

Leukaemia Section

Short Communication

+8 or trisomy 8

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Clinics and pathology

Disease

Chronic myelogenous leukaemia (CML)

Epidemiology

+8 is one of the major anomalies additional to the t(9;22), with i(17q), + der(22), before +19; found as a unique additional anomaly in 10%, with other in 25% of CML cases with clonal evolution; these additional anomalies may be present at the diagnosis of CML (in 10%, possibly with unfavourable significance), or may appear during course of the disease, they do not indicate the imminence of a blast crisis, although they also frequently emerge at the time of acute transformation; +8 is more often found in the myeloid than in the lymphoid blast crisis.

Prognosis

+8 has apparently no prognostic significance in CML.

Disease

Other chronic myeloproliferative diseases: polycythemia vera (PV), and idiopathic myelofibrosis (but not found in essential thrombocythemia).

Epidemiology

+8 is found in 20% of PV cases with an abnormal karyotype, mostly as the sole anomaly, may be accompanied with +9 (abnormal karyotypes in PV occur mainly with evolution, but the appearance of a clonal anomaly does not indicate progression of the disease); +8 is found in 10% of myelofibrosis cases with chromosome anomalies, sometimes with +9.

Prognosis

No prognostic significance.

Disease

Myelodysplastic syndromes (MDS): refractory anaemia (RA), refractory anaemia with ring sideroblasts (RARS), refractory anaemia with excess of blasts ± in transformation (RAEB±T), chronic myelomonocytic leukaemia (CMML).

Note

The present (unpublished) review of about 250 ANLL cases with +8 is a review of literature cases and may therefore be biased, although the percentages herein given are in accordance with those of large series.

Epidemiology

+8 is found in 15-20% of MDS; 5-10% of MDS with +8 are treatment-related MDS; +8 is present in each FAB subgroup: up to 30% of RARS cases have +8; 15-20% of other subgroups have +8.

+8 is: the sole anomaly in 55%, found with simple karyotypic changes in 20%, and part of a complex karyotype in the remaining 25% of cases.

Altogether, sex ratio is 1.5M/1F (1.8/1 in cases RAEB±T and CMML, 1/1 in RA or RARS).

- 15% of +8/MDS are found with -5/del(5q), often in complex karyotypes.

- 4% of +8/MDS are found with t(1;7)(q10;p10)(and 20% of t(1;7)/MDS-ANLL also associate +8).

- 4% as well are found with del(20q), mainly in simple karyotypes.

- +8 is strikingly found in independant subclones, with other subclones carrying other anomalies, in particular del(5q) or t(1;7) (e.g.: 46, XY, del(5q)/47, XY, +8).

Prognosis

Median survival would near 2 years.

Disease

Acute non lymphocytic leukaemias (ANLL)

Note

The present (unpublished) review of more than 500 ANLL cases with +8 is a review of literature cases and may therefore be biased, although the percentages herein given are in accordance with those of large series; we also add 39 unpublished t(11;19) to 101 published cases.

Epidemiology

+8 is found in 10-15% of ANLL; 10% of ANLL with +8 are treatment-related ANLL; +8 is present in each FAB subgroup (from M1 to M7) in a grossly equivalent percentage (but in M5a where the percentage is higher), in contrast to what has been previously claimed; cases may present with a preceding myelodysplasia.

+8 is: the sole anomaly in 40%, found with simple karyotypic changes in 35%, and part of a complex karyotype in the remaining 25% of cases.

altogether, sex ratio is 1.2/1 (1.6/1 in cases with a complex karyotype, 1/1 otherwise).

- 5-10% of +8/ANLL are found with -5/del(5q)and/or -7/del(7q), often associated, and nearly always in complex karyotypes.

- 5-10% also are found in t(15;17)/M3 cases, mostly as a single additional anomaly, while 1/3 of t(15;17) are accompanied with +8.

- 5-10% are found with inv(16), mainly in simple karyotypes (and 15% of inv(16) cases also carry +8).

- 5% are associated with +21, often parts of a complex karyotype.

- 5% also are found in 11q23 ANLL, mostly in t(9;11)(p22;q23) cases (and 20% of t(9;11) also carry +8, while 15% of t(11;19)(q23;p13.3)/ANLL or ALL (91 cases, 25 unpublished), 10% of t(6;11)(q27;q23)/ANLL, t(10;11)(p12;q23)/ANLL, and t(11;19)(q23;p13.1)/ANLL (49 cases, 14 unpublished) as well, and only 3% of t(4;11)(q21;q23)/ALL, have an additional 8 chromosome.

- Less than 5% are found with t(8;21)(q21;q21) often in simple karyotypes, and 10% of t(8;21) associate +8.

- Less than 5% also are associated with t(9;22)(q34;q11)/ANLL, mostly in complex karyotypes.

- 2% are associated with +9, either in simple or in complex karyotypes.

- 1% of +8/ANLL are found with t(1;7)(q10;p10), but as far as 20% of t(1;7) also associate +8.

- 15% of Down syndrome patients with MDS/ANLL have +8 in their leukaemic cells.

Clinics

From 2 studies on ANLL in adults with +8 solely: no specific FAB subgroup; median age was 60 years (vs 50 years in cases of +8 accompanying t(8;21), t(15;17) or inv(16)); no gross organomegaly; moderate WBC.

Prognosis

Of ANLL in adults with +8 solely: complete remission in 60-70% (vs 90% in cases accompanying t(8;21), t(15;17) or inv(16)); median survival was 13 months in one study, 20 months in another; taking all +8 cases, solely or not, median survival would be of about a year; +8 does not seem to alter the relatively good prognosis of t(8;21), t(15;17) or inv(16), while the (numerous) cases with a complex karyotype exhibit a poor outcome; age is an adverse feature.

Disease

Acute lymphocytic leukaemia (ALL)

Phenotype/cell stem origin

+8 is more often found in B-cell than in T-cell cases.

Epidemiology

- +8 is a rare anomaly in lymphoid malignancies (90% of +8 occur in myeloid malignancies); found in about 5% of ALL.

- Rarely found as a sole anomaly (5-10%), may be part of hyperploid karyotypes (>50 chromosomes mainly) without structural anomalies (20% of cases), mostly found in complex karyotypes with structural anomalies (2/3 of cases), these complex karyotypes being often hyperploid as well.

- Sex ratio: 1.5/1.

- Accompany (mostly in complex karyotypes): t(9;22)(q34;q11)/ALL, t(4;11) (see above) and other 11q23, del(6q), t(1;19)(q23;p13), dic(9;12) and other known primary anomalies.

Disease

Non-Hodgkin lymphomas

Epidemiology

+8 is exceptional; has been found associated with t(14;18)(q32;q21), t(8;14)(q24;q32), and other known or unknown anomalies.

Disease

Chronic lymphoproliferative diseases

Epidemiology

Very rare anomaly (to be noted that +8 is

exceptional in T-prolymphocytic leukaemia, in contrast with the frequency of i(8q), which occurs by completely different mechanisms, but gives, for parts, very similar genetic imbalances).

Genetics

Note

Genes (possibly) involved are unknown.

To be noted

Note

Karyotypes with +8 may be misinterpreted with a possible overlooked constitutional trisomy 8, a syndrome associating mild to moderate mental delay and (sometimes mild as well) bone anomalies; furthermore constitutional trisomy 8 has been said to be at increased risk of cancers, haematological malignancies in particular.

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