

Secondary myelodysplastic syndrome may happen same as paraneoplastic syndrome in a period of time and prior to the appearance of malignancy: A case study of 6 patients

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Abstract

Myelodysplastic syndrome is a bone marrow failure in which differentiation and maturity do not happen naturally and dysplasia exists in each of 3 cell categories in Bone marrow. Refractory anemia is one of the major complaints with which the patients come to hematology clinics, which in diagnostic considerations lead to MDS as diagnosis. Often there is no recognized reason for this, so it is called “primary MDS”. In practice, we meet some patients who have MDS criteria however we can also find specific reasons for it; therefore we call it “secondary MDS”. One of the most important reasons for secondary MDS is the side effects of medications used in chemotherapy and radiotherapy in patients who undergo these therapies. We observed 6 patients in this case study during lengthy follow up that were diagnosed as MDS and during follow up period malignancy appeared in 6 cases. Supportive and therapeutic measures in these patients did not considerably improve blood cell count, most patients required blood injection and antibiotics for infection treatment. However align with malignancy treatment such problems are completely resolved both in terms of clinical and laboratory.

Keywords: Myelodysplastic syndrome, Paraneoplastic syndrome, Malignancy

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Introduction

MDS or Myelodysplastic syndrome is a group of blood and marrow disorders. Stem cells do not mature in MDS and the number of immature and dysplastic cells increase¹⁻⁴. In most cases, the disease would progress gradually. So cytopenia would become worse and move toward bone marrow failure.

Approximately 80-90% of MDS cases occur among patients older than 60⁵. Each year, 1200 new cases of MDS are diagnosed in US^{1-4, 6}.

MDS patients' morbidity and mortality associated with low blood cell counts that may be in the form of anemia, bleeding arising from thrombocytopenia and infection arising from decrease in white blood cell counts⁷ and eventually patient would enter acute leukemia phase. In addition to this primary type of MDS, in practice we observe some patients who are similar to primary MDS patients in terms of laboratory, clinical and morphology of blood and marrow, but a reason for this type of disease would be mentioned, so the use of

“secondary MDS” term may become applicable. Typically, secondary MDS is the result of DNA damage from chemotherapy^{5, 8-11} or RT¹² to blood cells that specially occurs in the combination of radiation and Alkylating factors such as Busulfan, procarbazine, Nitrous urate that usually happens after a period of 5-7 years of this disease or for drugs such as topoisomerase inhibitors from MDS II during a 2 year period. So, secondary MDS may be a delaying complication of cancer treatment. MDS in aplastic anemia cases occur after receiving immune suppressive drugs during follow up period. Peripheral blood morphology, BMA, BMB and cytogenetic test would be conducted apart from CBC diff and Plt count for MDS diagnosis^{4, 13, 14}. Symptoms that are defined as MDS in peripheral blood and marrow are as follows: Peripheral Blood Cytopenia, ineffective haematopoiesis, dysgranulopoiesis (hypogranulation, pseudo pelger huet), dysmegakaryopoiesis (hypossegmented Megakaryocyte nucleus),

dyserythropoiesis¹⁵ and the increase of Blast counts. Of course dysplasia that involves all 3 cell categories was observed in marrow. In Am J Hematology study that was published in 1992, the relation between malignancy and MDS has been reported and some cases of diagnosis have been occurred prior to malignancy and some cases have been the same time or after diagnosis¹⁶. MDS diagnosis was also accomplished on the basis of available criteria.

Case study

Based on an investigation during 2007-2012, patients diagnosed as MDS based on MDS criteria, we have encountered with patients who can be involved in secondary MDS. The reason

for such patients' referral was cytopenia and they were diagnosed as MDS in marrow study, but most of them were young and since the beginning, there has been suspicion to systematic diseases, auto immune diseases¹⁷ or malignancy as the cause of cytopenia and MDS. Apart from supportive cares and treatments for MDS, it has been considered to search for malignancy or systematic diseases as a cause of MDS. However at the beginning we did not come into any specific conclusion. Most patients required blood injection in order to keep the level of appropriate Hb for ordinary activities.

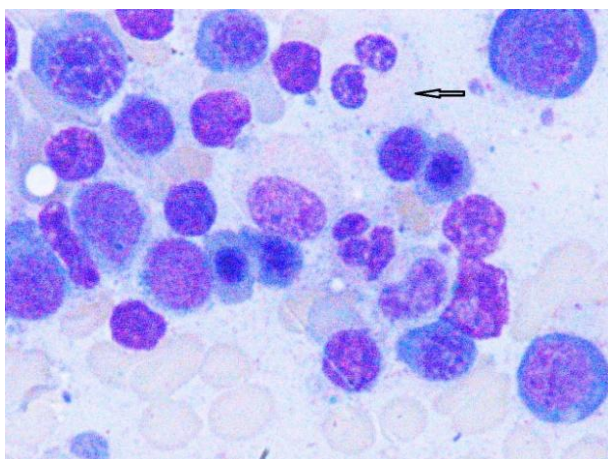
Age and sex specifications of such patients are identified in table 1.

Table 1: Patients' age and sex and type of malignancy in this case study

No.	Age	Sex	Interval before diagnosis (month)	Malignancy
1	27	FEMALE	7	Breast Cancer
2	45	MALE	9	Colon Cancer
3	40	FEMALE	12	Colon Cancer
4	28	FEMALE	6	HD
5	39	FEMALE	4	HD
6	52	MALE	20	Gastric Cancer

Presentation and characteristics of these patients are as below:

The first patients was a 27 year old female who has been referred because of Anemia and Leukopenia and during follow up due to Anemia continuity and refractory anemia, she underwent BMA and BMB and had MDS criteria (figure 1).



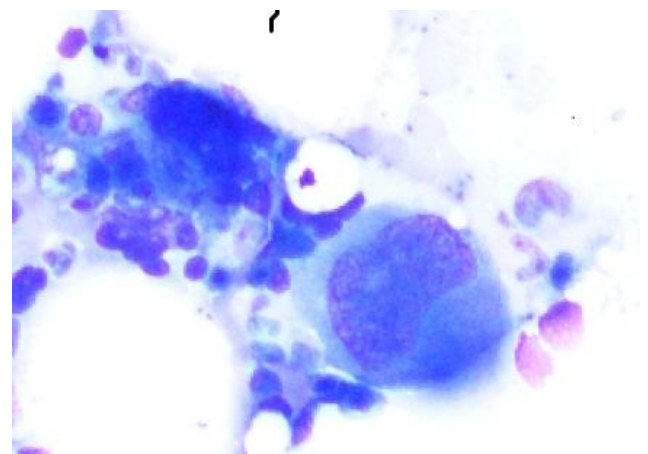
Dyserythropoiesis, Dysgranulopoiesis (pseudo pelger huet raw)

Figure 1: Patients was a 27 year old female

Besides repeated blood injection along with supportive and therapeutic measures she had been followed up and during a 7 month period,

she had a surgery because of Breast mass and she was diagnosed as breast cancer. Patient underwent chemotherapy and Anemia and Cytopenia has been completely resolved after the completion of treatment.

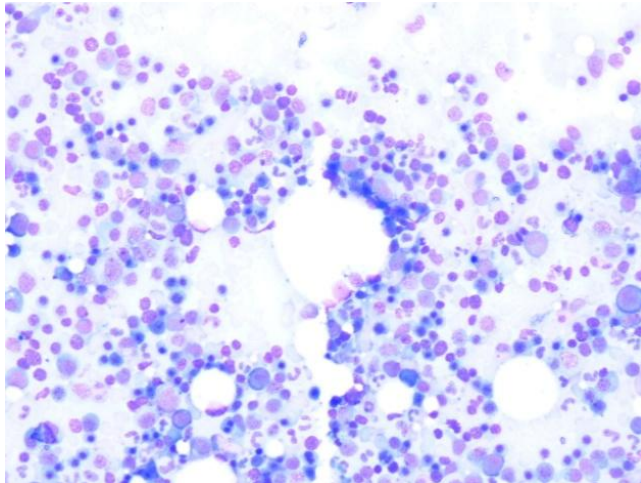
The second patient was a 49 year old man who was referred to clinic because of Macrocytic Anemia and low Retic count and he underwent BMA and BMB because of Anemia continuity and has diagnosed as MDS in BMA (figure 2A, 2B).



Unilobule megakaryocytic

Figure 2A: A 49 year old man with dysmegakaryopoiesis

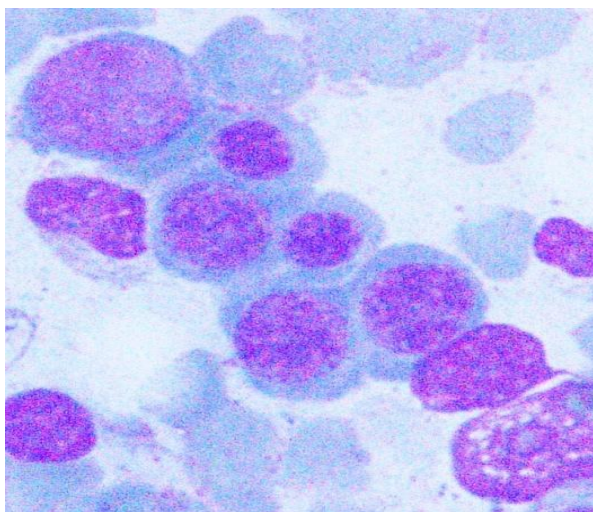
During follow up period, patient required blood injection once each 15 days, so thalidomide was started for him. He had frequent infections because of leukopenia and had a history of hospitalization. During follow up period and after 1.5 months of thalidomide initiation and 9 months later, he was affected by colon cancer and had no problem in CBC diff. after treatment of colon cancer.



Dyserythropoiesis, Dysgranulopoiesis

Figure 2B: 49 year old man who was referred to clinic because of Macrocytic Anemia

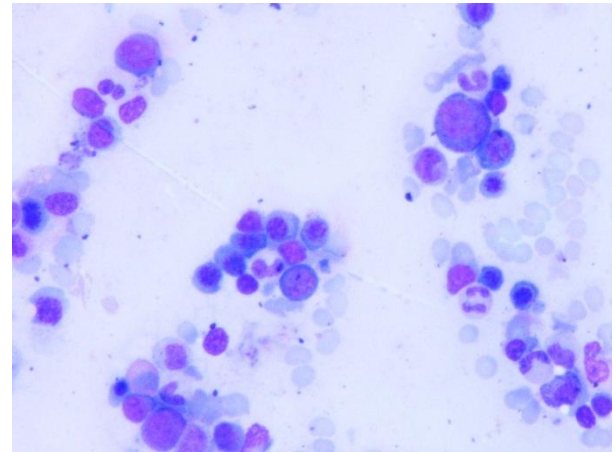
The third patient was a 40 year old female due to refractory anemia and leukopenia. She underwent BMA and BMB and had MDS criteria including dyserythropoies and dysgranulopoiesis (figure 3) who has been diagnosed by colon cancer during a 12 months follow up period.



Dyserythropoiesis

Figure 3: The third patient was a 40 year old female

The fourth patient was a 28 year old female who has been referred because of Macrocytic Anemia, thrombocytopenia and low Retic counts. During 6 months follow up interval, patient affected by neck mass and she was diagnosed as Hodgkin lymphoma. However she no need to blood transfusion but MDS criteria (figure 4) disappeared after treatment of oncology disease.



Dyserythropoiesis

Figure 4: a 28 year old female

The fifth patient was a 39 year old female who was referred because of severe Anemia and Cytopenia and she was diagnosed as MDS in BMA (figure 5). During a 4 month follow up period, she had a mass in supraclavicular area and after neck mass resection; she was diagnosed as Hodgkin's lymphoma and patients required blood injection and antibiotics for infection treatment. After the treatment of fourth and fifth patients, blood disorders are totally resolved. In next BMA review, Myelofibrosis or RS (reed-sternberg cell) wasn't seen.

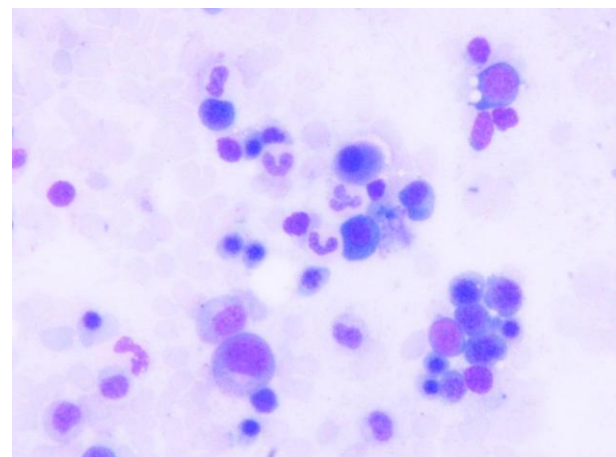


Figure5: 39 year old female

The sixth patient was a 52 year old male who had referred to clinic because of pancytopenia including thrombocytopenia and anemia and leukopenia and demonstrated MDS criteria in BMA. For this patient initiated nutrition drug but no needed to transfusion.

During a 20 month follow up period, no considerable progression in MDS observed and he underwent treatment because of gastric cancer and after the end of treatment, his blood disorders totally resolved.

Discussion

Often we observe Cytopenia in peripheral blood when coping with patients who have malignancy and anemia sounds very outstanding on this regard. Malignant cells may produce TNF and cytokine which may lead to the decrease of red cells production and long life. Also cytopenia may arise from chemotherapy, radiotherapy or infiltration of marrow by malignant cells. This case study represents that we can consider MDS as a paraneoplastic issue that is developed several months prior to cancer presentation.

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