Naso-Sinusal T ALL With Aberrant Expression of CD56 Mimicking NK/T Non Hodgkin Lymphoma

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Abstract T-acute lymphoblastic leukemia (T-ALL) represents 25 % of cases of acute lymphoblastic leukemia (ALL) in adults. The clinical presentation is dominated by a elevated number of white blood cells and in immunophenotype the lymphoblasts are generally Tdt positive and variably express CD1a, CD2, CD3, CD4, CD5, CD7, and CD8. NK/T non Hodgkin lymphoma is presented as a single lesion often ulcerated with torpid evolution affecting the nasal cavity, nasopharynx and/or palate. CD56 expression is while characteristic of NK-cells, and is also expressed on a subset of normal T cells. Its expression in ALL does not exclude the diagnosis and seems to be a prognostic factor of this disease. We report the case of a young woman with nasal cavity tumor which was initially diagnosed as T-cell lymphoma. This diagnosis was finally revised to conclude to T-ALL with CD56 aberrant expression.

Keywords CD56 expression · T-acute lymphoblastic leukemia · Naso-sinusal mass · NK/T lymphoma

Introduction

T-acute lymphoblastic leukemia (T-ALL) represents 25 % of cases of acute lymphoblastic leukemia (ALL) in adults.

In Morocco this incidence is not known. The clinical presentation is dominated by a elevated number of white blood cells, a large mediastinal mass with lymphadenopathy and hepatosplenomegaly. In immunophenotype the lymphoblasts are generally Tdt positive and variably express CD1a, CD2, CD3, CD4, CD5, CD7, and CD8. NK/T non Hodgkin lymphoma is presented as a single lesion often ulcerated with torpid evolution affecting the nasal cavity, nasopharynx and/or palate. There may be an extension to the nasal sinus, oropharynx, orbit or cranium base with involvement of cranial nerves. CD56 expression is while characteristic of NK-cells, and is also expressed on a subset of normal T cells. However neoplastic myeloid, lymphoid, plasmotoid dendritic or myeloma cells can also express CD56. Its expression in ALL does not exclude the diagnosis of T-cell ALL [1, 2]. This expression as well as age or leukocytosis at diagnosis seems to be a prognostic factor of T-ALL [3, 4]. In T-ALL CD56 expression has been reported for a small number of cases and an association with worse outcome has been suggested. We report the case of a young woman with nasal cavity tumor which was initially diagnosed as T-cell lymphoma. This diagnosis was finally revised to conclude to T-ALL with CD56 aberrant expression.

Case Report

A forty year old woman with no past medical history consulted in hematology unit for a tumor of the left cheek which appeared 3 months ago. The patient reported itching and sweating without fever or weight loss. The examination showed a performance status at one according to ECOG/World Health Organisation (WHO), a mass of the left cheek measuring 8 cm, no peripheral lymphadenopathy

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Fig. 1 Immunohistochemistry markers CD56 in the left and Tdt in the right

Fig. 2 Left jowl mass after induction chemotherapy course

and hepatosplenomegaly. The sinus CT-scan found a naso-sinusal tumor of $45 \times 32 \times 21$ mm extended to the left cheek. The tumor biopsy showed T-cell lymphoma with expression of T markers (CD3, CD5 and CD4) and negative to CD20. Biological exams in Hematology unit were completed by cells blood count: White Blood Cells 39,490 with $33\,217/\text{mm}^3$ lymphocytes (some of which are large with nuclei) 12 g/dl hemoglobin, $363,000/\text{mm}^3$ platelets). The lactic deshydrogenase and protein electrophoresis were normal. The patient received a cyclophosphamid vincristin and prednison (COP) chemotherapy pending the results of the bone marrow biopsy. Our pathologist reconsidered the diagnosis of the tumor biopsy and concluded to T-cells lymphoblastic lymphoma CD4+ CD5+ CD3+, Tdt+ and CD20–, EBV–with expression of CD56 antigen (Fig. 1). The examination of blood and bone marrow found an infiltration by lymphoblast so the final diagnosis was T-ALL with aberrant expression of CD56. The patient was included in MAR-ALL* local treatment of leukemia/lymphoblastic lymphoma. After the induction therapy, the response to treatment evaluation found a persistence of the mass with bone marrow infiltration. In consolidation treatment, physical examination revealed the left cheek mass (Fig. 2) whose measurements on computed tomography of the face remained virtually unchanged in comparison to those made in diagnosis: $44 \times 42 \times 23$ versus $45 \times 32 \times 25$ mm

(Fig. 3). The failure of chemotherapy led to a second line of treatment that resulted in a failure again.

Discussion

T-ALL typical presents with an elevated leukocyte count and often a large mediastinal mass or other tissue mass. Lymphadenopathy and hepatosplenomegaly are common. The sites of involvement are varied. They may well involve the nasal region that is known to be frequent in extranodal NK/T lymphoma. Indeed, extranodal NK/T-cell lymphoma is more prevalent in Asia, and the native American population of Mexico, Central America and South America. It occurs most often in adults, and is more common in males than females [2]. The classic form is presented as a single lesion often ulcerated with torpid evolution affecting the nasal cavity, nasopharynx and/or palate. There may be an extension to the nasal sinus, oropharynx, orbit or cranium base with involvement of cranial nerves. The almost constant expression of markers for association with EBV is a key to suspect its role in the development of these lymphomas [5].

In our patient the naso-sinusal involvement by ALL caused the confusion with nasal lymphoma for two reasons: the first reason is the site of involvement and the second is his association with CD56 expression. Indeed, the diagnosis of T-cell lymphoma which is more suitable for this type of tumor involvement has been mentioned in first and we considered treatment of aggressive lymphoma. A novel tumor biopsy exam coupled with peripheral blood and bone marrow examination, confirmed the expression of CD56 and the negativity of EBV. All this helped to conclude to a T-ALL diagnosis.

The prognosis of patients T-ALL compared to those with B-ALL is marked by a high risk of failure after induction therapy, early relapse and an isolated central nervous system relapse [6]. The prognostic factors identified so far include: age, WBC count at diagnosis, initial treatment response and cytogenetics. The predictive value

Fig. 3 Cranio-facial CT scan after induction chemotherapy course

* MARALL treatment include in induction: Steroid-Vincristine-Daunorubicin-L-Asparaginase-Intra-thecal

of immunophenotype on prognosis is controversial. Ravandi et al., from the analysis of 200, patients reported that the expression of CD56 was associated with a high incidence of central nervous system reaches the diagnosis while in another study Moreno et al. found that CD56 was the only independent prognostic factor for complete remission [3, 4]. Treating CD56 -expressing T-ALL is the same as T-ALL without CD56 expression. Response to therapy does not seem related to this marker.

T-ALL specifically express T antigen CD3. Other markers such as CD1a, CD2, CD4, CD5, CD7 and CD8 can be expressed, but none of them is specific. The expression of CD10 is less common (25 % of cases) and non-specific. The myeloid antigen CD34 and markers of natural killer (NK) cells can also exist. The expression of CD56 can be found in an unusual case without excluding the diagnosis of T-cells ALL [2]. It could cause confusion with lymphoma NK/T where the expression of CD56 is common with CD2 and certain cytotoxic molecules (such as granzyme B, TIA1 and perforin), while the CD3 T and other markers are negative (CD4, CD5, CD8, TCR δ , β F1, CD16 and CD57).

CD56 is a cell antigen which is expressed primarily on NK cells, activated T cells, the brain and cerebellum, and neuro-endocrine tissues. It is used as a phenotypic marker in certain malignancies, particularly in the lympho-proliferative large granular lymphocytic neoplasia. It is also expressed in rare cases of acute myeloid leukemia, nasal lymphomas associated with Epstein Barr virus (EBV) infection and multiple myeloma [7]. The expression of CD56 has been associated with an impact on prognosis in various malignancies.

In AML with t(15,17) and t(8,21) and in anaplastic large cell lymphoma, it was associated with a poor clinical response [8]. Montero showed that in a study of 30 cases of T-cell ALL with CD56 expression, CD56 was the only independent prognostic factor for a complete response to treatment [4]. In another subsequent studies with a larger number of patient Fischer et al. have not shown an adverse impact on outcome in T-ALL [8]. EBV gene

research can help to get a difference between T-cell ALL and T-cell lymphoma especially in case of aberrant expression of CD56. However, if its positivity allows to formally exclude T-cell ALL, its negativity does not exclude the diagnosis of T-cell lymphoma in which it may be absent. In our case it is true that the histological analysis coupled with immunohistochemistry was formal diagnosis of T-cell ALL expressing CD56, negativity of EBV has further confirmed this diagnosis. In addition Tdt would be a cheaper and better alternative to EBV studies to differentiate T cell lymphoma from T ALL.

References

1. Borowitz MJ, Chan JKC (2008) T lymphoblastic leukemia/lymphoma. In: Swerdlow SH et al (eds) WHO classification of tumours of haematopoietic and lymphoid tissues, vol 4. IARC Press, Lyon, pp 176–178
2. Ferry JA, Quintanilla-Martinez L, Chan JKC et al (2008) Extranodal NK/T-cell lymphoma, nasal type. WHO classification of tumours of haematopoietic and lymphoid tissues, vol 4. IARC Press, Lyon, pp 285–288
3. Ravandi F, Cortes J, Estrov Z et al (2002) CD56 expression predicts occurrence of CNS disease in acute lymphoblastic leukemia. *Leuk Res* 26(7):643–649
4. Montero I, Rios E, Parody R et al (2003) CD56 in T-cell acute lymphoblastic leukaemia: a malignant transformation of an early myeloid-lymphoid progenitor? *Haematologica* 7:26
5. Dupuis J (2004) Lymphomes non hodgkiniens T et NK périphériques. *EMC* 2:016
6. Goldberg JM, Silverman LB, Levy DE et al (2003) Childhood T-cell acute lymphoblastic leukemia: the Dana-Farber cancer institute acute lymphoblastic leukemia consortium experience. *J Clin Oncol* 21:3616–3622
7. Leandro F, Dalmazzo F, Rafael H et al (2009) The presence of CD56/CD16 in T-cell acute lymphoblastic leukaemia correlates with the expression of cytotoxic molecules and is associated with worse response to treatment. *Br J Haematol* 144(2):223–229
8. Fischer L, Gökbuget N, Schwartz S et al (2009) CD56 expression in T-cell acute lymphoblastic leukemia is associated with non-thymic phenotype and resistance to induction therapy but no inferior survival after risk-adapted therapy. *Haematologica* 94(2):224–229