J Clin Exp Hematopathol
Vol. 51, No. 2, Nov. 2011

Case Study

Myelodysplastic Syndrome of del 20q with Plasma Cell Dysplasia

Nagahito Saito,[1] Katsuhiro Higashiura,[1] Kazunori Ehata,[1] Shinji Kurosawa,[1] Kenta Honma,[1] Masayuki Abe,[1] Akihiko Kimura,[2] Mio Suzuki,[3] Shigeo Nakamura,[4] Hiroshi Shiku,[5] and Hong Kean Ooi[6,7]

Deletion of the long arm of chromosome 20 (del 20q) has been observed in patients with myelodysplastic syndrome (MDS) or myeloid malignancies. We experienced an MDS female case of del 20q accompanied by clusters of plasmacytic cells in bone marrow. Her bone marrow cells showed morphological abnormalities in three lineages and the chromosomal abnormality of 46, XX, del (20) (q11.2q13.3). Although the percentage of plasma cells was low in free cells, such cells showed nuclear abnormalities. In bone marrow clots, we also observed clusters of anti-CD38 and anti-CD138 antibody-positive cells. According to the FAB or WHO classification, the diagnosis was unclear. Therefore, we were obliged to term this case as MDS with plasma cell dysplasia. This patient was considered to be a rare case of MDS related to abnormalities in myeloid and B-lymphoid cells. 〔*J Clin Exp Hematopathol 51(2) : 141-145, 2011*〕

Keywords: myelodysplastic syndrome, del (20q), plasma cell, CD38, CD138

INTRODUCTION

Myelodysplastic syndrome (MDS) is a hematological disease derived from abnormal maturation and differentiation of stem cells and is clinically manifested as cytopenia.[1] MDS, especially a case with deletion of the long arm of chromosome 20 (del 20q), has been generally thought to be a result of abnormal maturation in the myeloid lineage.[2-4] We report herein a rare MDS case showing del 20q with hypo-γ-globulinemia, no M-protein in serum, no Bence-Jones proteinuria, and no high percentage of plasma cells among bone marrow free cells, but with plasma cell dysplasia in bone marrow clots. The relatively low percentage of plasma cells among bone marrow free cells seemed to mask the B-cell abnormality because clusters of plasmacytic cells positive for anti-CD38 and anti-CD138 antibody were observed in bone marrow clots. We had to draw our own conclusions about diagnosis in this case, namely, MDS of del 20q with plasma cell dysplasia that showed abnormalities of both myeloid and B-lymphoid lineages. No examination data were obtained to show that this case was a B-cell malignant disorder.

Received : July 8, 2011
Revised : July 24, 2011
Accepted : August 3, 2011

[1]Internal Medicine, Nemuro City Hospital, Nemuro, Hokkaido, Japan
[2]Orthopedics, Nemuro City Hospital, Nemuro, Hokkaido, Japan
[3]Internal medicine, Kushiro Rosai Hospital, Kushiro, Hokkaido, Japan
[4]Clinical Pathology, Nagoya University Hospital of Nagoya University Graduate School of Medicine, Nagoya, Japan
[5]Internal Medicine, Mie University Graduate School of Medicine, Tsu, Japan
[6]Veterinary Medicine, National Chung Hsing University, Taichung, Taiwan
[7]Veterinary Medicine, Yamaguchi University, Japan
Address correspondence and reprint requests to : Nagahito Saito, MD, PhD, Internal Medicine, Nemuro City Hospital, 1-2, Ariisocho, Hokkaido 087-8686, Japan
E-mail : nagahitosaito@k7.dion.ne.jp and Prof. Hong-Kean Ooi DVM. PhD. Department of Veterinary Medicine, National Chung Hsing University, 250 Kuo Kuang Rood, Taichung, 40227, Taiwan
E-mail : hkooi@mail.nchu.edu.tw

CASE REPORT

A 75-year-old Japanese female patient had been treated at our hospital as an outpatient with hypertension and diabetes mellitus undergoing oral administration of drugs. She had suffered a cerebral infarction 10 years previously and also a clinical episode of high fever after being vaccinated against the season's influenza half a year previously. She was admitted to our orthopedic division because of a bone fracture at her pubic arch caused by rocking vibration of a car seat while sitting in her family car driven along an asphalt-paved road in the city. Despite the urging of the orthopedist to consider a surgical approach to her fracture, she selected non-surgical conservative therapy. Her anemic condition was brought to our attention. To our disappointment, we could not examine the blood in the fractured region of her pubic arch.

Her hematological data were as follows : red blood cell count 2.23×10^{12}/L, hemoglobin 76 g/L, hematocrit 21.7%, white blood cell count 7.0×10^{9}/L, and platelet count 226×10^{9}/L. Iron, unsaturated iron binding capacity, total iron binding capacity, and ferritin in serum were 78 μg/dL, 111

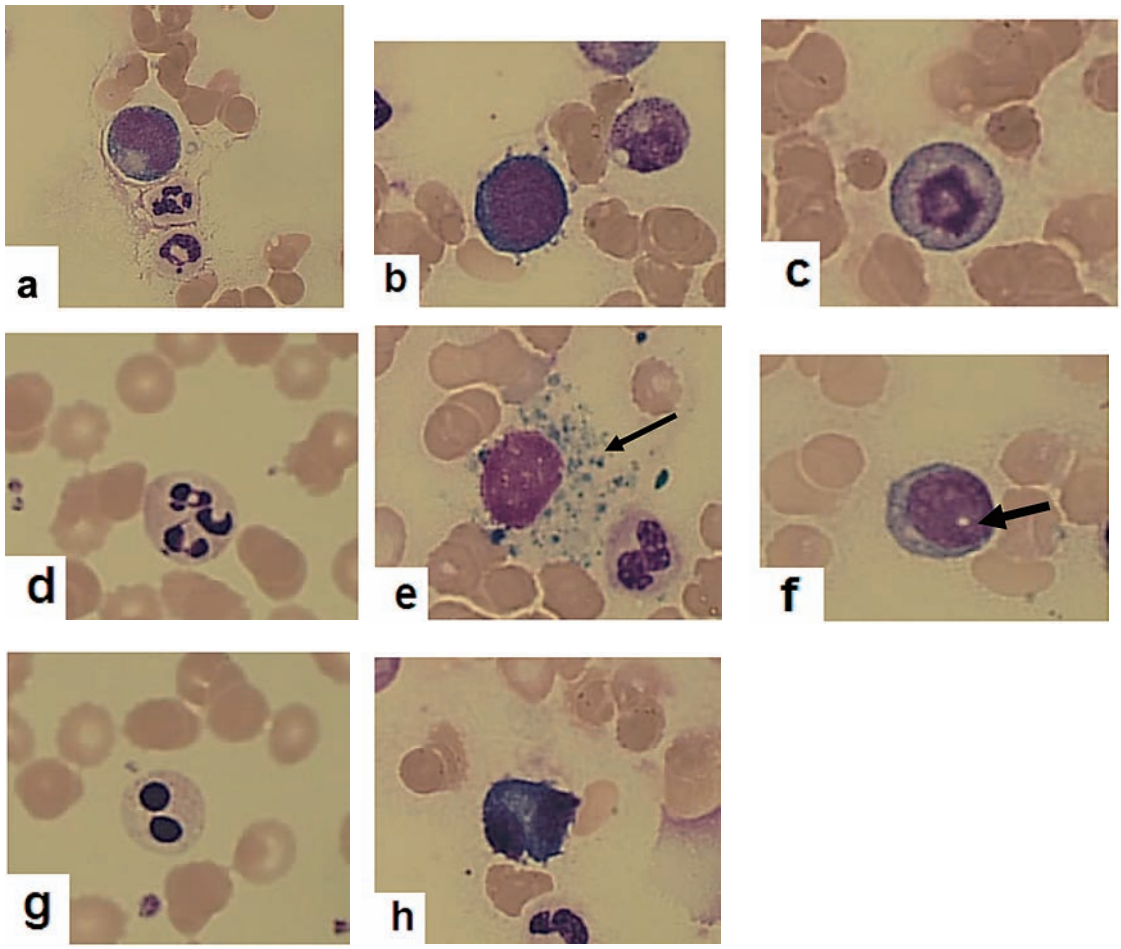

Fig. 1. Bone marrow smear (May-Grünwald-Giemsa stain). (***1a***) An indistinct cell. (***1b***) Micromegakaryocyte-like cell. (***1c***) Nuclear segmented erythroblast. (***1d***) Nuclear hypersegmented neutrophil with few granules. (***1e***) Reticulum cell (*arrow* indicates iron-phagocyting cytoplasm). (***1f***) Lymphoplasmacytic cell with nuclear pocket (*arrow*). (***1g***) Neutrophil with pseudo-Pelger-Huët nucleus. (***1h***) Plasma cell with lobulate nucleus.

μg/dL, 189 μg/dL, and 479 ng/mL, respectively, in which only ferritin was elevated. Blood urea nitrogen and creatinine were 38.1 mg/dL and 2.37 mg/dL, respectively. Her serum albumin was low (3.0 g/dL ; normal range, > 3.7 g/dL), indicating malnutrition. Serum immunoglobulins (Ig) consisting of IgG at a concentration of 740 mg/dL but with a low level of IgG4 (IgG1, 61.4% ; IgG2, 34.33% ; IgG3, 3.42% ; IgG4, < 0. 31%), IgA at 146 mg/dL, IgM at 185 mg/dL, IgE at 121 IU/mL, and IgD at 1. 7 mg/dL (the normal ranges of the 5 classes of aforementioned serum Ig are 870~1,700, 110~470, 23~250, 0~170, and < 9, respectively) were observed. Sedimentation test (ESR), C-reactive protein, antinuclear antibody, and anti-DNA antibody were > 140 mm/hr, 4.8 mg/dL, × 80, and × 160, respectively. D-dimer and thrombin/anti-thrombin III complex were elevated (3.6 μg/dL and 11.6 ng/mL) because of hyper-coagulation induced by bone fracture. Since her fracture occurred in an unusual region and by an unexpected accident, we performed bone marrow aspiration given her anemia, suspecting a myeloma-like disorder. Our orthopedist did not identify any abnormal lesion in her bone X-ray pictures. Free cells in aspirated bone marrow revealed hypocellularity with only 1.2% of plasma cells showing nuclear lobulation or pocket in free cells. Such plasma cells could not be light-microscopically qualified as typical myeloma cells. Morphological abnormalities of blood cells in three lineages were also observed. Reticulum cell possessed iron in the cytoplasm (Fig. 1). A chromosomal abnormality was shown as 46, XX, del (20) (q11.2q13.3) (18 cells/20 analyzed cells, Fig. 2). Moreover, in the aspirated bone marrow clots, the clusters of plasmacytic cells were found to be positive for anti-CD138 or anti-CD38 antibody (Fig. 3). Urinary Bence-Jones protein was negative. Electrophoresis of serum did not reveal any evidence of M-protein.

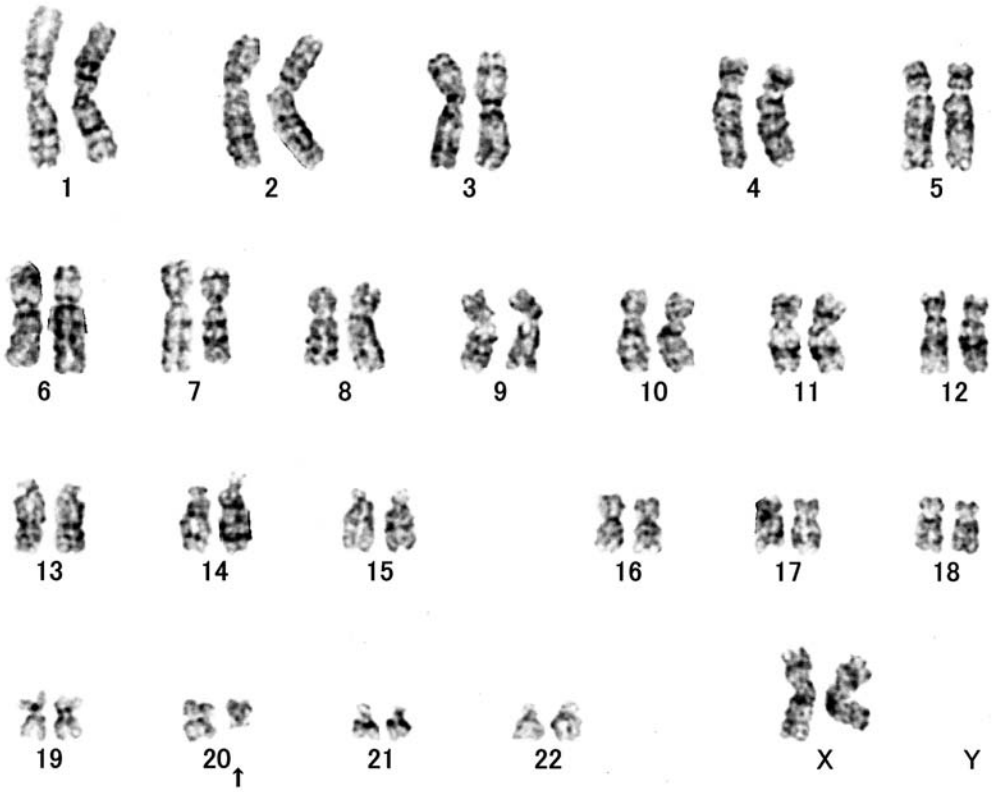

Fig. 2. Chromosomal abnormality. Deletion of long arm in chromosome 20 (*arrow*).

DISCUSSION

This case showed morphological abnormalities of blood cells in three lineages with abnormal iron metabolism indicated by elevated ferritin in serum and by iron-positive staining in the cytoplasm of reticulum cells. Although the patient showed normocytic anemia, slightly renal dysfunction, and malnutrition, the iron-containing reticulum cells on her bone marrow smears showed that her anemia was refractory against iron supplementation. Her chromosomal abnormality, del (20) (q11.2q13.3), is reported to occur predominantly in the myeloid lineage.[5] Therefore, she was initially diagnosed as having refractory anemia or cytopenia in MDS according to the FAB[6] or WHO[7] classification. Although the increase of plasma cells could not be counted in her bone marrow free cells, plasma cells showed several nuclear aberrations. Her bone fracture at her pubic arch, which was attributed to the slight vibration of a car seat that occurred during a ride in a car being driven on an asphalt-paved road, suggested that she had deteriorated to the point at which her bone was pathologically vulnerable to fracture. Clusters of plasmacytic cells positive for anti-CD38 or anti-CD138 antibody were observed in her bone marrow clots. Such plasmacytic cells might be considered to belong to a certain category of myeloma cells, as supported by the observation that rabbit cells were transformed into CD138-expressing malignant cells when primary human myeloma cells were injected into an immunodeficient rabbit.[8] In this case, we could not identify the plasmacytic cells as typical myeloma ones in multiple myeloma. Meanwhile, the chromosomal abnormality of del 20q has been considered to be a common MDS-associated cytogenic change concerning the myeloid lineage.[9] This chromosomal change was also presented in myeloproliferative disorders (MPD)[10,11] such as polycythemia vera and essential thrombocythemia, which are not disorders in the myeloid lineage. In the lymphoid lineage, some del 20q-MDS cases with myeloma,[12] with monoclonal gammopathy of undetermined significance,[13] and with small cell lymphocytic lymphoma[14] were also reported. Recently, an uncommon case of chronic myeloid leukemia with myeloma was reported in an elderly woman.[15] However, almost all of these reported MDS cases were complicated with B-cell disorders that had arisen after therapy with alkylating agents.[16] On the other hand, *in vitro*, both anti-CD38- and del 20q-positive cells were observed in the Epstein-Barr virus-transformed lymphoid cell line from the cells of a del 20q-MDS case.[17] These reports might indicate that the del 20q-associated cytogenic finding is associated with a chromosomal abnormality related to not only myeloid but also other lineages. Alternatively, MDS with B-cell abnormality might be related to a viral infection such as

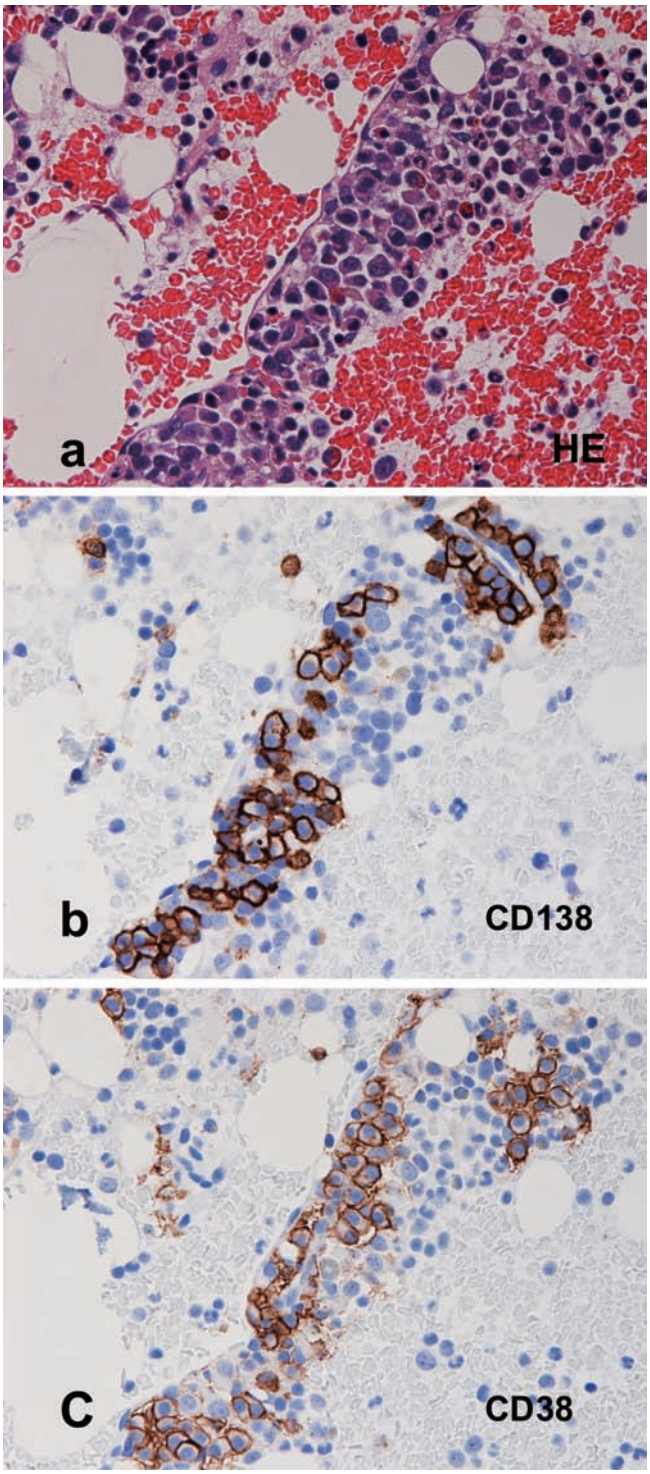

Fig. 3. Bone marrow clot. (***3a***) A cluster of plasma cells is seen (hematoxylin & eosin stain). (***3b***) Immunostain for anti-CD138 antibody. Plasma cells in cluster are positive. (***3c***) Immunostain for anti-CD38 antibody. Plasma cells in cluster are positive.

Epstein-Barr virus. We cannot explain the significance of the low level of IgG4 in this patient's serum IgG because this elderly MDS case with both plasmacytic cell dysplasia and a low level of IgG4 is the first of its kind reported globally. The slightly elevated anti-nuclear antibody, anti-DNA antibody, ESR, and C-reactive protein in her serum might be telltale signs of abnormal functions of her B-cells, although the localized inflammation upon her bone fracture would have induced several immunological reactions in her body. The clusters of anti-CD38- and anti-CD138-positive cells exist not as free cells but in clots accompanied by MDS. In general, some elderly subjects with or without MDS show immunological abnormalities as previously discussed.[18,19] We could not draw any conclusions on the causal relationship between her immunological abnormalities and anti-CD138- or anti-CD38-positive cells.

When we consider this rare MDS case, there is some possibility that a certain type of MDS might be related to B-cell abnormality as a pathological factor. Nonetheless, we experienced a truly rare case that showed coincidental abnormal transformations in myeloid precursor cells and B-cells.

REFERENCES

1 Nimer SD: Myelodysplastic syndromes. Blood 111:4841-4851, 2008
2 Wang PW, Iannantuoni K, Davis EM, Espinosa R III, Stoffel M, *et al*.: Refinement of the commonly deleted segment in myeloid leukemia with del (20q). Genes Chromosomes Cancer 21:75-81, 1998
3 Demory JL, Dupriez B, Fenaux P, Laï JL, Beuscart R, *et al*.: Cytogenetic studies and their prognostic significance in agnogenic myeloid metaplasia: A report on 47 cases. Blood 72:855-859, 1988
4 Kim IS, Kim HJ, Yoo KH, Sung KW, Kim SH: A boy with acute lymphoblastic leukemia acquired clonal and nonclonal cytogenetic abnormalities including del (7q) and del (20q) without clinical evidence of disease after sex-mismatched cord blood transplantation. J Pediatr Hematol Oncol 28:540-543, 2006
5 Li T, Xue Y, Zhang J, Chen S, Pan J, *et al*.: Isodicentric 20q- in two cases of B-cell acute lymphocytic leukemia with the respect (9;20) (p11;q11.2) and t(9;22) (q34;q11.2). Cancer Genet Cytogenet 181:55-59, 2008
6 Bennet JM, Catovsky D, Daniel MT, Flandrin G, Galton DA, *et al*.: Proposals for the classification of the myelodysplastic syndromes. Br J Haematol 51:189-199, 1982
7 WHO Classification of Tumours, Tumours of Haematopoietic and Lymphoid Tissues. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, *et al*. (eds): 4th ed, Lyon, IARC, 2008
8 Yata K, Yaccoby S: The SCID-rab model: a novel *in vivo* system for primary human myeloma demonstrating growth of CD138-expressing malignant cells. Leukemia 18:1891-1897, 2004
9 Steensma DP: The changing classification of myelodysplastic syn-

dromes: what's in a name ? Hematology Am Soc Hematol Educ Program 645-655, 2009

10 Douet-Guibert N, Basinko A, Morel F, LeBris MJ, Ugo V, *et al*.: Chromosome 20 deletions in myelodysplastic syndromes and Philadelphia- chromosome-negative myeloproliferative disorders: characterization by molecular cytogenetics of commonly deleted and retained regions. Ann Hematol 87:537-544, 2008

11 Schaub FX, Jäger R, Looser R, Hao-Shen H, Hermouet S, *et al*.: Clonal analysis of deletions on chromosome 20q and JAK2-V617F in MPD suggests that del 20q acts independently and is not one of the predisposing mutations for JAK2-V617F. Blood 113:2022-2027, 2009

12 Jacobson J, Barligie B, Shaughnessy J, Drach J, Tricot G, *et al*.: MDS-type abnormalities within myeloma signature karyotype (MM-MDS): only 13% 1-year survival despite tandem transplants. Br J Haematol 122:430-440, 2003

13 Nilsson T, Nilsson L, Lenhoff S, Rylander L, Astrand-Grundström I, *et al*.: MDS/AML-associated cytogenetic abnormalities in multiple myeloma and monoclonal gammopathy of undetermined significance : evidence for frequent *de novo* occurrence and multipotent stem cell involvement of del (20q). Genes Chromosomes Cancer 41:223-231, 2004

14 Cotter PD, Tumewu P, Browett PJ: Deletion of long arm of chromosome 20 in a patient with small cell lymphocytic lymphoma. Cancer Genet Cytogenet 70:142-143, 1993

15 Ide M, Kuwahara N, Matsuishi E, Kimura S, Gondo H: Uncommon case of chronic myeloid leukemia with multiple myeloma. Int J Hematol 91:699-704, 2010

16 Orazi A, Czader MB: Myelodysplastic syndromes. Am J Clin Pathol 132: 290-305, 2009

17 White NJ, Nacheva E, Asimakopoulos FA, Bloxham D, Paul B, *et al*.: Deletion of chromosome 20q in myelodysplasia can occur in a multipotent precursor of both myeloid cells and B cells. Blood 83:2809-2816, 1994

18 Saito N, Hirai K, Torimoto Y, Taya N, Kohgo Y, *et al*.: Plural immunoglobulin synthesis in a single cell: An ultrastructural study of two cases with three M-proteins. Ultrastruct Pathol 22:421-429, 1998

19 Saito N, Konishi K, Ohota S, Kondo T, Kato M, *et al*.: Plural light chains in a single plasma cell of a monoclonal gammopathy of undetermined significance case: An ultrastructural study. Hum Cell 20:10-14, 2007