

# Leukaemia Section

## Mini Review

### +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; +8 may arise after interferon and/or imatinib treatment. It's significance is unknown.

### Disease

**Other chronic myeloproliferative diseases:** polycythemia vera (PV), and idiopathic myelo-fibrosis (but not found in essential thrombocy-themia).

### 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The present (unpublished) review of about 250 MDS cases with +8 is a review of literature cases and may therefore be biased, although the percentages herein given are in accordance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 25-30% of RARS cases have +8; 15-20% of other subgroups have +8

+8 is: the sole anomaly in 55-65%, found with simple karyotypic changes in 20%, and part of a complex karyotype in the remaining 25% of cases.

Altogether, sex ratio is significantly unbalanced, near 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-AML 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

Progression from MDS towards AML would occur in about half cases of +8 solely. Median survival in these cases would be about 1.5-2 yrs.

## Disease

Acute myeloid leukaemias (AML)

### Note

The present (unpublished) review of more than 500 AML 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 AML; 10% of AML with +8 are treatment-related AML; +8 is present in each FAB subgroup (from M1 to M7) in a grossly equivalent percentage (but in M3, where the percentage is lower (2% as the sole anomaly, 10% altogether), and in M5 where the percentage is higher (10% as the sole anomaly, 20-30% altogether)), in contrast to what has been previously claimed; cases may present with a preceding myelodysplasia. +8 is not more frequent in treatment related leukaemias.

+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/AML 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 AML, mostly in t(9;11)(p22;q23) cases (20% of t(9;11) carry +8), while 15% of t(11;19)(q23;p13.3)/AML or ALL (91 cases, 25 unpublished), 10% of

t(6;11)(q27;q23)/AML, t(10;11)(p12;q23)/AML, and t(11;19)(q23;p13.1)/AML (49 cases, 14 unpublished) as well, and only 3% of t(4;11)(q21;q23)/ALL, have an additional 8 chromosome; +8 is also frequently associated to a t(1;11)(p32;q23)

- 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)/AML, mostly in complex karyotypes.

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

- 1% of +8/AML 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/AML have +8 in their leukaemic cells.

+8 is also found in 15% of t(9;22)(q34;q11) and 25% of t(7;12)(q36;p13) cases.

## Clinics

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

## Prognosis

Prognosis of AML 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 mths in one study, 20 mths in another, around 1 year in most; 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. +8 can be associated with intermediate or poor prognosis.

## 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).

### Disease

Solid tumours

Desmoid fibromatosis and Dupuytren's contracture; +8 is found, mostly as the sole anomaly, in 25% of cases.

Clear cell sarcoma with t(12;22)(p11;p11) : +8 is found in 55% of cases of clear cell sarcoma.

Ewing tumors with t(11;22)(q24;q12) : +8 is found in 35% of cases of Ewing tumors.

Myxoid liposarcoma with t(12;16)(q13;p11) : +8 is found in 15% of cases of myxoid liposarcoma.

Synovial sarcoma with t(X;18)(p11;q11) : +8 is found in 10% of cases of synovial sarcoma.

Hepatoblastoma: +8 is found (with other anomalies) in 35% of cases of hepatoblastoma.

Wilms tumor: +8 is found (with other anomalies) in 25% of cases of cases of Wilms tumor.

... and others.

## Genetics

### Note

Genes (possibly) involved are unknown. The leukaemias with +8 appear to be a heterogenous group, with different clinical and cytologic presentations, and different expression profiles as well.

+8 is likely to be a secondary event, even in the cases where no known primary anomaly is associated to the +8, and also even in the trisomy 8 solely cases, where cryptic events -such as cryptic translocations or deletions, or mutations- remain to be found as primary events.

Imprinting data gave no particular results.

Constitutional trisomy 8 patients have an increased risk of developing a leukaemia

## 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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