Secondary Non Hodgkinian Lymphoma in a Patient Treated for Hodgkin Disease: A Case Report with Comprehensive Literature Review

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Abstract

The introduction of the intensive radiotherapy and chemotherapy has transformed the prognosis of Hodgkin disease and the long-term complications of the therapy became more frequent. Furthermore, the carcinogenic effect of the used therapeutical agents leading to a high incidence of second malignancies was clearly demonstrated. We present here a case of a patient treated for Hodgkin disease who developed 15 years later a secondary non Hodgkin lymphoma. The objective of this presentation is to describe this rare metachronous association of two malignancies and to discuss the etiological links.

Introduction

The occurrence of second malignancies in long surviving patients treated for cancers is widely reported in the literature and many documented studies have proven the role of some therapeutical agents in the incidence of second cancers, this was the case of secondary acute myeloid leukemia in which the role of cytotoxic drugs was well documented, however, secondary non Hodgkin lymphomas are less common and their pathogenesis remains controversial.

Case presentation

A 14 years old Moroccan patient presented to our institution in 1995 with multiple diffuse cervical lymphadenopathies associated to weight loss and night sweats, the physical examination found splenomegaly without hepatomegaly, computed tomography of the chest and the abdomen showed diffuse mediastinal and retroperitoneal lymphadenopathies. The biopsy of the cervical lymph nodes revealed on the histological examination a diagnosis of scleronodular subtype of Hodgkin lymphoma which was classified stage IIIB. The patient was treated initially with 6 cycles of chemotherapy following COPP regimen (association of Cyclophosphamide, Prednisone, Procarbazine, and Vincristine) followed by mantle field irradiation, we obtained a complete remission at the end of the treatment and the patient remained in good control for 15 years. In January 2011 he presented a righteous letarocervical mass evoking bulky lymphadenopathy associated to an intermittent fever and night sweats, the mass biopsy revealed on the histological examination a diagnosis of non Hodgkinian lymphoma confirmed by immunohistochimestry study with a positive staining to CD20 and EMA, and negative staining to CD30, CD3, CD15. The lymphoproliferative index was about 80%. Scanography showed multiple diffuse lymphadenopathies on the mediastinum, the abdomen, and the pelvis, with nodular splenomegaly and nodular lesions on the lungs, biological analysis showed an elevated lactate deshydrogenase rate, and the disease was classified stage IVBb. The patient undergoes now a salvage chemotherapy based on R-ESHAP protocol (association of Rituximab, Etoposide, Cisplatine, Cytarabine, and Methylprednisolon)

Discussion

In 1979, Horokian et al reported 6 cases of Non Hodgkin Lymphomas (NHL) occurring in patients treated for Hodgkin disease (HD) [1], this metachronous association of malignancies have been largely studied in the literature resulting in an incidence varying from 0.88% to 16.80% [2], the summary of the most important reviews are reported in (Table1).

Numerous theories and hypothesis could help to better understand the etiological link between the secondary NHL and the treated HD in the case that we report.

Postradiation theory: The impact of radiation therapy on the occurrence of second solid tumors is well established, but this relationship is less documented in the case of second hemopathies. Mauch PM et al in an analysis of 794 patients treated for HD with radiation alone or combined to chemotherapy reported a relative risk (RR) of 10.6 per 10,000 person-years for developing secondary NHL in patients treated with...
radiation alone, this risk was increased to 16.1 in patients treated with radiation combined to chemotherapy [6], however, evidence of linking radiation exposure to LNH occurrence is still not confirmed.

Cancerogenic effect of chemotherapy theory: DNA single or double brin damage caused by cytotoxic drugs, more evidently with alkylating and topoisomerase II inhibitors agents, might lead to the development of second malignancies. This hypothesis was well established in the pathogenesis of secondary acute myeloid leukemia (AML) to cancer chemotherapy treatment, and Pedersen-Bjergaard et al have reported different genetic pathways in leukemogenesis in patients presenting with therapy-related AML. [10] In the case of secondary NHL there is a lack of biological proofs to support this theory.

Immunodepression theory: Observation from Post-transplant lymphoproliferative disorders (PTLD) suggests the role of Epstein-Barr virus as a result of loss of immune control of EBV-positive B lymphocytes [11], in spite of that, there is no clinical evidence to say that whether HD treatment is related to a chronic immunodepression underlying a secondary lymphoproliferative disease such as LNH.

Transforming HD theory: In 1983 Miettinen et al suggested that lymphocytic predominant Hodgkin disease subtype may sometimes change into a more malignant lymphoma of the Hodgkin's or non-Hodgkin's type [12], nevertheless, even if common progenitor and genetic pathways were described, the question of whether LNH could be a part of the natural history of HD development remains uncertain.

Conclusion

The long survival and the heavy therapeutical strategy in patient treated for Hodgkin disease are the leading factors?in the occurrence of second cancers, many effort are made to desescale the therapeutical approach to avoid this complication.

References

Illustrations

Illustration 1

Table 1: The frequency and the relative risk of secondary Non Hodgkinian Lymphoma in patients treated for Hodgkin disease. (N: Total number of patients; NA: Not available; RR: Relative risk; sNHL: Secondary Non Hodgkinian Lymphoma)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Period of follow-up</th>
<th>N</th>
<th>sNHL</th>
<th>%</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swerdlow <em>et al.</em> [4]</td>
<td>2000</td>
<td>1983-1993</td>
<td>5,519</td>
<td>50</td>
<td>0.9</td>
<td>14 (10.5-18.3)</td>
</tr>
<tr>
<td>Bhattacharya <em>et al.</em> [5]</td>
<td>1996</td>
<td>1955-1996</td>
<td>1,380</td>
<td>6</td>
<td>0.43</td>
<td>20.9 (7.7-42.0)</td>
</tr>
<tr>
<td>Tucker <em>et al.</em> [9]</td>
<td>1988</td>
<td>1988-1995</td>
<td>1,307</td>
<td>9</td>
<td>0.59</td>
<td>0.5 (1.1-33.5)</td>
</tr>
</tbody>
</table>
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