

Histiocytic Sarcoma of Bone Marrow With Partial Cohesive Neoplastic Cells and Hemophagocytosis: a Case Report

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Case Report

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Abstract

Background: Histiocytic sarcoma (HS) is a rare hematolymphoid neoplasms whose cells show morphologic and immunophenotypic features of mature tissue histiocytes. We herein report a HS case without nodules or lymphadenectasis confirmed with the help of immunohistochemistry (IHC) on bone marrow (BM) biopsy and smear.

Case presentation: A 63-year-old female patient with a history of cerebral infarction presented with fever, retching and hypodynamic sign for three weeks. The peripheral blood examination showed aggressive pancytopenia accompanying with the positivity for Epstein-Barr virus (EBV) antibody. The computed tomography and abdomen ultrasound scan didn't reveal any nodules or lymphadenectasis other than hypersplenotrophy. Significantly, the BM aspirate shows vast pleomorphic tumor cells atypically distributed in both forms of single diffuse and cohesive. The hemophagocyte phagocytized granulocytes on BM smear exhibited the lymphoma related hemophagocytic syndrome. Immunohistochemically, neoplastic cells were immunopositively for macrophage-associated antigen cluster of CD4, CD68, CD163, but negative for the T-cell, B-cell and myeloid lineage markers of CD15, CD20, PAX-5, CD5, CD30, CD3, CD56, CD38, CD138, ALK and MPO, confirming the hypothesis of HS in BM.

Conclusion: The rare HS case of bone marrow with atypically partial cohesive pleomorphic tumor cells had the hemophagocytic syndrome, presented highly aggressive clinical course and challenged to the diagnoses.

Background

Histiocytic sarcoma (HS) is a rare hematopoietic neoplasm derived from the monocyte/macrophage system [1]. HS has a wide patient age range from infancy to old age with median age of 52 years and a slight male predominance [2]. Clinically, HS could affect solitary organs such as lymph nodes, gastrointestinal tract, soft tissue, skin, bone marrow, spleen and even central nervous system, usually associated with other analogical hematologic malignancies of follicular lymphoma, mantle cell lymphoma and acute/chronic lymphocytic leukemia [3, 4]. Given its rarity, complicated organs symptoms and histologic overlap with diverse mimics, the diagnosis of histiocytic sarcoma had been extremely challenged.

According to the 2016 World Health Organization (WHO) classifications, cytomorphology and immunohistochemistry generally help to strictly distinguish HS from B-cell, T-cell or anaplastic cell lymphoma, even other associated lymphocytic leukemia. HS cells are usually single diffuse variety in morphology and immunohistochemically positive for one or more histiocytic markers of CD68, CD163, lysozyme and CD4 [5]. We herein report a rapid invasiveness HS case without nodules and lymphadenectasis, involving a 63-year-old female patient diagnosed as bone marrow HS with atypically cohesive clusters neoplastic cell accompanying with EBV infection.

Case Presentation

A 63-year-old woman experienced retching, poor appetite, systemic hypodynamia and low-grade fever without any obvious incentive, who sought medical advice in the First Affiliated Hospital of Chengdu Medical College on April 29, 2019 and then suffered from the failure of antibiotic therapy. As the persistent fever and headache especially at night with a maximum temperature of 39 °C for 3 days, the patient was referred to the General Hospital of Western Theater Command PLA on May 18, 2019 for the evaluation of lacunar infarction and anemia. On physical examination, the subcutaneous nodule and superficial lymph node enlargement were not palpated. The peripheral blood examination showed aggressive pancytopenia with erythrocyte of $2.66 \times 10^{12}/L$, hemoglobin of 75 g/L, blood platelet count as 78×10^9 and erythrocytes sedimentation rate of 140 mm/h, accompanying severe infection with hypersensitive C-reactive protein of 137.3 mg/L, procalcitonin of 5.06 ng/mL and positive for Epstein-Barr virus antibody. The magnetic resonance imaging (MRI) on head identified that the lacunar ischemia scattered on the bilateral frontal parietal lobes. The abdomen ultrasound and contrast-enhanced computed tomography only revealed the hypersplenotrophy without any solid nodules or lymphadenectasis. BM biopsy and smear were performed for definitive diagnosis, followed by Wright–Giemsa staining for 25 min at room temperature and Hematoxylin-Eosin staining for 30 min at 37 °C. The BM biopsy revealed markedly tumor cell proliferation in the stroma of BM with diffuse architecture (Fig. 1). Moreover, the BM aspirate showed that BM karyocytes were active proliferation with abundant cohesive clusters or singly diffuse scattered malignancy cells in the scanning view (Fig. 2A-2C). These cells varied in morphology of irregular round, oval, spindle-shaped and tadpole shape with abundant basophilic cytoplasm, grooved, strip-like pleomorphic nuclei and faintly visible nucleoli. Furthermore, a frequent phenomenon that hemophagocyte phagocytized granulocytes, erythrocyte and pigment granules appeared in BM smear, which commonly hinted malignant histiocytosis, hemophagocytic syndrome, lymphoma and lymphocytic leukemia (Fig. 2D). Immunohistochemical staining of neoplastic cells (antibody dilution, 1:100; MaiXin, Technologies, Inc., FuJian, China) was negative for CD20, paired box PAX-5, CD5, CD30, CD3, CD56, CD15, CD38, CD138, ALK, MPO while it was positive for CD4, CD68, CD163 (Fig. 3), ruling out B-cell lymphoma, T-cell lymphoma, and myeloid origin. In view of the iconic immunohistochemical marker, abundant hemophagocytes and the positive EBV infection, this HS case was confirmed.

Unfortunately, the rapid invasiveness of HS gave rise to the patient's poor physical condition. The functional gastrointestinal disorders, pleural and abdominal pelvic effusion occurred successively within three days. Soon she had septic shock with electrolyte disturbance and metabolic acidosis on May 23, 2019 and finally died of respiratory failure on May 24, 2019. We were unable to collect more information on the cytogenetic or treatment of this HS case.

Discussion

Histiocytic sarcoma, also formerly known as “true histiocytic lymphoma”, is rare because of its prevalence rate less than 1% of all non-Hodgkin's lymphomas [4]. The differential diagnosis of HS

involves various lymphomas, histiocytic and dendritic cell neoplasms, melanomas, metastatic carcinoma and pleomorphic sarcomas [5], which is confronted with challenges of misdiagnosis and requires proficient recognition of clinic features, the atypical-morphology of tumor cell, the expression of histiocyte-associated makers.

Microscopically, HS is characterized by large and pleomorphic cells with “Pac-Man”-like nuclei and abundant vacuolated cytoplasm [6]. Commonly, a predominant noncohesive proliferation diffused among HS neoplastic cells, no matter in solid nodules with reactive eosinophilic infiltration stroma [7] or in bone marrow with abundant phagocytes [8]. Moreover, although the association of HS with other lymphocytic leukemia/lymphomas had been frequently reported in recent years, most of which still presented as the noncohesive or single diffuse proliferation cells in biopsy [9–11]. The atypical cohesive growth pattern of large neoplastic cells only appeared in several cases of B-cell lymphomas of plasma blastic lymphoma (PBL) [12, 13], T-cell lymphomas of anaplastic large cell lymphoma (ALCL) [14, 15], other metastatic carcinoma to bone marrow [16] and one case of classic Hodgkin lymphoma (CHL) [17]. Interestingly, in this case, a rare sight that neoplastic cell in tightness cohesive clusters with symplasm morphological was distinctly observed on this bone marrow smear, even accompanying with the hemophagocytosis and EBV infection. Thus the mimic cohesive morphology of large neoplastic cells deserves additional attention in terms of differential diagnosis for this case.

The immunohistochemistry (IHC) helps to differentiate HS from other large neoplastic cells lymphomas of B cell type or T cell type. WHO classified PBL as an uncommon mature B-cell lymphoma, occurring most frequently in HIV-positive patients, but exceptions do exist, which was characterized by positive expression of the following postgerminal centre B cell associated and plasma cell associated markers: multiple melanoma oncogene (MUM1) epithelial membrane antigen (EMA) and CD138 [13]. The ALCL is defined as a CD30 + peripheral T-cell neoplasm that is not reproducibly distinguishable on morphological grounds from ALCL-ALK+, but lacks the ALK protein and exists the case of ALCL-ALK- [18, 19]. This HS case is strictly profiled by the crucial marker of CD163, CD68 and CD4 [5, 20], differentiated with typical absence of CHL maker (CD15), myeloid maker (MPO), T cell of ALCL (CD30, ALK) and B cell (CD20, CD138, PAX-5).

Additionally, most studies have demonstrated that BRAF V600E mutations occur in nearly two-thirds of HS, while the tumor-suppressor gene CDKN2A was the frequently altered gene (46%) [21, 22]. A targeted next-generation sequencing (NGS) study recently demonstrated recurrent mutations activating the 57% mitogen-activated protein kinase (MAPK) pathway (MAP2K1, KRAS, NRAS, BRAF, PTPN11, NF1, CBL) and the 21% phosphoinositide 3-kinase (PI3K) pathway (PTEN, MTOR, PIK3R1, PIK3CA) in HS cases, respectively. Unfortunately, the death of our patient in this case terminated the gene-related determination. Anyway, these hadoop findings of gene mutation or arrangement should contribute to the diagnosis and treatment of HS.

Abbreviations

HS: Histiocytic sarcoma; BM: bone marrow; EBV: Epstein-Barr virus; WHO: World Health Organization; MRI: magnetic resonance imaging; PBL: plasma blastic lymphoma; ALCL: anaplastic large cell lymphoma; CHL: classic Hodgkin lymphoma; IHC: immunohistochemistry; MUM1: multiple melanoma oncogene; EMA: membrane antigen; NGS: next-generation sequencing; MAPK: mitogen-activated protein kinase.

Declarations

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Authors' contributions

Yang Liang performed histopathology analysis and wrote original draft; Yihua Chen took charge of project administration; Guangjie Wang provided the resources of patient's tissue samples. Li Mao contributed to the conceptualization and review&editing of manuscript.

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Availability of data and materials

is available upon request from the corresponding author

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of Chengdu Medical College (2019-E-65) and was performed in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

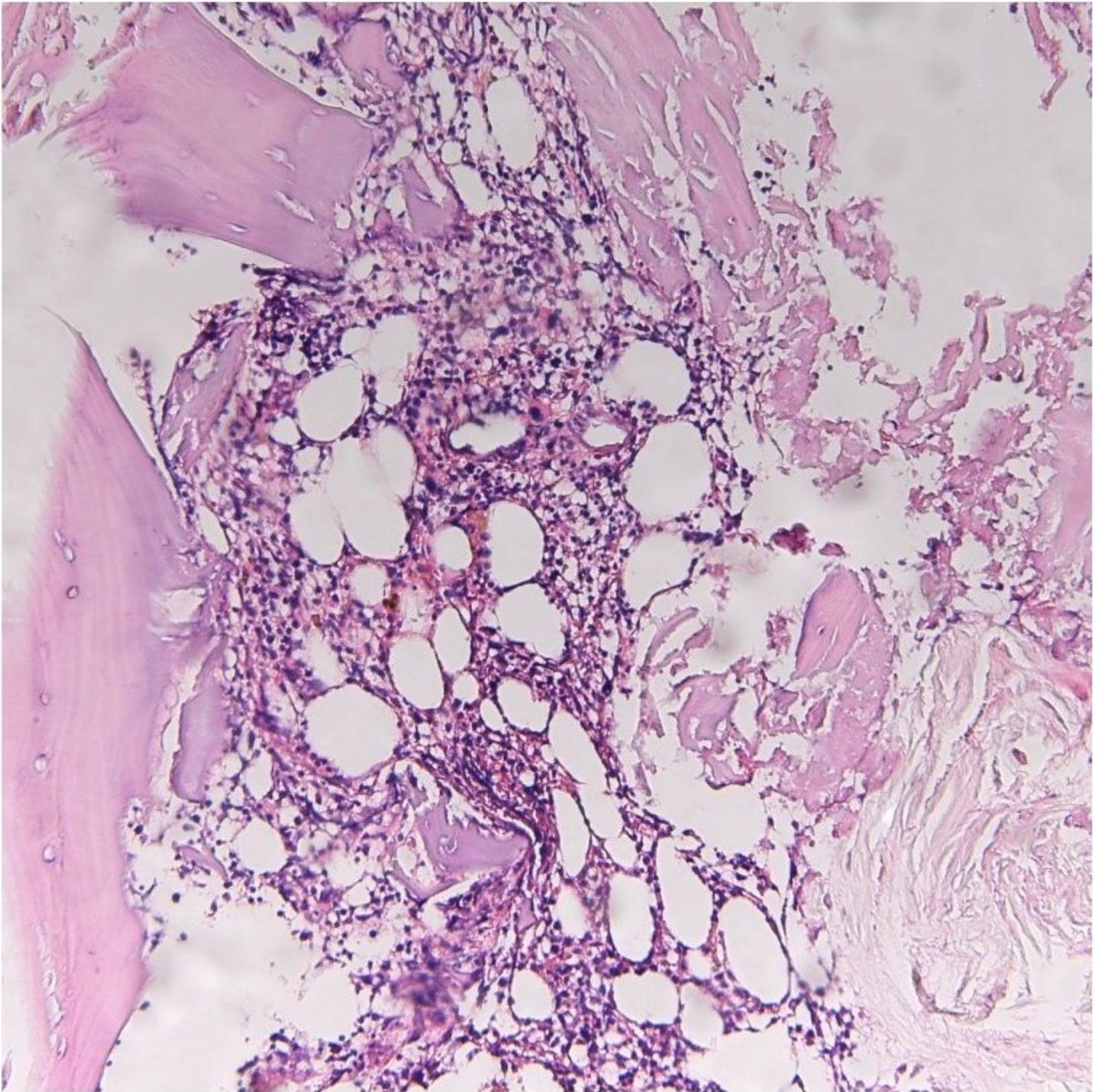


Figure 1

The karyocytes of BM are apparently active proliferation and some atypical neoplastic cells occur in the stroma of BM with diffuse architecture (hematoxylin and eosin stain, x100)

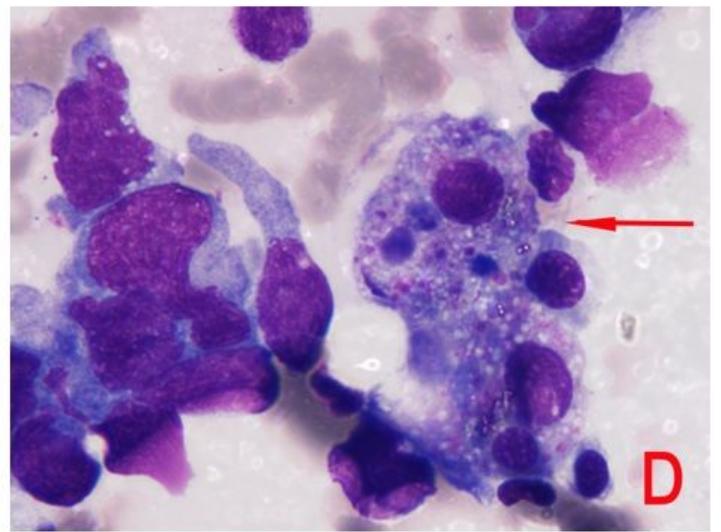
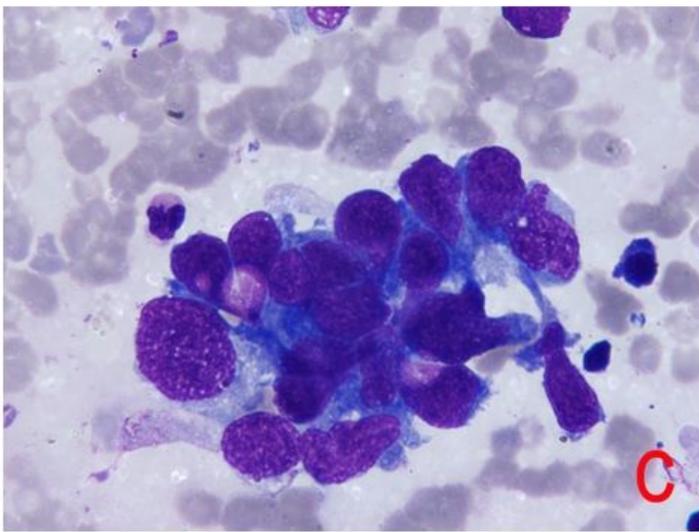
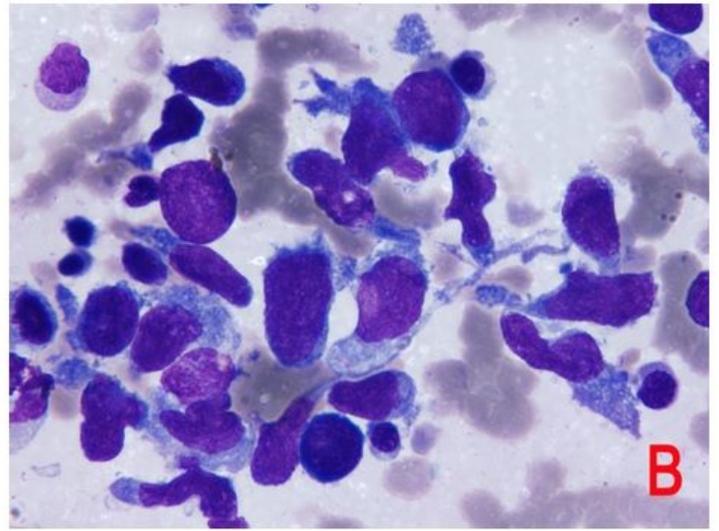
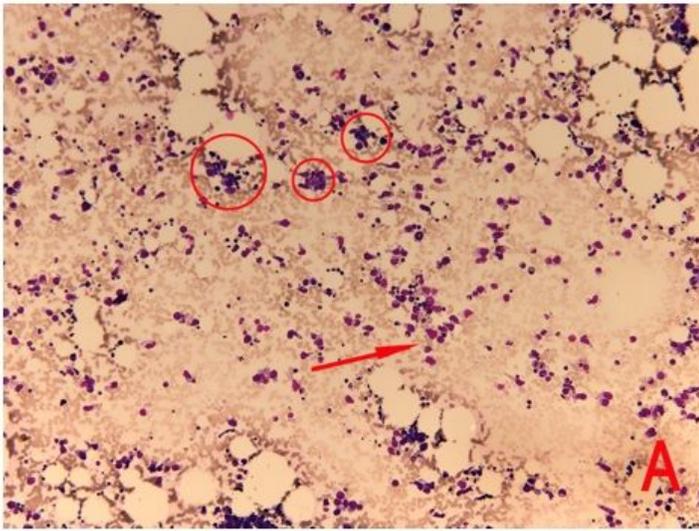


Figure 2

Cytologic findings of the bone marrow: karyocytes are active proliferation that are composed of 80% cohesive clusters (red roll) or singly scattered (A, red arrow) neoplastic cells and 20% normal myelocyte (Wright-Giemsa staining, x200); These cells are irregular round, oval, spindle-shaped and tadpole shape with basophilic cytoplasm, and the nuclei has some unconsPICuous nucleoli (B,C, Wright-Giemsa staining, x1000); Emophagocyte phagocytize granulocytes, erythrocyte and pigmentgranules (D, Wright-Giemsa stain, red arrow, x1000).

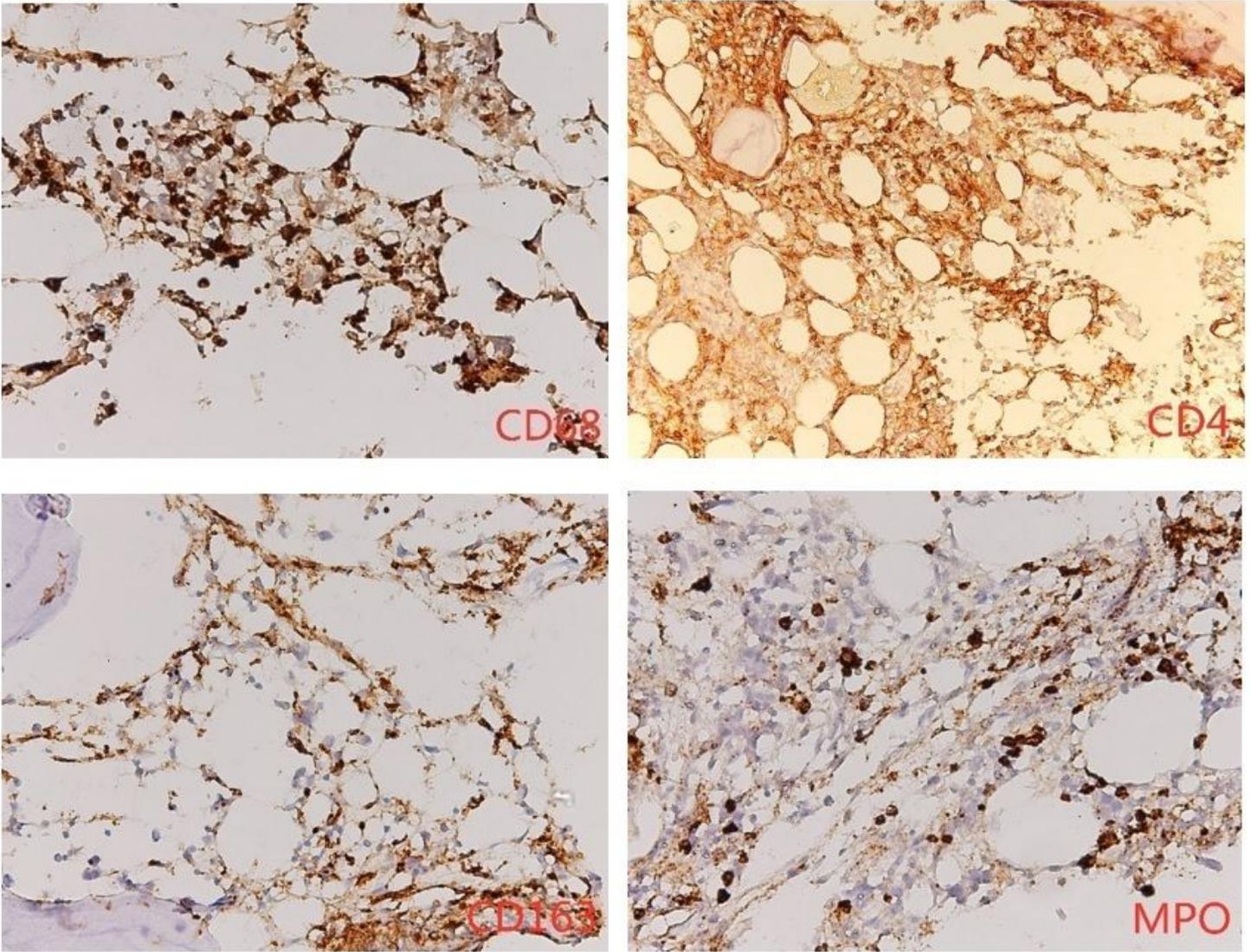


Figure 3

Immunohistochemical staining of neoplastic cells are positive for CD4, CD68 ,CD163 and negative for MPO (magnification, x 100)