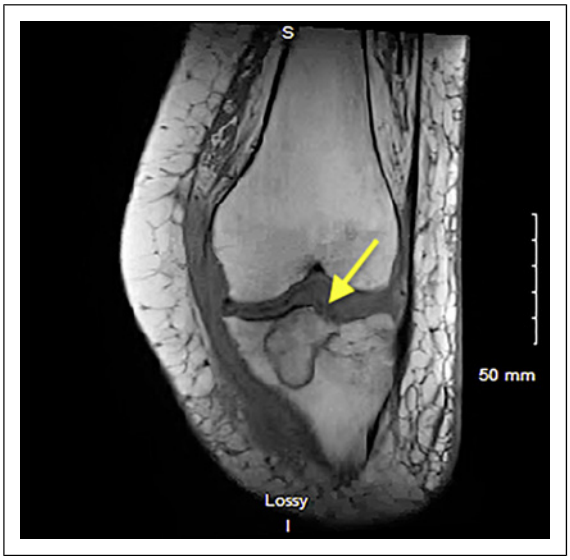

Fig. 2. MRI left knee with anteromedial 1.8 × 3.9 cm enhancing fluid collection concerning for abscess.

[1]. While the most common location for MS is in the visceral soft tissue [7, 8], this patient had an atypical presentation by having 18 soft tissue masses identified on CT scan compared to a retrospective radiological study where greater than 95% of patients with MS had 3 or less localizations with a mean value of 44.9 ± 27.8 mm [7]. With *Staphylococcus capitis* bacteremia on admission, it is possible that this patient had a combination of multiple MS lesions in addition to multiple abscesses, totaling up to the 18 lesions identified on CT scan; however, multiple wound cultures and paracentesis were negative for bacteria, and the patient failed to improve after adequate coverage with empiric antibiotics along with incision and drainage. It is also important to note that bone marrow biopsy with cytogenetic analysis was ultimately unable to be performed for this patient prior to transitioning to comfort care status, and the thrombocytopenia attributed to sepsis could have also been secondary to bone marrow dysfunction. This patient may have acutely developed AML, as described in a similar case report where a patient complained of pain secondary to MS for 17 months with normal bone marrow and peripheral blood examinations until the last month of her life where a diagnosis of AML was made [9].

The disease process of MS is still not completely understood; however, it may be facilitated by cell adhesion molecules, chemokine receptors/ligands, and aberrant FAS-MAPK/ERK signaling. It was previously theorized that homophilic binding of CD56 (neural cell adhesion molecule) from leukemic blasts to tissues expressing CD56 facilitated increased uptake of myeloid cells in localized tissue; however, it was later demonstrated that there was no significant difference in CD56-positive leukemic blasts in patients with or without MS [10]. CD11b (surface β2 integrin member macrophage 1 member) has been theorized to play a role in the development of MS due to a higher rate of CD11b blasts in patients with MS with concurrent AML compared to patients with AML alone. Although it was pointed out that the increased risk may be simply due to the monoblastic/myelomonocytic differentiation, leukemic cells with monoblastic/myelomonocytic differentiation have increased CD11b expression [2]. Also supporting the theory that monoblastic differentiation leads to increased risk of MS is the association with the somatic loss of RAS-MAPK/ERK signaling or metastasis-suppressor RAF kinase inhibitor protein in 50% of MS with synchronous AML cases compared to 14% of cases of AML alone [11]. Increased CCR5/CCL3 interaction and overexpression of CXCR4 and CXCR7 have also been observed in MS patients [12].

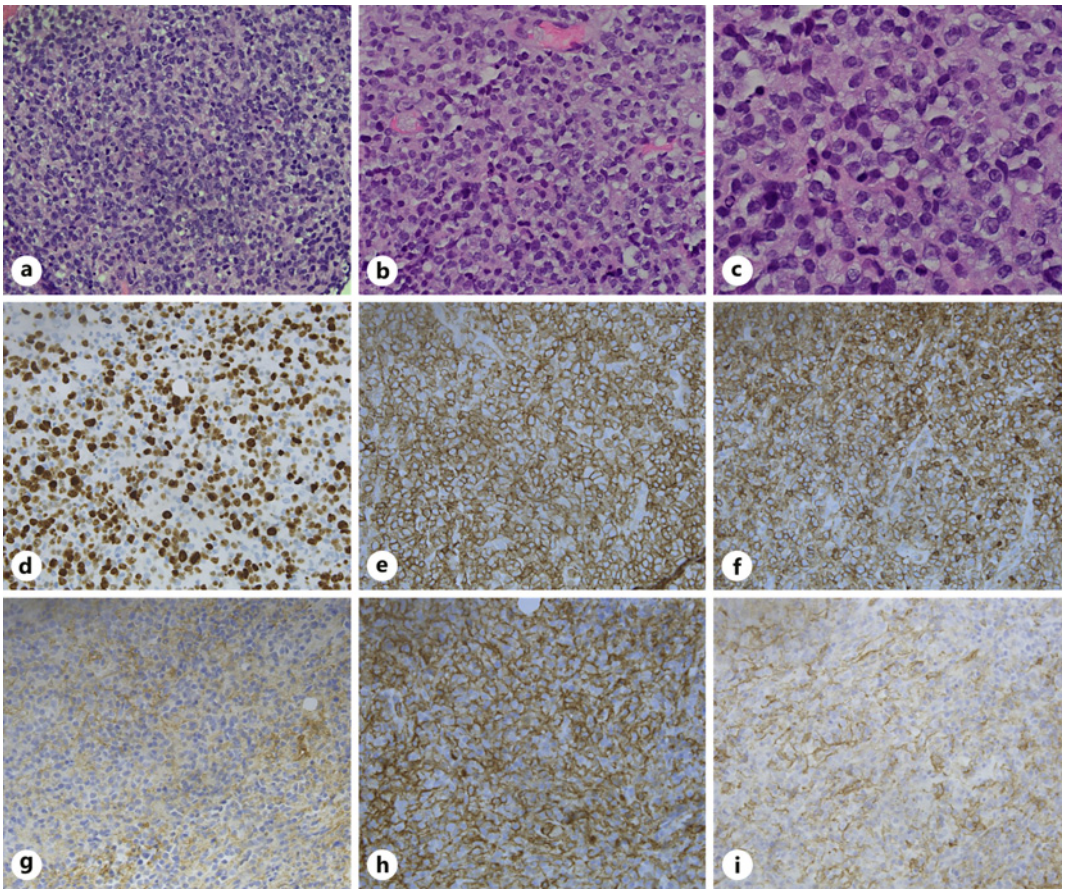

Fig. 3. Hematoxylin and eosin (H&E) and immunohistochemical stains of left abdominal sidewall mass. The H&E stains (**a–c** in order are at ×40, ×60, and ×100 magnifications) show large pleomorphic nuclei with irregular contour, immature chromatin, and prominent nucleoli. The immunohistochemical stains (at ×40 magnification) shown in figures (**d–i**) in order are Ki-67 (high-proliferative index), CD43 (positive), CD45 (positive), CD123 (weak and focal positivity), CD33 (positive), and CD14 (weak positivity).

When testing for MS, histological examination is used to classify into blastic, immature, or mature groups according to degree of myeloid differentiation [1]. Immunohistochemistry panel includes CD68-KP1 as the most commonly expressed marker, then MPO, CD117, CD99, CD68/PG-M1, lysozyme, CD34, terminal deoxynucleotidyl transferase, CD56, CD61, CD30, glycophorin A, and CD4 [1]. This panel differentiates MS from lymphoblastic lymphoma, Burkitt lymphoma, diffuse large B-cell lymphoma, blastic plasma dendritic neoplasm, neuroblastoma, rhabdomyosarcoma, primitive neuroectodermal tumor, and medulloblastoma [1]. The KI-67 index is frequently high (50–95%). While CD43 and lysozyme are viewed as the most sensitive markers for MS as there is a reported 100% expression in most case studies, they are not specific markers. MPO, which is expressed in 66–96% of MS cases, is used to differentiate MS from lymphoma, although MPO may be under-expressed in some monocytic or poorly differentiated MS [1, 13]. Cytogenetic studies for MS typically reveal a panel of different chromosomal abnormalities including: MLL rearrangement, t(8;21), monosomy 7, trisomy 8, trisomy 11, trisomy 4, inversion (16), monosomy 16,16q deletion, 5q deletion, and 20q deletion [1]. Patients with AML and t(8;21) have a higher incidence of

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Positive	Negative
Ki67: in >80% of cellularity	CD3
BCL6: Rare, weakly positive cells	CD20
MUM1: Rare positive cells	CD10
BCL2: Scattered positive cells	BCL1
CMYC: Weakly positive in majority of tumor cells	CD21
CD30: Weakly positive in a subset of tumor cells (~5%)	CD5
CD43: Diffusely positive	PAX5
CD45: Diffusely positive	CD138
MPO: Scattered positive cells	CD34
ERG highlights endothelial cells	CD2
CD68: Positive in a subset of tumor cells	TdT
Lysozyme: Positive in a subset of tumor cells	CD1a
CD4: Positive in a majority of tumor cells	CD117
CD123: Positive in a majority of tumor cells	CD56
CD33: Diffusely positive	AE1/3
CD14: Positive in a majority of tumor cells	CK8/18
TCL1: Rare positive cells	SOX10
	EBER (ISH)

Fig. 4. Immunohistochemistry of left abdominal sidewall lesion core biopsy.

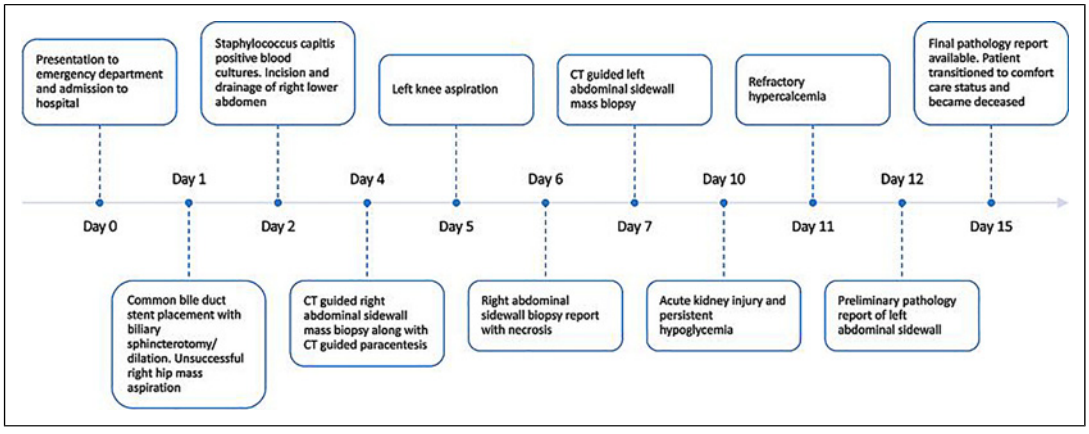

Fig. 5. Clinical course timeline.

up to 18% of developing MS with a less favorable prognosis [14]. This prompted researchers to suggest that those patients be considered for early aggressive therapy including bone marrow transplantation [14].

The treatment of MS involves using the same induction chemotherapy as would be used with AML with systemic idarubicin and cytarabine. Surgery and/or radiotherapy can also be used for symptomatic lesions or tumors causing local organ dysfunction/obstruction. Allogeneic hematopoietic stem cell transplantation is used for patients who achieved complete

remission with AML-induction protocols [15]. Prognostication is currently limited due to lack of large prospective series with the rarity of disease and the variation in tumor location, timing of presentation, tumor genetics, and treatment strategies [15]. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000535600).

Conclusion

The diagnosis of MS can be very difficult as presented above. This case is a reminder of the importance of early tissue biopsy for patients with persistent lactic acidosis and lesions of unknown origin. This case also highlights the importance of immunohistochemistry and cytogenetic testing for culture-negative lesions to diagnose and differentiate MS from other etiologies.

Statement of Ethics

Written informed consent was obtained from the patient's next of kin for publication of this case report and any accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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Author Contributions

Nicholas Nelson wrote the main text of the manuscript and collected photographs. Durva Masih assisted with the literature review and editing for the manuscript. Ahmed Sabri and FNU Monika prepared the biopsy H&E and IHC images seen in Figure 4 and reviewed the immunohistochemistry/cytogenetic section of the discussion. Muazzam Mirza treated the patient and provided mentorship and editing for the manuscript. All authors approved the final version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in the article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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