Feline Myelodysplastic Syndrome: A Case Report

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Abstract: Myelodysplastic syndrome (MDS) is a rare heterogeneous myeloid clonal disorder originating from hematopoietic stem cells, with weakness and anemia as the most common clinical signs. Owing to the dysplasia of myeloid precursor cells, MDS is frequently characterized by pancytopenia and a history of chronic non-regenerative anemia, which can be fatal in severe cases.Due to the insufficient understanding of myelodysplastic syndrome (MDS) and the high difficulty in its definitive diagnosis, affected animals often require frequent blood transfusions for supportive maintenance during treatment. Early definitive diagnosis and treatment of MDS can significantly reduce the frequency of blood transfusions, alleviate the pressure on pet owners, and prolong the survival time of affected animals.We herein report a case of feline myelodysplastic syndrome (MDS), with the aim of providing clinical diagnostic and therapeutic insights for veterinarians.

Key words： myelodysplastic syndrome（MDS）；non-regenerative anemia；bone marrow cytology；azacitidine

Myelodysplastic syndrome (MDS), also known as primary myelodysplasia, is a heterogeneous group of rare diseases affecting young to middle-aged animals, and is considered as a pre-leukemic condition. Affected animals present with clinical signs including fever, weakness, severe non-regenerative anemia, and/or thrombocytopenia, and/or leukopenia, and may progress to acute leukemia[1]. The pathogenesis of this disease remains poorly understood; potential underlying causes include monoclonal proliferation of hematopoietic stem cells, as well as impaired differentiation and maturation of bone marrow progenitor cells. Currently, there is no standard treatment protocol for this disease, which carries a poor prognosis, with most affected animals having a short survival time.

Azacitidine is a demethylation inhibitor, which exerts its pharmacological effects by interfering with the activity of RNA transcription enzymes and DNA methyltransferase 1 (DNMT1). It is currently used in human clinical practice to prolong the survival time of patients with myelodysplastic syndrome (MDS). In this study, a case of feline MDS was treated with a combination regimen of azacitidine and prednisolone, and the treatment process was analyzed, with the aim of investigating the clinical efficacy of azacitidine in feline MDS.

1. Case Presentation

1.1 Signalment

A 4-year-old spayed female Domestic Shorthair (DSH) cat, weighing 3.27 kg, with up-to-date vaccinations and regular parasite prevention.

1.2 History

The cat had a history of severe non-regenerative anemia. It was previously treated at an external hospital for suspected feline leukemia virus (FeLV) infection and cytauxzoonosis, with medications including prednisolone [2 mg/(kg·*d*)], cyclosporine [8 mg/(kg·*d*)], atovaquone [52 mg/(kg·*d*)], azithromycin [10 mg/(kg·*d*)], doxycycline, erythropoietin (EPO), a commercial pet hematopoietic supplement (Buxue Gan Jing), vitamin B12, and zidovudine [11 mg/(kg·*d*)], but no satisfactory therapeutic response was achieved. The cat received 3 blood transfusions within the past month, and was subsequently referred to our hospital for further treatment.

2. Physical Examination

The cat presented in good mental condition with a body temperature of 39.4℃, heart rate of 150 beats/min, respiratory rate of 34 breaths/min, body condition score (BCS) of 2/5, and 6% dehydration. Mucous membranes were pale, and capillary refill time (CRT) was less than 2 seconds. The cat showed normal appetite and water intake, with unremarkable urination and defecation.

3. Diagnosis

3.1 Complete Blood Count

The packed cell volume (HCT) was 11.3% (reference range: 30.3%–52.3%), reticulocyte count was 1.8×10^9/L (reference range: 3–50×10^9/L), and total platelet count was 99×10^9/L (reference range: 151–600×10^9/L), indicating severe non-regenerative anemia. The corrected total white blood cell count was 8.85×10^9/L (reference range: 2.87–17.02×10^9/L). Manual differential counting of blood smears revealed segmented neutrophils accounting for 81%, band neutrophils 2%, and lymphocytes 17%. All leukocyte subsets except band neutrophils fell within normal reference ranges. Eight nucleated red blood cells were observed per 100 white blood cells counted.

3.2 Serum Biochemistry

No significant abnormalities were detected via IDEXX 10-item serum biochemistry panel.

3.3 Bone Marrow Cytology

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Bone marrow aspiration was performed at the femoral trochanteric fossa, and multiple cytological smears were prepared for differential counting of 500 bone marrow nucleated cells. All bone marrow smears demonstrated consistent findings with high cellularity and significant hemodilution. Scant bone marrow particles were visible with myeloid hyperplasia (hematopoietic cells >75%, adipocytes <25%); bone marrow particles are shown in Figure 1. The differential count of 500 nucleated cells yielded the following results:

- Erythroid series (45.5%): orthochromatophilic normoblasts 14%, polychromatophilic normoblasts 17.5%, basophilic normoblasts 11%, rubriblasts 3%. Rubriblasts in the cat's bone marrow are presented in Figure 2.
- Myeloid series (31.5%): segmented neutrophils 18%, band neutrophils 3%, metamyelocytes 2%, myelocytes 0%, promyelocytes 1%, myeloblasts 7.5% (13.6% of non-erythroid nucleated cells).
- Lymphocytes: 21%
- Monocytes: 2%
- The myeloid-to-erythroid (M:E) ratio was decreased at approximately 1:1.43 (feline normal reference range: 1.21–2.16), accompanied by erythroid hyperplasia. Myeloid precursor cells were diminished with incomplete maturation stages. Erythroid precursors were markedly increased (Figure 3); although maturation stages were complete, disordered erythropoiesis was evident. Binucleation (Figure 4), megaloblastoid change, and asynchronous nuclear-cytoplasmic maturation were identified in polychromatophilic and orthochromatophilic normoblasts. Megakaryocytic lineage was adequate (1–5 megakaryocytes per 10 high-power fields) with normal platelet production, and no hemoparasites were observed. Lymphoid cells consisted of small mature lymphocytes within normal quantitative limits. No evidence of immune-mediated destruction, such as erythrophagocytosis by macrophages or erythroblastic islands, was identified on any bone marrow cytology slide.

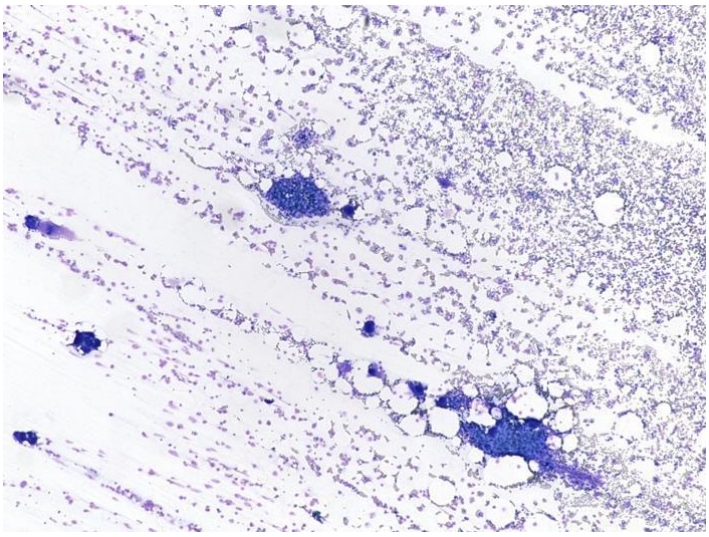

Fig.1 A few unit particles fromlowpower（Wright-Giemsa staining，40×）

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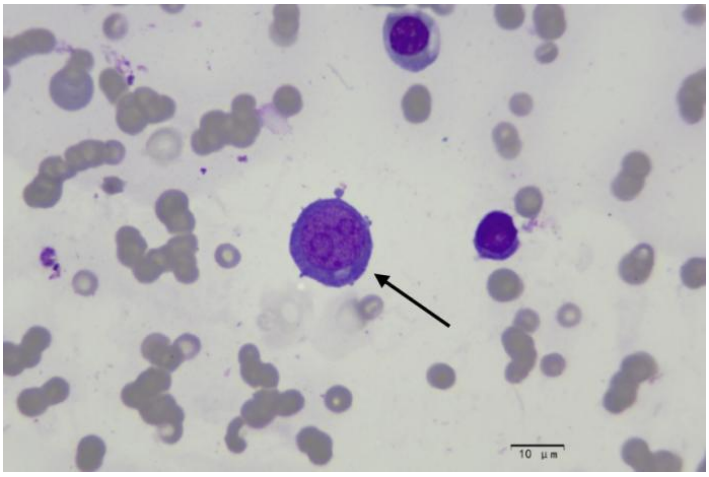

Fig.2 Bone marrow cytology smear of the cat（Wright-Giemsa staining，1 000×）

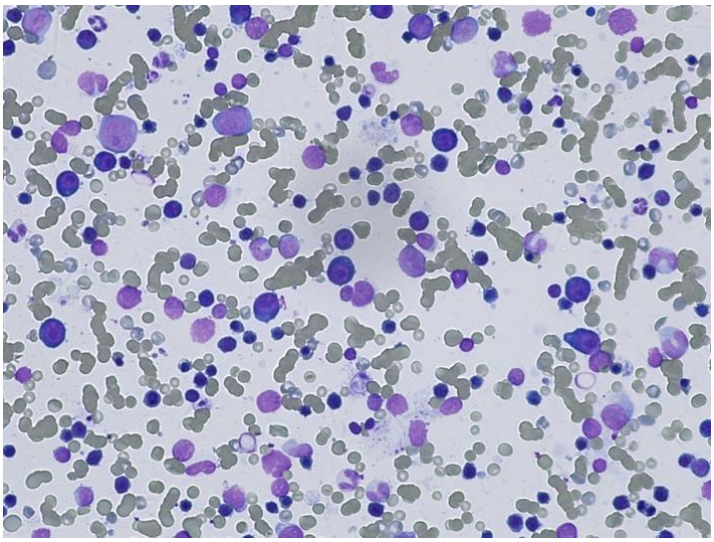

Fig.3 A closer view of the erythroid precursors（Wright-Giemsa staining，200×）

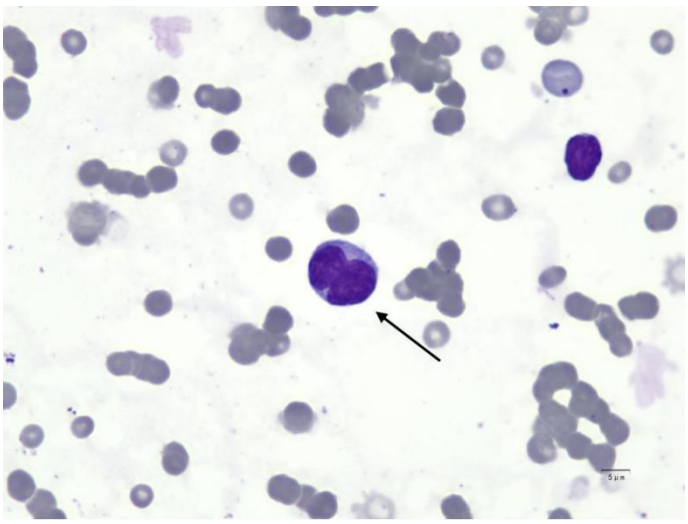

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Fig.4 Bone marrow cytology smear of the cat（Wright-Giemsa staining，1 000×）

Arrow：binucleate cell

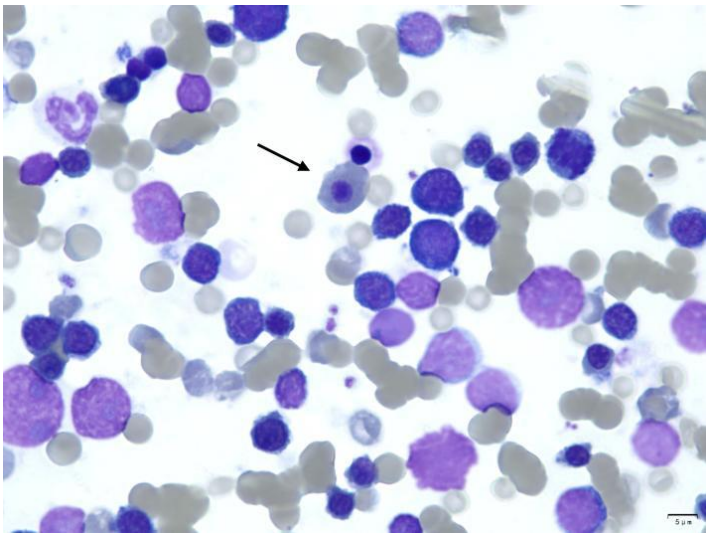

Fig.5 Bone marrowcytology smear of the cat（Wright-Giemsa staining，1 000×）

Arrow：asynchronous maturation between the nucleus and cytoplasm

3.4 Imaging Examination

Abdominal ultrasonography revealed hepatomegaly with rounded hepatic margins and increased parenchymal echogenicity. The pancreas exhibited coarse parenchymal echotexture with mild hyperechogenicity of peripancreatic fat. The splenic tail was rounded, splenic body thickness measured 1.33 cm, perisplenic fat was hyperechoic, and a small volume of peritoneal effusion was present. Ultrasonographic images of the spleen are shown in Figure 6.

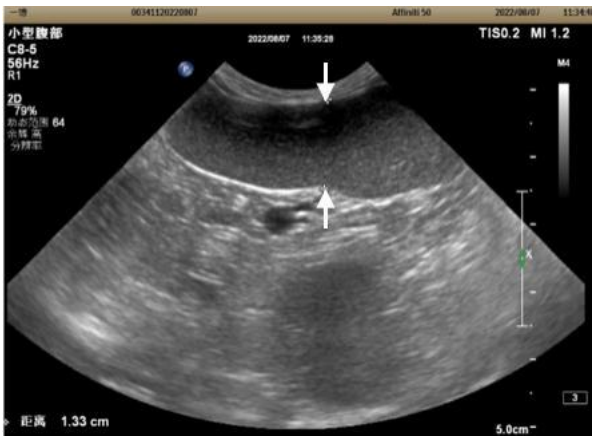

Fig.6 Longitudinal sonographic image of spleen

Arrow：Spleen diameter is approximately 1.33cm

3.5 Additional Diagnostic Tests

Fecal examination yielded no parasite ova. Polymerase chain reaction (PCR) testing for feline leukemia virus (FeLV) and Mycoplasma haemofelis returned negative results.

3.6 Diagnosis results

The cat presented with a chronic, severe non-regenerative anemia, and PCR assays for pathogenic microorganisms capable of inducing feline non-regenerative anemia were negative. Systemic illness and inflammatory causes of anemia were ruled out based on complete blood count, serum biochemistry, and abdominal ultrasound findings. Bone marrow cytology demonstrated blast cell proportion <20%, myeloblast proportion >6%, M:E ratio <1, and characteristic erythroid dysplasia (binucleation and megaloblastoid change). The definitive diagnosis was myelodysplastic syndrome (MDS-RAEB or MDS-EB).

4. Treatment and Outcome

A combination regimen of azacitidine and prednisolone was administered, with adjunctive medications including S-adenosylmethionine, vitamin B12, folic acid, and doxycycline.

- Azacitidine protocol: Subcutaneous injection at 35-70 mg/($m^2 \cdot d$) for 4 consecutive days per treatment cycle, for a total of 3 cycles, with a 30-day interval between cycles.
- Prednisolone dosage: 1.5 mg/(kg·d).

For the first cycle, azacitidine was dosed at 70 mg/($m^2 \cdot d$). On the day of initial administration, the cat developed worsening anemia, vomiting, diarrhea, and lethargy. Supportive care included transfusion of 50 mL fresh whole blood, lactated Ringer's solution (LRS) for fluid resuscitation, maropitant, bismuth subcarbonate, omeprazole, and metronidazole to control gastrointestinal adverse effects. For the second and third cycles, azacitidine was reduced to 35 mg/($m^2 \cdot d$) administered subcutaneously for 4 days; only soft stool was noted during treatment without other notable adverse reactions.HCT and platelet counts steadily increased throughout chemotherapy, with serial changes documented in Figure 7. Prednisolone tapering was initiated on day 24 after completion of the third cycle. When the dose was reduced to 0.25 mg/($kg \cdot d$), HCT declined, prompting an upward adjustment to 0.5 mg/($kg \cdot d$). On day 190 following the third cycle, HCT rose to 40.9%, and prednisolone was tapered to 0.25 mg/($kg \cdot d$) for long-term maintenance. At the time of manuscript writing, the cat's HCT remained stable at approximately 41% with excellent overall clinical condition. The survival time from initial diagnosis to date totals 792 days.

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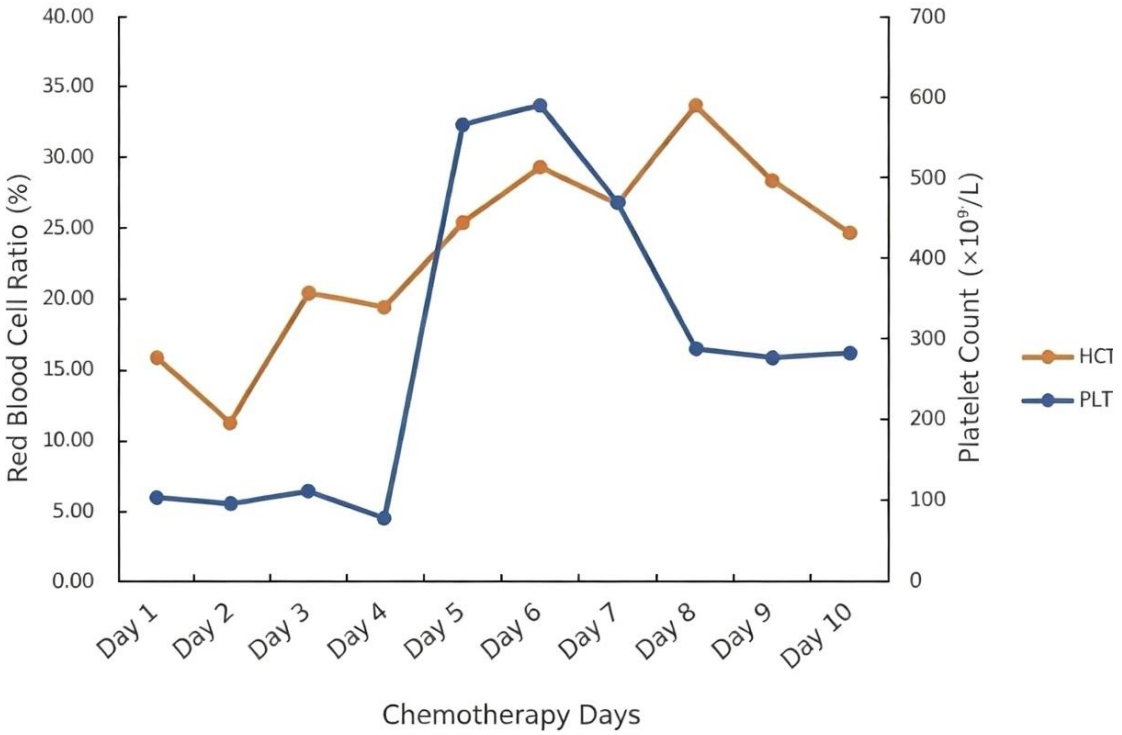

Fig.7 Trends of hematocrit and platelet count during three cycles of chemotherapy

Days ofchemotherapy；Hematocrit；Platelet count

5. Discussion

This report represents the first publicly documented case in China describing azacitidine therapy for feline myelodysplastic syndrome (MDS). This case progressed to classic multilineage cytopenia dominated with severe non-regenerative anemia. Systemic disease, infectious etiologies, drug reactions, toxicosis, and nutritional deficiencies as underlying causes of non-regenerative anemia were excluded via signalment, medical history, clinicopathology, and imaging. Bone marrow hypercellularity confirmed myeloproliferation. Nucleated cells predominantly composed of erythroid precursors. The M:E ratio was depressed accompanied by erythroid hyperplasia, Characterized by rubriblasts and basophilic normoblasts accounting for 14% of erythroid cells. Concurrent cytopenia, erythroid dysplastic features (asynchronous nuclear-cytoplasmic maturation, binucleation, megaloblastoid change), rubriblasts comprising <50% of erythroid cells, and myeloblasts <20% of non-erythroid nucleated cells excluded acute leukemia, establishing a diagnosis of MDS-RAEB[2-4].

MDS is a heterogeneous clonal myeloid disorder originating from hematopoietic stem cells with incompletely elucidated pathogenesis, likely driven by somatic mutations or dysfunction of hematopoietic stem cells. It is a rare hematologic disease, with only approximately 80 cases reported globally to date[4-7].

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MDS is characterized by myeloid dysplasia including left shift, hypersegmentation, and asynchronous nuclear-cytoplasmic maturation. Key laboratory findings include severe non-regenerative anemia or multilineage cytopenia (predominantly erythroid and thrombocytic reduction, with occasional leukopenia).

No standardized diagnostic criteria for MDS in dogs and cats exist in veterinary medicine,diagnosis is adapted from the minimal diagnostic criteria for human MDS. Criteria include: (1) cytopenia affecting one or more lineages, with all alternative causes of cytopenia ruled out; (2) dysplastic cells in erythroid, myeloid, or megakaryocytic lineages accounting for ≥10% , or myeloblast proportion <20%[2]. Small animal MDS is commonly classified via a modified French-American-British (FAB) system overseas[8], consisting of three subtypes: MDS-erythroid predominance (MDS-Er), MDS-refractory cytopenia (MDS-RC), and MDS-excess blasts (MDS-EB), with MDS-EB carrying the poorest prognosis. A retrospective analysis of 34 cats with myelodysplasia，13 cats were diagnosed with MDS-EB patients with a median survival of only 0.7 months, among which 9 cats died or were euthanized within 30 days due to critical disease. Eight cats diagnosed with MDS-RC had a median survival of 11.7 months[8].

No standardized therapeutic protocols of MDS for veterinary are currently established[9-11]. A case report by Masaharu Hisasue et al. successfully managed one MDS-EB cat with azacitidine combined with prednisolone and vitamin K2[7]. Based on the above chemotherapy regimen, this case was treated with the combined protocol of azacitidine and prednisolone. Common adverse effects of azacitidine include nausea, anorexia, gastrointestinal upset, constipation, injection site reactions (erythema, pruritus, inflammation), myelosuppression, and fever[12]. In this case, the 70 mg/($m^2 \cdot d$) azacitidine dose induced severe vomiting, diarrhea, and lethargy, which resolved with supportive care. Dose reduction to 35 mg/($m^2 \cdot d$) eliminated severe adverse events, with only one blood transfusion required throughout chemotherapy.

Several limitations of this study should be noted. Human MDS protocols typically administer six azacitidine cycles, with treatment discontinuation criteria based on normalized bone marrow cytology and peripheral blood parameters. This case ceased chemotherapy after only three cycles without post-treatment bone marrow cytology re-evaluation, relying solely on clinical remission and blood parameters returned to normal, compromising diagnostic rigor. Furthermore, human MDS diagnostic guidelines mandate comprehensive testing including Bone marrow cytology，bone marrow core biopsy (to assess cellularity, CD34 immunohistochemistry, fibrosis grading, and megakaryocyte cytochemistry) and karyotype analysis. Due to restricted diagnostic resources in china veterinary practice compared to human medicine, only a bone marrow cytology examination was conducted in this case; although slide interpretation followed standards set by international veterinary cytopathologists, diagnostic certainty remains limited. Previous research findings indicate that FeLV infection is associated with the development of tumors such as MDS and AML, and may lead to tumor recurrence in affected animals[7]. This case lacked FeLV ELISA testing, precluding definitive exclusion of FeLV-associated disease and limiting accurate prognostic assessment.

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By summarizing the clinical management of this feline MDS case, this manuscript systematically reviews the clinical manifestations and diagnostic principles of MDS, and discusses the dose of azacitidine and treatment cycle for feline MDS, aiming to provide clinical reference for veterinary practitioners.

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