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Original Paper

Myelodysplastic Syndrome Combined with Systemic Lupus Erythematosus: A Case Report

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Abstract

The literature on myelodysplastic syndrome combined with systemic lupus erythematosus is rarely reported. We reviewed and analysed the clinical data of a patient with myelodysplastic syndrome combined with systemic lupus erythematosus who had skin petechiae and fever as the main symptoms, and reviewed the relevant theories. There may be a close relationship between myelodysplastic syndrome and systemic lupus erythematosus, and further research is needed on the pathogenesis. When patients with autoimmune diseases (including systemic lupus erythematosus) presented with blood cell reduction，it is important to pay attention to them, and early bone marrow examination should be carried out to screen for the presence of hematological malignancies.

Keywords

Myelodysplastic syndrome, Systemic lupus erythematosus, Autoimmune disease, case report

1. Case Information

1.1 Medical History

The patient, female, 52 years old, presented to our hospital in November 2019 with a chief complaint of "diagnosed with myelodysplastic syndrome for over 2 years, with a 5-day history of fever". In May 2017, scattered bleeding spots appeared on the skin of both lower limbs without obvious triggers, which gradually increased with the course of the disease, and relevant examinations confirmed the diagnosis of "myelodysplastic syndrome". The patient underwent three cycles of chemotherapy with

the HAG (HHA 2mg on days 1, 3, 5, and 7; Ara-c 0.05 qd on days 1-14; G-CSF 150ug q12h on day 0) regimen, achieving complete remission. However, the patient refused further chemotherapy. 5 days ago, the patient had fever without any obvious triggering cause, and her temperature was up to 39.5℃, accompanied by cough and coughing up sputum, which was white mucous sputum, with no wheeze, and there was no discomfort such as panic, chest tightness, and abdominal pain. Blood routine examination revealed a white blood cell count of 1.23*10^9/L, red blood cell count of 3.13*10^12/L, hemoglobin level of 75g/L, platelet count of 46*10^9/L, absolute neutrophil count of 0.97*10^9/L, absolute lymphocyte count of 0.18*10^9/L, and absolute monocyte count of 0.00*10^9/L. Bone marrow cytological examination showed severe hypoplasia of bone marrow proliferation, with a granulocyte-to-erythrocyte ratio of 3.39:1. The proportion of cells in the granulocytic series accounted for 48%, with an increased proportion of segmented neutrophils and reduced proportions in other stages, without apparent morphological abnormalities. The proportion of cells in the erythroid series accounted for 14%, mainly composed of intermediate to late-stage erythroblasts, some of which exhibited irregular nuclear shapes or megaloblastic changes, accounting for 28%. The mature red blood cells varied in size. The proportion of cells in the lymphocytic series accounted for 34%, without apparent morphological abnormalities. Platelet production was observed, and two granular megakaryocytes were found in the entire slide. Flow cytometry analysis showed that primitive myeloid cells accounted for approximately 3.8% of all nucleated cells, with an increased proportion and reduced granularity. They expressed CD34HLADRbri, CD13, CD33, and partially expressed CD15, CD64, and CD38dim, but did not express CD56, CD7, CD96, CD19, CD15, CD14, or CD123. Conclusion: The proportion of primitive myeloid cells was increased, accounting for approximately 3.8% of all nucleated cells, with an increased proportion and reduced granularity, and an abnormal phenotype. Chromosomal examination report: [cp]45~47,XX,Ip-,-5,6q+,6p+,-7,-9,+9,9q+,-11, -14,-17,-18,-19，-20,+21, +mar1~mar3[8]. Conclusion: Few cells were analyzed, with only 8 cells in the metaphase phase available for analysis, demonstrating a highly complex mixed abnormal karyotype.

1.2 Previous Medical History and Physical Examination

The patient had a history of systemic lupus erythematosus for 4 years, presenting with symptoms of dry mouth, dry eyes, oral ulcers, and photosensitivity. The patient was on long-term treatment with hydroxychloroquine tablets at a dose of 0.2g twice daily.

Physical examination: T: 38.9℃, P: 85 beats/min, R: 19 breaths/min, BP: 140/103mmHg. The patient was conscious with an anemic appearance, and no enlargement of superficial lymph nodes. Heart rate was 76 bpm, with regular rhythm and strong heart sounds, without murmurs in the valve areas. The abdomen was soft, without tenderness or rebound tenderness. The liver and spleen were not palpable below the rib cage. Physiological reflexes were present, and pathological reflexes were absent. No edema was observed in the lower extremities.

Dermatological examination: The eyelids and cheeks (Figure 1) showed butterfly-shaped infiltrative and slightly edematous purplish-red patches. The boundaries of the patches were still clear, with a

darker center and bruising. Purple-black crusts were present in the central area of the cheek erythema, with dryness and no exudation. The anterior chest (Figure 2), upper extremities, and hands showed circular and annular erythematous plaques measuring 1-5cm in diameter. The erythematous edges were slightly elevated, with white scales and scabs, on the surface, some of which merged into larger patches. The lower extremities showed densely distributed petechiae and ecchymoses.

Figure 1. Facial Skin Lesions

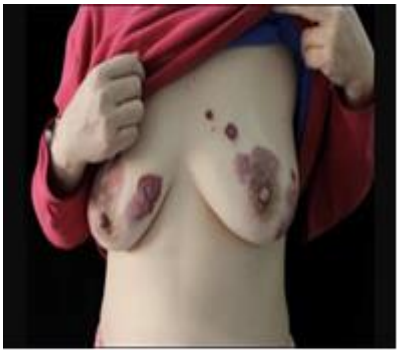

Figure 2. Anterior Chest Skin Lesions

1.3 Laboratory Examination

Histopathological examination(Figure 3): Marked hyperkeratosis was observed, with the epidermis generally normal. Basal cell liquefaction degeneration was present, and the superficial dermis showed a band-like infiltration of lymphocytes, accompanied by extensive bleeding. Lymphoid tissue cell infiltration was observed around the blood vessels in the mid to lower dermis. Diagnostic suggestion: The specimen exhibited hemorrhage accompanied by excessive keratosis, suggesting a possible association with a paraneoplastic tumor. Follow-up is recommended. Antinuclear antibody test: Antinuclear antibodies IgG (+), homogeneous type, titer 1:640; anti-ds-DNA antibodies IgG type 177.6IU/mL; anti-Sm antibodies (++); anti-SSA (++) antibodies; anti-nucleosome antibodies (+); anti-histone antibodies (+). Immunoglobulin G: 41.4g/L; Immunoglobulin A: 4.64g/L; Complement C3: 0.38g/L; Complement C4: 0.13g/L. Erythrocyte sedimentation rate: 88mm/h. No obvious abnormalities were found in hepatitis typing. Tuberculosis T-spot test: Negative. Treponema pallidum specific antibody TPPA (-).

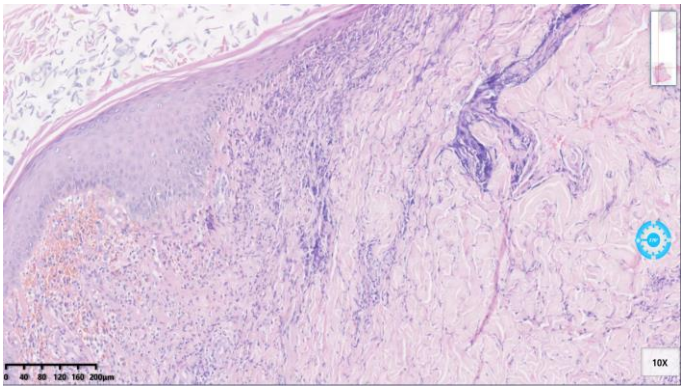

Figure 3. Histopathological Image 10x

1.4 Diagnosis and Treatment

Diagnosis: 1. Myelodysplastic syndrome 2. Systemic lupus erythematosus.

After admission, the patient received decitabine plus reduced-dose DA (DNR: 60mg on day 1, 40mg on days 2-3; Ara-C 0.1g q12h on days 1-7) chemotherapy. Post-treatment examination revealed white blood cell count (1.50-2.52)*10^9/L, hemoglobin level (75-96)g/L, platelet count (62-71)*10^9/L, and absolute neutrophil count (1.5-2.0)*10^9/L. Partial regression of lower extremity ecchymoses was observed. During hospitalization, the patient developed a mixed bacterial and fungal infection, which was treated with antibiotics (meropenem, linezolid) and antifungal agents (voriconazole, sulfonamides). The patient was discharged from the hospital with recovery of body temperature and improvement of the infectious symptoms.

2. Discussion

Myelodysplastic syndrome (MDS) is a hematopoietic stem cell disorder characterized by ineffective hematopoiesis in the bone marrow, peripheral blood cell reduction, and a tendency to progress to acute leukemia. It has a poor treatment response. Treatment options mainly depend on the patient's risk stratification and include immunomodulatory therapy, demethylating agents, and hematopoietic stem cell transplantation. Research has found a correlation between MDS and immune dysfunction, with possible lymphocyte clone abnormalities, T and B cell dysfunction, and the presence of autoantibodies in patients (Zhang, He, & Liu, 2007). The patient had a history of systemic lupus erythematosus, and this admission was accompanied by symptoms of butterfly erythema on the face, photosensitivity, and oral ulcers. Laboratory examination indicated leukopenia, thrombocytopenia, abnormal autoantibodies, and complement reduction, confirming the diagnosis of systemic lupus erythematosus (SLE). Systemic lupus erythematosus can involve multiple systems in the body, leading to blood cell reduction and impaired cellular immune function. The long-term use of immunosuppressive agents, viral infections, and genetic factors increase the risk of secondary tumors (Ladouceur, Bernatsky, Ramsey-Goldman, & Clarke, 2018). Research findings indicate that the incidence of hematological malignancies in SLE patients is approximately 2.75%, with non-Hodgkin lymphoma (NHL) being the main type, while reports of MDS

are rare (Liu, Zhang, Wang, Song, & Zhang, 2021; Gorshein, Weber, & Gore, 2020). Our center reported a case of MDS combined with SLE and reviewed the relevant literature.

The types of hematological malignancies that occur in SLE mainly include non-Hodgkin lymphoma, MDS, and acute myeloid leukemia (AML) (Lu, Bernatsky, Ramsey-Goldman, et al., 2013). There may be a close clinical connection between MDS and SLE. Immunosuppressive therapy, clinical factors, viral infections, and genetic factors may be risk factors for tumors in SLE patients. Approximately 20% of MDS or CMML patients may have systemic inflammation and autoimmune diseases (SIADS), and MDS patients with SIADS have a worse prognosis (Moura, Santiago, Neto, Gomes de Souza, & Moura, 2017). A report shows that SLE accounts for 30% of MDS patients with autoimmune disease (Mekinian, Grignano, Braun, et al., 2016). Conversely, patients with autoimmune diseases for 10 years or more have a higher risk of developing into MDS (Wilson, Neogi, Prout, & Jick, 2014). In a multicenter case-cohort study, Bernatsky et al. reported an increased risk of hematologic malignancies in SLE patients treated with immunosuppressive agents, which may be relevant, including cyclosporine, methotrexate, and azathioprine (Alexandra, Sasha, Rosalind, & Ann, 2018). Zhang Shengtao et al. reported 9 cases of rheumatic diseases combined with myelodysplastic syndrome, of which 4 cases had a history of rheumatic diseases before the diagnosis of MDS, and all 9 cases exhibited active rheumatic disease manifestations at the time of diagnosis. Among these 9 patients, 2 had combined rheumatoid arthritis, and 4 were diagnosed with SLE or SLE combined with polymyositis (Zhang, He, & Liu, 2007). According to a report, Some patients diagnosed with MDS have abnormalities in SLE and rheumatoid arthritis related anti autoantibodies before diagnosis (Kelmenson, Wagner, McNair, et al., 2020). Moura et al. reported a case of SLE combined with chronic myelomonocytic leukemia (formerly classified as a subtype of MDS, now an independent disease) and suggested conducting comprehensive bone marrow examinations when patients have abnormal blood counts (Moura, Santiago, Neto, Gomes de Souza, & Moura, 2017). These patients exhibited both immune dysfunction and hematopoietic dysfunction, possibly due to immune dysregulation leading to different rheumatic disease manifestations. A study comparing 2,471 MDS patients with 42,886 Medicare controls found that MDS patients were more likely to have autoimmune phenomena (23% vs. 14%), with the most common autoimmune diseases being chronic rheumatic heart disease, rheumatoid arthritis, myelodysplastic anemia, psoriasis, and rheumatic polymyalgia (Anderson, Pfeiffer, Landgren, Gadalla, Berndt, & Engels, 2009). Another analysis of 110 patients with autoimmune diseases with unexplained hematopenia found that unexplained hematopenia was an early manifestation of clonal hematological diseases represented by MDS, and there was a significant correlation between MDS and SLE (OR 1.82, 95% CI 1.04-3.16). It is also recommended that when the patient's examination reveals high serum iron, high MCV and presence of serum monoclonal band, bone marrow examination should be performed to exclude haematologic malignancy or bone marrow toxicity (Aristea, Panayiotis, et al., 2013). Amy et al. (2022) evaluated the association between autoimmune diseases and the risk of MDS in a

population-based study, and SLE is a potential elevated risk factor for individuals with MDS (Amy, Michelle, et al., 2022).

It has been found that prolonged immune stimulation promotes the aggregation of bone marrow-derived suppressor cells, and such aggregated suppressor cells release inhibitory cytokines, such as TGF-β and IL-10, which in turn cause a decrease in the number of blood cells and developmental abnormalities (Meirow, Kanterman, & Baniyash, 2015; Chen, Eksioglu, Zhou, et al., 2013). And this provides clues to the co-pathogenesis of MDS and autoimmune diseases. Other researchers have found that in high-risk MDS patients, there is an increase in the number of Tregs cells, which leads to the progression and worsening of both MDS and autoimmune diseases (AIDs) (Mailloux, Sugimori, Komrokji, et al., 2012; Kotsianidis, Bouchliou, Nakou, et al., 2009). However, studies have indicated that azacitidine has the capability to reduce the peripheral blood Tregs cell count (Costantini, Kordasti, Kulasekararaj, et al. 2013). Clinical studies concerning the concurrent occurrence of MDS and AIDs have revealed that upon reevaluation following azacitidine treatment, there is a decrease in the number of Tregs cells in peripheral blood. Simultaneously, clinical symptoms of MDS and AIDs have improved. This phenomenon suggests that the abnormality in T cells may be one of the mechanisms underlying the co-occurrence of MDS and AIDs (Al Ustwani, Ford, Sait, et al., 2013).

The molecular mechanisms underlying the occurrence of MDS and SLE are not fully understood, involving cytokines, stimulation of immunomodulatory drugs, immune cell disorders, and genetic polymorphisms. Bernatsky et al. found that SLE-related SNPs, such as CD40 rs4810485 and HLA rs1270942, may be associated with diffuse large B-cell lymphoma (DLBCL), and TNFAIP3 SNP rs7749323 may be associated with MALT lymphoma (Alexandra, Sasha, Rosalind, & Ann, 2018). The reduced number or dysfunction of regulatory T cells in MDS patients may be related to the development of autoimmune diseases (Mailloux & Young, 2010). However, further research is needed to determine whether these variations have predictive effects on the occurrence of MDS.

In conclusion, there may be a clinical connection between MDS and SLE, and the mechanisms underlying their development require further investigation. When SLE patients present with blood cell reduction, attention should be paid to that, and timely comprehensive bone marrow examination is recommended to screen for the presence of hematological malignancies and avoid misdiagnosis, enabling timely diagnosis and treatment.

References

Al Ustwani, O., Ford, L. A., Sait, S. J., et al. (2013). Myelodysplastic syndromes and autoimmune diseases--case series and review of literature. *Leukemia research, 37*(8), 894-9.

Alexandra Ladouceur, Sasha Bernatsky, Rosalind Ramsey-Goldman, & Ann E Clarke. (2018). Managing cancer risk in patients with systemic lupus erythematous. *Expert Review of Clinical Immunology*. http://doi.org/10.1080/1744666X.2018.1519394

Amy M Linabery, Michelle A Roesler, et al. (2022). Personal history of autoimmune disease and other medical conditions and risk of myelodysplastic syndromes. *Cancer epidemiology*, *76*, 102090. http://doi.org/10.1016/j.canep.2021.102090

Anderson, L. A., Pfeiffer, R. M., Landgren, O., Gadalla, S., Berndt, S. I., & Engels, E. A. (2009). Risks of myeloid malignancies in patients with autoimmune conditions. *br J Cancer*, *100*(5), 822-828.

Aristea Papageorgiou, Panayiotis D Ziakas, et al. (2013). Indications for bone marrow examination in autoimmune disorders with concurrent haematologic alterations. *Clinical and experimental rheumatology*, *31*(1), 76-83.

Chen, X., Eksioglu, E. A., Zhou, J., et al. (2013). Induction of myelodysplasia by myeloid-derived supprssor cells. *J Clin Invest*, *123*(11), 4595-4611. http://doi.org/10.1172/jci67580

Costantini, B., Kordasti, S. Y., Kulasekararaj, A. G., et al. (2013). The effects of 5-azacytidine on the function and number of regulatory T cells and T-effectors in myelodysplastic syndrome. *Haematologica*, *98*(8), 1196-205.

Gorshein, E., Weber, U. M., & Gore, S. (2020). Higher-risk myelodysplastic syndromes with del(5q): does the del (5q) matter? *Expert Rev Hematol*, *13*(3), 233-239.

Kelmenson, L. B., Wagner, B. D., McNair, B. K.et al. (2020). Timing of elevations of autoantibody isotypes prior to diagnosis of rheumatoid arthritis. *Arthritis Rheumatol*, *72*(2020), 251-261.

Kotsianidis, I., Bouchliou, I., Nakou, E., et al. (2009. Kinetics, function and bone marrow trafficking of CD4+CD25+FOXP3+ regulatory T cells in myelodysplastic syndromes (MDS). *Leukemia*, *23*(3), 510-8.

Ladouceur, A., Bernatsky, S., Ramsey-Goldman, R., & Clarke, A. E. (2018). Managing cancer risk in patients with systemic lupus erythematous. *Expert Rev Clin Immunol*, *14*(10), 793-802. http://doi.org/10.1080/ 1744666X.2018.1519394

Liu, X. M., Zhang, Y. G., Wang, S. Y., Song, J. Q., & Zhang, X. P. (2021). A case report of MDS-5q-1 with systemic lupus erythematosus. *Laboratory Medicine*, *36*(05), 574-576.

Lu, M., Bernatsky, S., Ramsey-Goldman, R., et al. (2013). Non-lymphoma hematological malignancies in systemic lupus erythematosus. *Oncology*, *85*(4), 235- 240. http://doi.org/10.1159/000350165

Mailloux, A. W., & Young, M. R. (2010). Regulatory T-cell trafficking: from thymic development to tumor-induced immune suppression. *Crit Rev Immunol*, *30*(5), 435-447. http://doi.org/10.1615/critrevimmunol.v30.i5.30

Mailloux, A. W., Sugimori, C., Komrokji, R. S., et al. (2012). Expansion of effector memory regulatory T cells represents a novel prognostic factor in lower risk myelodysplastic syndrome. *Journal of immunology* (Baltimore, Md: 1950), *189*(6), 3198-208.

Meirow, Y., Kanterman, J., & Baniyash, M. (2015). Paving the road to tumor development and spreading:myeloid-derived suppressor cells are ruling the fate. *Front Immunol*, *6*, 523. http://doi.org/10.3389/fimmu.2015.00523

Mekinian, A., Grignano, E., Braun, T., et al. (2016). Systemic inflammatory and autoimmune manifestations associated with myelodysplastic syndromes and chronic myelomonocytic leukaemia: a French multicentre retrospective study. *Rheumatology* (Oxford, England), *55*(2), 291-300.

Moura, C. A., Santiago, M., Neto, J., Gomes de Souza, V. H., & Moura, C. G. (2017). Chronic myelomonocytic leukemia mimicking hematologic systemic lupus erythematosus. *Lupus*, *26*(2), 204-207. http://doi.org/10.1177/0961203316657436

Wilson, A. B., Neogi, T., Prout, M., & Jick, S. (2014). Relative risk of myelodysplastic syndromes in patients with autoimmune disorders in the general practice research database. *Canc Epidemiol*, *38*(5), 544-9.

Zhang, S. T., He, P. G., & Liu, W. L. (2007). Rheumatic diseases associated with myelodysplastic syndromes: nine cases report. *Chinese Journal of Rheumatology*, *11*(07), 423-425.