

Leukaemia Section

Mini Review

Biphenotypic Acute Leukaemia (BAL)

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Clinics and pathology

Epidemiology

Biphenotypic acute leukaemia (BAL) is an uncommon disease. As strict diagnostic criteria have only recently been established, the precise incidence among acute leukaemias is uncertain, although it is likely to account for approximately 5% of all acute leukaemias. BAL can be de novo or secondary to previous cytotoxic therapy. It has been included in the WHO classification of haemopoietic malignancies as acute leukaemia of ambiguous lineage.

Clinics

As with other types of acute leukaemia, BAL presents with the symptoms resulting from cytopenias. The blast count at diagnosis does not tend to differ from that in acute myeloid leukaemia (AML) or acute lymphoid leukaemia (ALL). BAL can present at any age, including children, although it is more common in adults.

Cytology

Morphology The morphology of the blasts in BAL is not consistent. The cells may display myeloid differentiation features such as azurophilic granules or Auer rods, or have lymphoid/undifferentiated morphology. From those cases with myeloid features, the most common FAB subtype is M1 and M5. In some cases, there appears to be two blast populations: one larger population resembling myeloid blasts and another, with smaller lymphoid appearing blasts.

Immunophenotype This is essential to establish the diagnosis of BAL. The blasts co-express myeloid and lymphoid markers. Diagnosis is based on a published scoring system adopted by the European Group of Immunological Classification of Leukemias (EGIL) and the WHO. This system aims to differentiate true BAL from acute leukemias with aberrant expression of

a marker from another lineage. The score encompasses the number and degree of specificity of the markers expressed by the leukaemic cells.

The markers considered to be most specific are:

- B-lymphoid lineage: CD79a, CD22, cytoplasmic immunoglobulin.

- T-lymphoid lineage: CD3, anti-TCR, and

- Myeloid lineage: myeloperoxidase by cytochemistry or flow cytometry. Most cases express early haemopoietic markers such as CD34.

The score allows four groups to be identified. The most common group, accounting for 60-70% of cases, are those which co-express myeloid and B-lymphoid antigens. Less commonly the blasts co-express myeloid and T-lymphoid antigens. Co-expression of T and B-lymphoid markers and those with trilineage differentiation are rare.

Treatment

BAL has proven to be very difficult to treat with many cases being resistant to induction chemotherapy and those that enter remission have a high risk of relapse. There is no agreement on how the disease should be treated. The majority of patients receive treatment according to the morphology of the blasts, with either AML or ALL induction. If patients enter complete remission, consideration should be given to consolidation with stem cell transplantation.

Prognosis

The prognosis of BAL in adults is worse than AML or ALL. Four year overall survival has been quoted at 8%, although the numbers in this study are low. The most important good prognostic features emerging from limited data are age (<60 years), absence of the Philadelphia chromosome and achievement of complete remission. BAL is associated with over-expression of P glycoprotein (Pgp). As Pgp phenotype is often associated with treatment outcome in patients

with acute leukaemia, it is likely that over-expression may worsen the prognosis in BAL.

Cytogenetics

Cytogenetics morphological

Clonal and complex chromosome abnormalities are frequent in BAL but none are specific or characteristic to BAL. From the limited data that we have, the most common findings are t(9;22)(q34;q11) and abnormalities of chromosome 11, particularly 11q23.

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