i(5)(p10) in hematological malignancies

Adriana Zamecnikova
Kuwait Cancer Control Center, Kuwait annaadria@yahoo.com

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Abstract
Isochromosome of the short arm of chromosome 5 is an infrequent chromosome anomaly that has been reported in myeloid, and less frequently in lymphoid malignancies, including leukemia and lymphomas.

Keywords
AML, acute monoblastic leukemia, isochromosome 5p, clonal evolution.

Clinics and pathology

Disease
Chronic or acute myeloid malignancies and lymphoid neoplasms.

Note
See also i(5)(p10) in acute myeloid leukemia

Epidemiology

Chronic myeloproliferative disorders (MPD) in 8 (4M/4F aged 19 to 81 years; median 66 years): 1 chronic myeloid leukemia (Markovic et al., 2000) and 7 MDS (Christodoulou et al., 2004; Lessard et al., 2007; Herry et al., 2010; Jimenez-Sousa et al., 2010; Douet-Guilbert et al., 2011; Reddi et al., 2012; Giudici et al., 2013).

Acute myeloid leukemia (AML) in 18 (9M/9F aged 8 to 86 years, median 64 years): 2 AML (Flach et al., 2011; Hartmann et al., 2014), 2 acute myeloblastic leukemia without maturation (M1) (Calabrese et al., 2000; Choi et al., 2007), 2 acute myeloblastic leukemia with maturation (M2) (Tamura et al., 1998; Herry et al., 2007), 1 acute promyelocytic leukemia (M3) (Goldschmidt et al., 2010), 2 acute myelomonocytic leukemia (M4) (El-Rifai et al., 1997; Panani 2006), 8 acute monoblastic leukemia (M5) (Yunis 1984; Slovak et al., 1991; Schoch et al 2001; Schmidt et al., 2004; Gervais et al., 2008; Paar et al., 2013) and 1 acute erythroleukemia (M6) (Herry et al., 2010) patient.

Multiple myeloma was diagnosed in a single male (Sawyer et al., 2014).

Lymphoid malignancies in 12 patients. B-cell lymphomas in 7 (3M/4F aged 55, 71, 78 and 86 years, 3 unknown) (Hashimoto et al., 1995; Dierlamm et al., 1997; Wlodarska et al., 1999; Hernandez et al., 2001; Bastard et al., 1992; Cook et al., 2004; Johnson et al., 2008), and there was a 54-years old male with chronic lymphocytic leukemia (Jarosova et al., 2010). 3 patients were diagnosed with T-cell lymphoid malignancies (2M/1F aged 38 and 69 years, 1 unknown) (Heinonen et al., 1994; Lepretre et al., 2000; Nelson et al., 2008) and an 11- years old male with bilineage or biphenotypic leukemia (La Starza et al., 1993).

Etiology

38 patients (20 M/18 F aged 8 to 86 years; median 69 years). Myeloid malignancies mainly (26 patients): 18 AML, 7 MDS and 1 CML. In 10 of the 18 AML patients the cells were of monoblastic (8 patients)/monocytic (2 patients) lineage. Among them, 4 had therapy-related MDS, 1 had therapy-related AML (t-MDS/t-AML), and one patient had chronic myelogenous leukemia in myeloid blast phase. The primary diagnoses for patients with t-MDS/t-AML were mediastinal germ cell tumor (Christodoulou et al., 2004), carcinoma of the ovary (Lessard et al., 2007), breast carcinoma (Gervais et al., 2008) and multiple myeloma (Jimenez-Sousa et al., 2010; Reddi et al., 2012).
The occurrence of i(5)(p10) was not restricted to myeloid malignancies as it was also detected in 8 patients with B-cell and in 3 with T-cell lymphoid malignancies.

**Prognosis**

i(5)(p10) is frequently part of complex karyotypes representing clonal evolution that may reflect genomic instability. Most of these patients showed a more aggressive course of the disease and poor response to chemotherapy (Paar et al., 2013).

**Genetics**

**Note**

The formation of i(5)(p10) may be observed in two patterns: (1) i(5)(p10) replacing a normal chromosome 5 leading to the loss of the long arm of chromosome 5 and duplication of its short arm. (2) It occurs as a supernumerary +i(5)(p10) chromosome, with two normal copies of chromosome 5, resulting in 5p tetrasomy, that has been reported in AML and B-cell lymphoid malignancies, but not in MDS.

**Cytogenetics**

**Note**

Because of their similar cytogenetic appearance, the incidence of i(5)(p10) may be underestimated as it might have been misinterpreted as 5q deletion, a known chromosome abnormality in myeloid malignancies. Therefore, to discriminate between 5q deletion and i(5)(p10), fluorescence in situ hybridization using locus specific probes for 5p/5q sequences is recommended.

**Cytogenetics morphological**

Presents as i(5)(p10) resulting in 5q deletion in 7 MPD, 6 AML, 1 CLL, 1 mature B-cell neoplasm and 3 T-cell lymphoid malignancies. Among them, sole anomaly in 1 MDS (Douet-Guilbert et al., 2011), sole additional anomaly to +8 in 1 MDS (Jimenez-Sousa et al., 2010), to -Y in 1 MDS (Reddi et al., 2012) and found as +8 and complex karyotypes in 2 AML (El-Rifai et al., 1997; Henry et al., 2007). In 1 MDS patient, 2 copies of isochromosome 5p and a single normal chromosome 5 have been detected (Giudici et al., 2013). Presents as a supernumerary +i(5)(p10) in 11 out of 17 AML, in the bilineage or biphenotypic leukemia, in 1 MM an in 6 out of 7 B-cell lymphomas. Among them, +8 was found in 8 AML patients (Panani 2006; Yunis 1984; Schoch et al 2001; Slovak et al., 1991; Calabrese et al., 2000; Flach et al., 2011) while it was a sole additional anomaly to +8 in 3 patients (Schoch et al 2001; Panani 2006). Found with 14q32 rearrangement and complex karyotypes in 3 out of 6 B-cell lymphomas and as part of complex karyotypes in the remaining patients.

**Result of the chromosomal anomaly**

**Fusion protein**

Oncogenesis

Isochromosome of the short arm of chromosome 5 represents a rare but recurrent chromosome anomaly in hematological malignancies.

Its occurrence has been mainly associated with myeloid malignancies, especially AML with
monocytic lineage, but it has also been reported in lymphoid disorders, including leukemia and lymphomas. When present in a single copy, i(5)(p10) results in 5p trisomy and 5q monosomy, that might be similar to a 5q- syndrome. Therefore, loss of material from chromosome 5q arm and gain of 5p material may play a key pathogenic role in these patients. In contrast, when presents as a supernumerary +i(5)(p10) chromosome, the formation of isochromosome leads to 5q disomy and 5p tetrasomy, thus duplication of its short arm leading to copy gain imbalances could contribute to proliferative advantage of the cells. i(5)(p10) is mainly observed as an additional chromosomal abnormality to known anomalies such as trisomy 8 in myeloid malignancies or is part of a complex karyotypes, likely representing a secondary cytogenetic event in the majority of patients.

References

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