Cancer Genetics 207 (2014) 124–127

Cancer Genetics

# Isolated trisomy 2 in bone marrows of patients with suspected hematopoietic malignancies

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Isolated trisomy 2 in hematopoietic malignancies is rare, having been reported in only eight cases. Of these cases, the majority are older males. The underlying hematologic malignancies range from myelodysplastic syndrome (MDS) to acute myeloid leukemia (AML). The molecular pathogenesis and prognostic significance of isolated trisomy 2 remains unknown. Herein, we report 11 cases of isolated trisomy 2 in hematologic disorders seen in the Mayo Clinic Cytogenetics laboratory from 1996–2012. The majority were older males between the ages of 63–93 years. The underlying bone marrow pathologic diagnoses ranged from no diagnostic features of malignancy to AML. Our data suggest that isolated trisomy 2 could represent an age-related phenomenon since all 11 cases were age 63 and over. It appears that isolated trisomy 2 harbors little prognostic significance and that, instead, the prognostic significance is driven by the underlying pathologic diagnosis. For example, whereas 3 of the cases with AML survived only 7–10 weeks post–bone marrow biopsy, 1 of the cases without diagnostic features of malignancy survived 10 additional years. Therefore, trisomy 2 as a sole abnormality should not be considered as definitive evidence for a myeloid neoplasm in the absence of diagnostic morphologic criteria.

**Keywords** Trisomy 2, MDS, AML, PMF



Isolated trisomy 2 in hematopoietic malignancies is a rare finding that has been reported in eight cases in the literature (1–7). These cases are typically older males ranging from 64–84 years old, presenting with various myeloid neoplasms including myelodysplastic syndrome (MDS), refractory anemia (RA) subtype; MDS, RA with excess blasts (RAEB-II) subtype; MDS, RAEB in transformation (RAEB-t) subtype; chronic myelomonocytic leukemia in transformation (CMML-t); acute myeloid leukemia (AML) arising out of prior MDS; acute monoblastic and monocytic leukemia (AMoL; FAB (French-American-British classification system) M5); and relapsed AML (Table 1). The significance of isolated trisomy 2 is not known, but has been postulated to be an age-related phenomenon (3).

To further investigate the possible diagnostic and prognostic significance of isolated trisomy 2 in hematologic malignancies, we report the hematopathologic and genetic studies from 11 cases seen at our institution.

## Materials and methods

Cases with isolated trisomy 2 in bone marrow specimens were identified from 1996 to 2012 in our cytogenetics laboratory. G-banding was performed according to standard cytogenetic methods using trypsin and Leishman stain. Although 20 metaphases are routinely examined, only 9 and 15 metaphases were identified in cases 8 and 4, respectively.

## Results

We identified 11 cases with isolated trisomy 2 in bone marrow specimens. The specimens were all from older patients, ranging from 63–93 years old, and 7 of 11 were male. Their hematopathologic evaluations represent a range of findings including two without diagnostic features of malignancy (Table 2).

Received January 16, 2014; received in revised form February 25, 2014; accepted February 27, 2014.

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2210-7762/$ - see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.cancergen.2014.02.011

**Table 1** Cases of isolated trisomy 2 in bone marrow hematopoietic disorders reported in the literature

| Patient | Age (y) | Sex | Result | Pathology report | Reference |
|---|---|---|---|---|---|
| 1 | 74 | M | 47,XY,+2[a] | MDS, RA subtype | (1) |
| 2 | 75 | M | 47,XY,+2[a] | MDS, RAEB-t | (2) |
| 3 | 87 | M | 47,XY,+2[5]/46, XY[35] | MDS transformed into AML | (3) |
| 4 | 80 | F | 47,XX,+2[22]/46, XX[8] | CMML-t | (3) |
| 5 | 64 | M | 47,XY,+2/46, XY[a] | MDS, RA subtype | (4) |
| 6 | 73 | M | 47,XY,+2[5]/46, XY[8] | MDS, RAEB-II subtype | (5) |
| 7 | 84 | M | 47,XY,+2[8]/46, XY[8] | AMoL; FAB M5 | (6) |
| 8 | N/A | M | 47,XY,+2[19] | AML in relapse | (7) |

*Abbreviations:* MDS, myelodysplastic syndrome; RA, refractory anemia; RAEB, refractory anemia with excess blasts; RAEB-t, refractory anemia with excess blasts in transformation; AML, acute myeloid leukemia; CMML-t, chronic myelomonocytic leukemia in transformation; AMoL, acute monoblastic and monocytic leukemia; FAB, French-American-British classification system; N/A, not available.

[a] Number of metaphases not reported.

**Table 2** List of the patients with isolated trisomy 2 seen in the Mayo Clinic cytogenetics laboratory between 1996 and 2012

| Patient | Age (y) | Sex | Result | Pathology report |
|---|---|---|---|---|
| 1 | 87 | M | 47,XY,+2[4]/45, X,-Y[3]/46,XY[13] | No diagnostic features of malignancy |
| 2 | 84 | M | 47,XY,+2[11]/46, XY[9] | No diagnostic features of malignancy |
| 3 | 78 | M | 47,XY,+2[17]/46, XY[3] | MDS, RCMD subtype |
| 4 | 82 | M | 47,XY,+2[6]/46, XY[9] | MDS, RCMD subtype |
| 5 | 72 | F | 47,XX,+2[2]/46, XX[18] | MDS, RAEB-1 subtype |
| 6 | 93 | F | 47,XX,+2[19]/46, XX[1] | MDS, RAEB-1 subtype |
| 7 | 67 | F | 47,XX,+2[3]/46, XX[17] | PMF |
| 8 | 82 | M | 47,XY,+2[9] | AML, NOS |
| 9 | 75 | M | 47,XY,+2[20] | AML, NOS |
| 10 | 69 | M | 47,XY,+2[13]/46, XY[7] | AML, MRC |
| 11 | 63 | F | 47,XX,+2[17]/46,X, idic(X)(q13)[1]/46,XX[2] | AML, MRC |

*Abbreviations:* MDS, myelodysplastic syndrome; RCMD, refractory cytopenia with multilineage dysplasia; RAEB, refractory anemia with excess blasts; PMF, primary myelofibrosis; AML, acute myeloid leukemia; NOS, not otherwise specified; MRC, myelodysplasia-related changes.

Case 1, 47,XY,+2[4]/45,X,-Y[3]/46,XY[13], was an 87-year-old male who had mild thrombocytopenia and mild anemia. The bone marrow was normocellular (30%; M:E ratio 1.7:1.0) with intact trilineage hematopoiesis and no increase in blasts. Erythropoiesis was mildly megaloblastoid without convincing evidence of myelodysplasia. The patient did not receive any treatment. He survived 10 years after the identification of the trisomy 2. His chromosome study also showed an absence of the Y chromosome in 3 of 20 metaphases—a known age-related phenomenon (8).

Case 2, 47,XY,+2[11]/46,XY[9], was an 84-year-old male with thrombocytopenia. The bone marrow was mildly hypercellular (50%) with mild panhyperplasia and no increase in blasts. Overall findings were compatible with peripheral sequestration and/or destruction of platelets (M:E ratio 3:1). Additional clinical information was not available.

Case 3, 47,XY,+2[17]/46,XY[3], was a 78-year-old male with severe anemia, neutropenia, and thrombocytopenia. The bone marrow showed a hypercellular bone marrow (80–90%) with myeloid maturation arrest at the myelocyte stage, megaloblastoid erythropoiesis, and dysplastic megakaryocytes. The abnormal megakaryocytes were characterized by distinctly separate nuclear lobes. There was 3% blasts. The findings were most suggestive of MDS. No additional clinical information was available; however, a bone marrow specimen collected 11 weeks after this study showed similar findings, except for an increase in blasts to 8%.

Case 4, 47,XY,+2[6]/46,XY[9], was an 82-year-old male with anemia and neutropenia. The bone marrow was mildly hypercellular (40%; M:E ratio 0.3:1) with erythroid hyperplasia and megaloblastoid erythropoiesis, mild dysgranulopoiesis, and increased dysplastic megakaryocytes that consisted of mononuclear forms and micromegakaryocytes. Blasts were <3%. The overall findings were consistent with MDS, refractory cytopenia with multilineage dyspoiesis subtype. Additional clinical information was not available.

Case 5, 47,XX,+2[2]/46,XX[18], was a 72-year-old female whose initial bone marrow showed moderate to marked hypercellularity (70–75%) with a slightly increased myeloblast percentage (5–6%), granulocytic and erythroid dysplasia, normal-appearing megakaryocytes and ring sideroblasts. The findings were consistent with a diagnosis of MDS, RAEB-1 subtype. No further clinical information was available. A follow-up bone marrow 4 years later showed persistent MDS with a borderline increase in blasts (5–6%) and development of monocytosis. Chromosomes were normal at that time.

Case 6, 47,XX,+2[19]/46,XX[1], was a 93-year-old female whose bone marrow was slightly hypercellular (40%) with mild panhyperplasia, dyserythropoiesis, dysplastic megakaryocytes, and a borderline increase in blasts (5%). The findings were consistent with MDS, RAEB-1 subtype. No additional clinical information was available.

Case 7, a female, was initially diagnosed with a myeloproliferative neoplasm for which the pathology and cytogenetics reports were not available for our review. The clinical notes indicated that multiple interval bone marrow biopsies showed a similar pathologic picture, with trisomy 2 in all metaphases. She was treated with hydroxyurea for about 5 years, and after becoming transfusion dependent, she received four cycles of Dacogen. She was then admitted on a clinical trial treatment of pomalidomide; however, no clinical improvement was seen. At this time, her fluorescence in situ hybridization (FISH) test for *BCR-ABL1* was normal, and