CASE REPORT

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Myeloid Sarcoma in the Sinonasal Cavity with Orbital Involvement: A Case Report

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ABSTRACT

Introduction: Myeloid sarcoma (MS) is a tumor mass that arises outside of the bone marrow area and is composed of either mature or not myeloid blasts of white blood cells. Acute myeloid leukemia (AML), chronic myeloid leukemia (CML) with an imminent blast crisis, and other underlying undiagnosed myeloproliferative disorders are frequently linked to MS, an uncommon disease. Without a history of leukemia, MS is difficult to diagnose and might be misdiagnosed for lymphoma or undifferentiated carcinoma. For patients, correct tissue diagnosis based on immunohistochemistry and histomorphology is important.

Case Presentation: Here, we present a 27-year-old woman who had a surgical procedure in The Department of Otorhinolaryngology-Head and Neck Surgery with the chief complaint of right nasal congestion and growing right eye protrusion. A solid mass in the right sinonasal region with infiltration into the retrobulbar area was confirmed by a head computed tomography (CT) scan. Cells with small to medium-sized cells, finely distributed chromatin, tiny nucleoli, and sparse cytoplasm were examined under a microscope. These cells were grouped in diffuse, linear, or Indian file patterns. Microscopic examination revealed morphology of myeloid tumor. Immunohistochemistry analysis emphasized the diagnosis of myeloid sarcoma. The patient then had chemotherapy, comprising of six cycles of docetaxel and carboplatin. After completing chemotherapy, a reduction in the size of the tumor mass was observed.

Conclusions: MS was diagnosed based on histological, radiographic, and immunohistochemical studies. Additional immunohistochemistry analysis testing is necessary to rule out a number of differential diagnoses when diagnosing MS in patients without a history of leukemia or hematological malignancy. The positive expression of myeloid markers such as CD68, CD15, CD33, and CD34 supports a diagnosis of MS.

INTRODUCTION

Myeloid sarcoma (MS) is a type of malignancy that develops outside of the bone marrow area and is caused by the growth of white blood myeloblastic cells, both mature and immature [1,2]. In 1811, MS was first described. Because myeloperoxidase (MPO) causes the internal cells to turn green, it is also known as a green tumor or chloroma. Granulocytic sarcoma was the designation given to it in 1966 due to differences in its microscopic appearance [2]. Subsequently, in 2002 the World Health Organization (WHO) declared this tumor an MS.

MS appears to be the most frequently used term [3]. Due to the rarity and difficulty of treating MS cases, there is no conclusive literature on the prevalence of myeloid MS worldwide. Acute myeloid leukemia (AML) patients are often affected by MS, which has an incidence rate of between 2.5–9.1% in the entire AML patient group [2,3]. Myelodysplastic or chronic myeloid leukemia (CML) with impending blast crisis are less common diseases that arise early in AML [2]. Primary MS, also known as isolated MS, is the state before cells invade the bone marrow in people who have no prior history of leukemia, myelodysplastic syndrome, or myeloproliferative neoplasm [3].

Imaging is the preferred technique since MS diagnosis requires the presence of a tumor mass that effaces local tissue [3]. Conventional imaging methods include

CT, MRI, and positron emission tomography (PET) [4]. The skin (leukemia cutis), lymph nodes, genitalia, gastrointestinal tract, bone, and central nervous system (CNS) are the areas most commonly affected [5]. The location influences how MS patients present clinically [6]. Granulocytic sarcoma, monoblastic or myelomonocytic sarcoma, megakaryoblastic/megakaryocytic sarcoma, and infrequently, erythroblastic sarcoma are the subtypes of MS that can be distinguished based on the hemato-pathological features.

According to the degree of maturation, the WHO divides MS into three subtypes: differentiated or mature, which has a preponderance of promyelocytes and more mature cells along with an abundance of eosinophils; blastic, which is characterized primarily by myeloblasts with little evidence of maturation; and immature, which is composed primarily by myeloblasts and promyelocytes [7]. When MS is poorly differentiated or there is no history of leukemia or hematological malignancy, diagnosis can be difficult. It may be mistaken for lymphoma, Ewing sarcoma, poorly differentiated carcinoma, or other hematological cancers when viewed under a light microscope. If the origin of the cells cannot be identified morphologically, further immunohistochemistry analysis is necessary.

Anti-CD34, anti-CD43, anti-CD45, anti-CD68, anti-CD56, anti-lysozyme, anti-myeloperoxidase, and anti-CD117 antibodies are used in immunohistochemical (IHC) staining for myeloid origin. MS also frequently expresses anti-CD11c, anti-CD13, and anti-CD33, while a smaller percentage expresses additional markers. Anti-MPO, anti-CD117, anti-CD99, anti-CD68/PG M1, anti-lysozyme, anti-CD34, anti-TdT, and anti-CD56 are the next most frequently expressed markers, after anti-CD68-KP1 [3,5].

CASE PRESENTATION

A 27-year-old woman presented with a chief complaint of right nasal obstruction that had been ongoing for four months before hospital admission, accompanied by increasing protrusion of the right eye. Initially, the patient reported nasal obstruction without epistaxis, nasal odor, or olfactory disturbances. Upon physical examination of the right ocular region, the patient presented conjunctival injection with proptosis and pain with or without applied pressure **(Figure 1A** and **1B).**

Subsequently, the physical examination extended to the right and left nasal cavities using a nasal endoscope. In the right nasal cavity, a narrowing of the nasal cavity was observed with a reddish-colored mass, hindering the assessment of other structures within the nasal cavity (**Figure 1C**). Conversely, the left nasal cavity exhibited signs of narrowing nasal cavity with serous secretions, eutrophic inferior turbinate, medial displacement due to mass, stomatal complex narrowing, and a mass on the nasopharyngeal wall (**Figure 1D**).

A computed tomography (CT) scan of the head was performed, showing the presence of a solid mass in the right sinonasal area with infiltration into the retrobulbar region, accompanied by the destruction of the sinus walls, nasal septum, cranial base, and infiltration into the parasellar area **(Figure 2)**.

On June 30, 2022, the patient underwent surgery to extirpate the sinonasal mass and FESS (Functional Endoscopic Sinus Surgery). Fragmented tissue was obtained and sent to The Pathology Department with a volume of approximately 3 cc and with dimensions of 0.4 x 0.3 x 0.1 cm, having a whitish-brown color, and displaying elastic consistency. The patient underwent routine blood laboratory tests revealing mild anemia, a slight decrease in hematocrit levels, and a minor increase in platelet and erythrocyte counts **(Table 1)**.

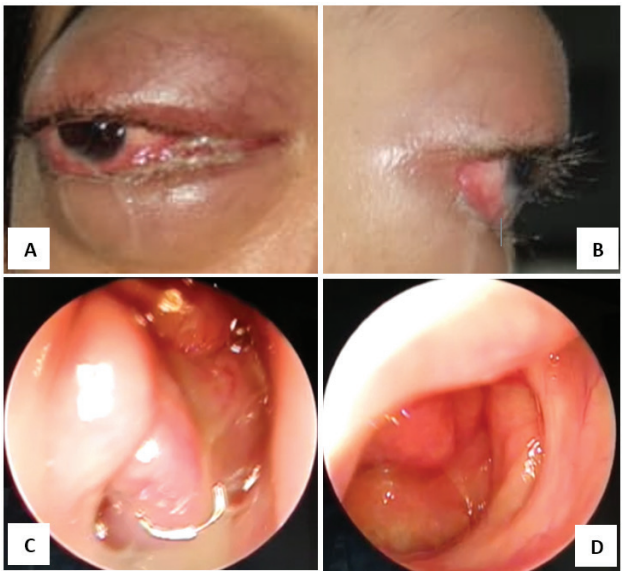

Figure 1. Local examination of the right eye region and an examination of the right eye showed proptosis and a red eye: (A) Anterior view; (B) Lateral view. The inspection of the right and left nasal cavity: (C) The right nasal cavity showed a narrowed nasal cavity with a reddish-colored mass, hindering the assessment of other structures within the nasal cavity; (D) The left nasal cavity demonstrated a narrowed nasal cavity with serous secretions, eutrophic inferior turbinate, medial displacement due to mass, and stomatal complex narrowing.

Table 1. The patient's blood count results

Tests	Value	Reference Value
Hb(g/dL)	10.3	11.40–15.00
WBC (x10^3/mm3)	9.38	4.73–10.89
Ht (%)	33	35–45
Platelet (x10^3/uL)	443	189–436
RBC (x10^6/mm3)	5.81	4.0–5.70
Differential Count	0/2/69/21/8	0–1/1–6/50–70/ 20–40/2–8

Hb=hemoglobin; WBC=white blood cells; Ht=hematocrit; RBC=red blood cell

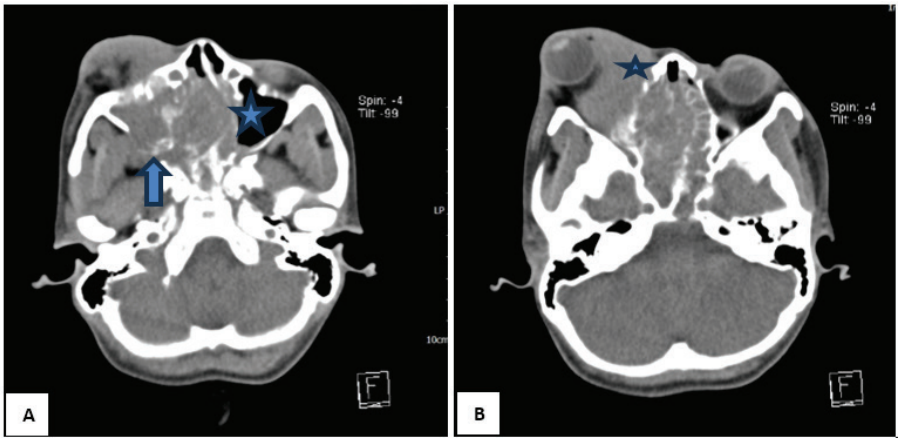

Figure 2. Head CT-Scan.
(A) A mass in the right maxillary sinus causing destruction of the sinus walls (arrow) and deviation of the nasal septum to the left (star); (B) Mass infiltration into the right medial rectus muscle and retrobulbar area (star).

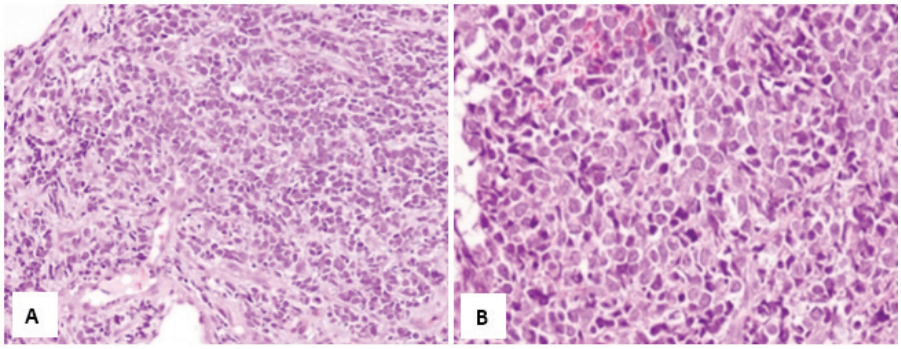

Figure 3. Microscopic view of the mass.
(A) The tumor cells were arranged in a linear pattern (H&E; X 100);
(B) Proliferation of round-oval nuclei cells with irregular nuclear membranes, finely dispersed chromatin, small nucleoli, and scanty cytoplasm (blast-like) (H&E; x400).

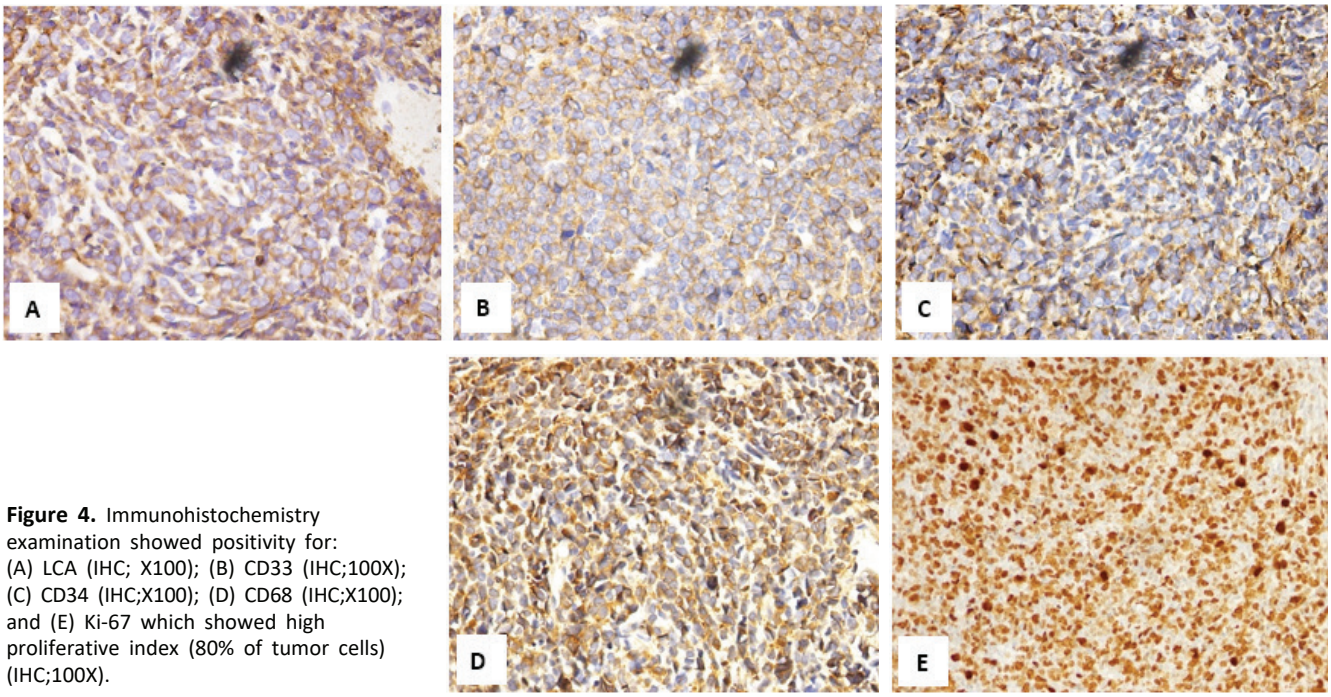

Figure 4. Immunohistochemistry examination showed positivity for:
(A) LCA (IHC; X100); (B) CD33 (IHC;100X); (C) CD34 (IHC;X100); (D) CD68 (IHC;X100); and (E) Ki-67 which showed high proliferative index (80% of tumor cells) (IHC;100X).

The tissue obtained from the sinonasal region was microscopically examined, revealing diffusely arranged blast cells in a linear or Indian file pattern **(Figure 3A).** The tumor mass consists of the proliferation of round-oval nuclei cells with irregular nuclear membranes, finely dispersed chromatin, small nucleoli, and scanty cytoplasm (blast-like) **(Figure 3B)**. Based on the morphology on microscopic examination, there are several differential diagnoses, namely non-Hodgkin lymphoma, neuroendocrine carcinoma, and undifferentiated carcinoma.

Further evaluation was carried out through an immunohistochemical (IHC) examination. Immunohistochemical examination revealed positive results for CD68-KP1, LCA, CD33, and Ki67, focal positivity for CD34 **(Figure 4),** as well as negative findings for CD20, CD3, CD15, AE1/3, MPO, CD56, chromogranin, synaptophysin, TdT, and CD117**.**

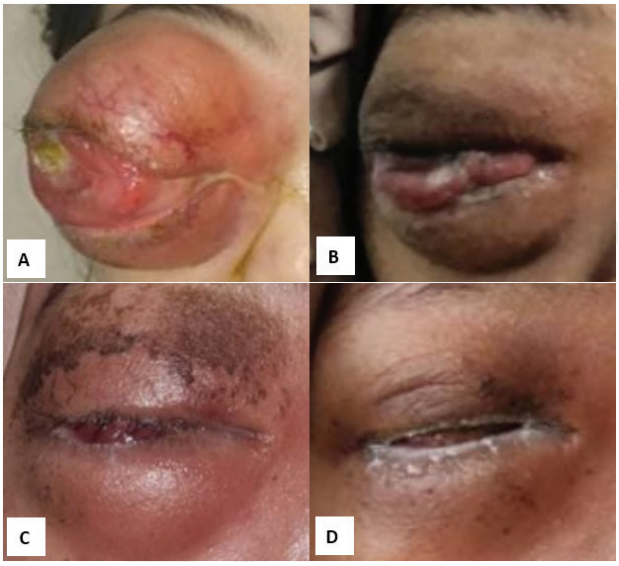

Figure 5. Clinical photographs of the patient. (A) and (B) pre-chemotherapy; (C) and (D) post-chemotherapy. There is a visible reduction in the orbital mass in the post-chemotherapy compared to the size of the tumor mass in pre-chemotherapy.

The diagnosis of MS was established based on histopathological, radiological, and immunohistochemical analyses. Afterward, the patient underwent chemotherapy involving six cycles of carboplatin and docetaxel. The chemotherapy was completed on December 29, 2022, and a reduction in tumor mass was observed **(Figure 5)**.

On 18 January 2023, the patient entered the hospital with complaints of headache for 2 months. Head contrast MRI (17 January 23) showed the impression of a solid mass residue in the nasal cavity. The patient was planned to undergo an elective VP Shunt but the patient and their family declined the procedure and she died at home.

DISCUSSION

Patients of any age can develop MS. The male-to-female ratio is somewhat higher at 1.2:1, with a mean age of 56 years and a range of 1 month to 89 years. Although this tumor can develop in any part of the body and at any age, it most frequently occurs in the skin, lymph nodes, and subperiosteal bone. Only a small percentage of cases report rhinopharyngeal involvement, with the orbital region, skull, and epidural space being the most commonly affected locations. The prevalence of head and neck involvement ranges from 12 to 43%. Common clinical signs of rhinopharyngeal MS include nasal congestion and hearing loss [8]. The patient in the case report reported having nasal congestion for four months, followed by eyeballs that were jutting forward more and more. Imaging is a crucial diagnostic and prognostic tool since multiple sclerosis can occur anywhere in the body. Since MS typically manifests as a soft tissue mass, CT imaging is typically the preferred modality [3].

According to histopathology, the tumor cells are usually tiny to medium-sized, with small nucleoli, finely scattered chromatin, round to oval nuclei, and a rapid rate of mitosis. Additionally, the size and development stages of these cells can vary. The cytoplasm exhibits either sparse cytoplasm or nuclei that are exposed [1,8]. The cellular structures of MS are scattered and lack clear borders. Closely spaced cells that exhibit solid patterns, infiltration, and occasionally linear or “Indian file” patterns might make up the tumor [6]. In this case, the tumor mass comprises small to medium-sized cells arranged diffusely that are closely adherent and densely arranged, with some of them exhibiting a linear or “Indian file” pattern. These cells possess round to oval nuclei, finely dispersed chromatin, small nucleoli, scanty cytoplasm, and easily identifiable atypical mitosis.

MS is infiltrated by myeloid cells, including myeloblasts, monoblasts, and less commonly, promyelocytes. As a result, it is divided into monoblasts, granulocytic sarcomas, and myelomonocytic sarcomas. Furthermore, it is divided into three categories according to the stage of development of the cells: blastic, immature, and mature. Blastic MS is composed of myeloblasts with low maturation. Immature MS is composed of myeloblasts, promyelocytes, and eosinophilic myelocytes. Mature MS is characterized by a high number of eosinophils, promyelocytes, and more developed cells. Either a diffuse pattern or an Indian file pattern is visible in the arrangement [3,4,7]. While monocytic neoplasms are more difficult to detect and require the use of immunohistochemistry and auxiliary tests like flow cytometry, fluorescence in situ hybridization (FISH), cytogenetics, and molecular studies, eosinophilic metamyelocytes are helpful diagnostic indicators in cases of granulocytic differentiation [5]. The diagnosis is further validated by immunophenotyping. While flow cytometric analysis can be performed on cell suspensions, immunohistochemistry on paraffin-embedded tissue slices is more commonly used for maturation evaluation and lineage affiliation identification [7].

MS are usually positive for myeloid and monocytic markers, i.e. CD33, CD68, lysozyme, and the more immature markers such as CD117 and CD34, CD61, glycophorin, CD4, etc. In addition, CD99 and TdT may also be positive. Moreover, CD56 can be detected in around 20% of MS cases [4]. The most reliable indicators for myeloid differentiation are MPO and CD117, but CD68 is the most widely expressed monocytic precursor marker [9]. MPO, a significant component of neutrophilic myeloid cells’ main granules, validates an MS/GS diagnosis. Although MPO is expressed in most MS/GSs, 30% of MS/GSs lack MPO, and some monocytic and poorly differentiated MS/GSs do not express it. Therefore, to validate the diagnosis of GS, other indicators must be present. The recent case’s negative MPO reactivity indicated a poorly differentiated MS/GS

with a bad prognosis [8]. Therefore, to validate the diagnosis of GS, other indicators must be present. The recent case's negative MPO reactivity indicated a poorly differentiated MS/GS with a bad prognosis [6].

Our cases demonstrated positive results of the IHC for CD68-KP1, LCA, CD33, and Ki67, focally positive for CD34, and negative results for CD20, CD3, CD15, AE 1/3, MPO, CD56, chromogranin, synaptophysin, TdT, and CD117. Positive results on CD68 and negative on MPO, tend to be monoblastic MS. Apart from that, the case showed negative results for CD 117 and TdT, which are markers expressed in immature type MS. Morphologically, it shows blast type cells and no eosinophils are found so it tends to be blastic type MS. CD20 and CD3 immunohistochemistry were conducted to rule out lymphoma, while AE 1/3, synaptophysin, and chromogranin IHC tests were performed to exclude neuroendocrine carcinoma and undifferentiated carcinoma.

Non-Hodgkin lymphoma (lymphoblastic, Burkitt, and diffuse large B-cell lymphomas), lymphoblastic leukemia, melanoma, Ewing's sarcoma (EES), primitive neuroectodermal tumor (PNET), rhabdomyosarcoma, neuroblastoma, medulloblastoma, and undifferentiated carcinoma are among the conditions from which MS needs to be distinguished.

Histopathologically, MS and NHL are similar in that they both show scattered cells, however, MS also shows positive results for myeloid differentiation marker and negative results for lymphocyte markers like CD3, CD20, CD79, and PAX5, as well as infiltration of immature granulocyte cells and an Indian file pattern. Meanwhile, MS and PNET/EES can have positive CD99 expression and similar cell size and morphology. However, PNET/ESS often manifests as a soft tissue mass, showing a lobulated or nodular pattern, and rosette formation. Furthermore, neuroendocrine markers such as synaptophysin and neuron-specific enolase (NSE) were shown to be positive in the immunohistochemistry analysis. Neuroblastoma, medulloblastoma, and embryonic rhabdomyosarcoma differ in their immunohistochemistry, morphology, and clinical characteristics [6].

Traditionally, MS has a very bad prognosis. Leukemia typically develops from untreated MS cases in 6–12 months [5,10]. De novo MS is thought to have a better clinical history than those that occur concurrently with AML, and the prognosis of MS is thought to depend on different MS characteristics. Since just mild anemia was identified in this patient and no other abnormalities were found in the laboratory testing, a bone marrow examination was not performed.

Treatment options include surgery, radiation, or both. Surgery is not necessary for MS patients with symptoms, but excision or debulking might be taken into consideration before the beginning treatment. In cases of isolated MS, poor response to the chemotherapy regimen, recurrence after bone marrow transplantation, and when prompt symptom relief is required, radiotherapy should be taken into consideration [3]. The main treatment option for both isolated MS and MS with concurrent bone marrow involvement is systemic chemotherapy. This is mainly because isolated or primary MS eventually leads to AML in most cases, even if there is no primary bone marrow involvement. As a result, MS chemotherapy regimens often adhere to the same guidelines as AML. Nevertheless, there is currently insufficient information to pinpoint a particular chemotherapy regimen that is advantageous for MS [4]. For all MS patients, cytarabine-containing remission induction chemotherapy is a common treatment strategy [11].

CONCLUSIONS

We report a case of primary MS without a history of leukemia or myeloid neoplasia. The immunohistochemical findings showed a positive result of CD68-KP1, LCA, CD33, and Ki67, focal positivity for CD34 resulting in a diagnosis of MS. Although MPO is the most frequently expressed marker in MS, 30% of cases did not express MPO. The absence of MPO expression can be found in cases of some minimally differentiated and monocytic MS/GS. In addition, negative reactivity for MPO leads to a diagnosis of poorly differentiated GS with a poor prognosis. The case report showed positive results on anti-CD 68 and negative on MPO, histopathologically showed blast-type cells, and no eosinophils were found so this case is a blastic-type monoblastic MS.

DECLARATIONS

Ethics approval and consent to participate

This case report is by the ethical guidelines applicable at Dr. Mohammad Hoesin General Hospital, Indonesia.

Competing interest

This case report received no external funding

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