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Case Report

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Rituximab plus concurrent radiation therapy for the management of CD20 -positive peripheral T- cell lymphoma: A case report and review of literature

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Abstract

Peripheral T-cell lymphomas constitute an uncommon and heterogeneous group of predominantly nodal mature T-cell lineage non-Hodking neoplasms in adults. Although unusual, CD20 expression has been reported in peripheral T-cell lymphomas. Currently there is no consensus regarding the preference and benefits of CHOP chemotherapy over alternative treatments. Since it has failed to accomplish remission and improve overall survival an alternative management approach should be encouraged to pursue as initial treatment according to the National Comprehensive Cancer Network. We present the case of an 81-year-old patient with a stage III CD20-positive peripheral T-cell lymphoma who was successfully managed with rituximab and concurrent radiation therapy for 8 weeks with no relapses and no evidence of disease since 2011. Further research through clinical trials is needed to reach a consensus and establish an optimal first-line standard regimen for treatment of CD20-positive peripheral T-cell lymphomas. The use of rituximab and radiation therapy may represent a promising initial combination in the setting of documented early nodal CD20-positive peripheral T-cell lymphoma.

Background

Peripheral T-cell lymphomas (PTCL) constitute an uncommon and heterogeneous group of predominantly nodal post-thymic, mature, T-cell lineage neoplasms in adults [1]. Compared to their B-cell lineage counterparts PTCL account for less than 15 percent of non-Hodgkin´s lymphomas (NHL) and exhibit a more aggressive clinical course. PTCL have a poorer prognosis with inferior rates of response to chemotherapy and disease-free survival overall [2]. The median age of onset is 60 years with a male to female ratio of 1.9:1. One-third of patients have B symptoms at diagnosis while others may present with lymphadenopathy with or without associated fatigue [1,3].

PTCL must be distinguished from other subtypes of B-cell and T-cell lymphoid malignancies defined by the World Health Organization classification. Consequently, an adequate immunophenotype by immunohistochemistry or flow cytometry is essential to establish the diagnosis. The designation PTCL not otherwise specified, is reserved for PTCL that fail to meet criteria for inclusion in another category and it is the most common subtype of PTCL [3].

Although unusual, CD20 expression has been increasingly reported in PTCL and other T-cell lymphomas in the last twenty years [4-12]. Moreover, Hultin *et al.* found the presence of this B-cell surface antigen in a small group of normal T-cells in healthy individuals [13]. Further research is needed to determine the clinical reverence of CD20 and other markers thought to be restricted to B-cells in PTCL.

Cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) and CHOP plus etoposide (CHOEP) chemotherapy regimens are the most commonly used first-line treatment for PTCL patients [4-12]. However, there is currently no consensus regarding optimal standard first-line therapy for PTCL. Thus, participation of PTCL patients in clinical trials is the preferred management approach according to the National Comprehensive Cancer Network (NCCN) as CHOP and CHOEP have not provided the same favourable outcomes as seen in other lymphoid entities [14]. The CD20 positive PTCL described in the reviewed literature were treated with the same regimens of a classic PTCL and in a few cases rituximab was added [9-12]. Radiation therapy (RT) was considered as a sole treatment in a CD20-positive PTCL of the skin[6] and as palliative treatment in one report [7].

To our knowledge, this paper reports the first case report of a CD20-positive peripheral mature T-cell lymphoma successfully managed with rituximab and concurrent RT with no evidence of disease since 2011.

Case presentation

In July 2011, an 81-year-old man presented to Sarah Bush Lincoln Regional Cancer Centre with a one month history of progressively increasing swelling, redness and tenderness over his right ear. He denied fever, chills, weight loss, night sweats and other symptoms. Physical examination evidenced an erythematous lesion involving the

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right tragus, crus of helix and preauricular region associated with an induration of the skin below; the rest was unremarkable. The patient had a history of coronary artery disease with a stent placement in 2009 for which he took aspirin, pravastatin and atenolol. No family history of malignancies, no smoking or drinking habits and no known drug allergies.

The patient underwent a fine needle aspiration, which was non -diagnostic. A computed tomography of the neck showed a 3.3 x 3.3 x 2.8 cm, superficial, soft tissue mass with irregular margins anterior to the right external ear canal at the superficial lobe of the right parotid gland. There were no enlarged cervical lymph nodes or osseous abnormalities.

An excisional biopsy of the mass showed a diffuse infiltration of the parotid architecture by intermediate-sized atypical lymphocytes which exhibited an open vesicular chromatin, prominent nucleoli and scant cytoplasm. Other occasional scattered large neoplastic lymphocytes were present with multiple nuclear lobes, prominent nucleoli, and moderate to abundant cytoplasm. The atypical lymphoid cell infiltrates invaded vessel walls and nerves in addition to the surrounding adipose tissue.

The overall findings of the immunohistochemical analysis at GenPath were consistent with CD20-positive peripheral mature T-cell lymphoma (Table 1). The presence of CD3, CD5, CD7 and the absence of PAX-5 and CD79a confirmed the lymphoma lineage as T-cell.

A positron emission tomography–computed tomography (PET/CT) two months later showed a 2.4 x 2.3cm fluorodeoxyglucose (FDG)- avid focus within the right parotid gland with standard uptake value measuring up to 17. There were no suspicious FDG-avid cervical lymph nodes. In addition, a small mildly FDG-avid precarinal lymph node and a 5.5cm hypermetabolic subcutaneous mass on the upper right thigh were found. The biopsy of this mass was also consistent with CD20-positive peripheral T-cell lymphoma. Patient's International Prognostic Index was 3 and his disease was cataloged as stage III.

Table 1. Immunohistochemistry profile. The neoplastic cells were positive for CD3, CD20, CD5, CD7 and CD43. CD4 was weakly positive in a subset of the neoplastic cells. CD2 and CD8 stain scattered cells. The neoplastic cells were negative for CD56, ALK-1, BCL-6, BCL-1, CD79a, CD30, PAX-5, CD10, CD21, CD23, TdT and TIA-1. EBV immunohistochemistry (likely LMP1) was positive in extremely rare cells

Antibody	Result
CD20	Positive
CD3	Positive
CD5	Positive
CD10	Negative
CD23	Negative
CD43	Positive
BCL-1	Negative
BCL-2	Negative
BCL-6	Negative
CD79a	Negative
CD56	Negative
PAX-5	Negative
CD2	Negative
CD7	Positive
CD4	Rare Positive (Small Subset)
CD8	Negative
CD30	Negative
CD21	Negative
TIA-1	Negative
EBV	Negative
TdT	Negative

The patient underwent definitive RT to both areas along with a concurrent rituximab therapy. He was given 180 centiGrays and 200 centiGrays of RT for the cervical and inguinal lymphadenopathy respectively and rituximab weekly for 8 weeks. The treatment was well-tolerated and by the end of the third week these lymphadenopathies, including the precarinal FDG-avid lymph node evidenced by imaging studies, disappeared. This was corroborated with a subsequent PET/CT which was unremarkable and during follow-up assessment where the patient affirmed being symptom-free of his condition. He completed the regimen of RT and rituximab in September 2011 without complications or relapses and currently there is no evidence of disease.

Conclusions

It is known that PTCL display lower rates of response to conventional chemotherapy with an average ranging from 50 to 70 percent when contrasted to other B-cell and some T-cell NHL with almost 90 percent of response [15]. For instance, the International PTCL Project exposed a 32 percent 5-year overall survival and a 20 percent 5-year failure-free survival within 340 cases [1]. Controversially, as reviewed in literature, despite the statistics and the fact that no study has demonstrated significant benefit of CHOP or CHOEP over other treatment it remains the most used first-line regimen to treat PTCL and CD20-positive PTCL [8-12].

Patients with similar progressively increasing lymphadenopathy at onset as the one described in this case report exhibited no exception to the poor response to conventional chemotherapy [9-12]. To manage CD20-positive PTCL Hirata *et al.* [12] install CHOP chemotherapy and evidenced a 4-month disease-free survival. They rotated to etoposide, methylprednisolone, cytarabine and cisplatin (ESHAP) and after achieving no remission rituximab alone was started. Xiao *et al.* [9] noticed a refractory CD20-positive PTCL with more than one relapse in their patient treated with CHOP plus RT. A comparable outcome of 4-5-month disease-free survival as that of Hirata *et al.* was reported by Song *et al.* [10] after initiating CHOP plus rituximab. Two years later, Matnani *et al.* [11] documented a 3-month disease-free survival after 6 cycles of CHOP along with rituximab. Most of these patients experimented several relapses, the outcome remains unknown with the exception of one subsequent death which was reported within these cases. Furthermore, other intensive regimens sometimes resulted in more early deaths due to side-effects and toxicity [15].

Rituximab represents a tentative targeted treatment option for CD20-positive PTCL as it is for B-cell NHL. It has proved to be effective, but the degree of response cannot be assessed since there are few cases of CD20-positive PTCL reported in literature. So far rituximab has given mixed results when combined with CHOP chemotherapy, comparable to the response of CHOP chemotherapy in classic PTCL. Moreover, in some reports rituximab was given alone as last resource in patients with an advanced disease [12]. Therefore, its potential in CD20-positive PTCL is far from being explored and may be underestimated.

RT with or without chemotherapy can be helpful in early stages of PTCL, especially with involvement of localized areas according to the NCCN [14]. Nevertheless, it has not played a critical part in the treatment plan of CD20-positive PTCL as chemotherapy is preferred at onset. Magro *et al.* [6] used RT to treat a CD20-positive PTCL of the skin and Buckner *et al.* [7] considered RT as palliative treatment in a CD20-positive T-cell Lymphoma/Leukemia. However, in the majority of case reports RT did not play any role, not even with localized disease.

Since CHOP, CHOEP, ESHAP and other chemotherapy regimens have failed to accomplish remission and improve overall

survival for the majority of patients with CD20-positive PTCL an alternative management approach should be encouraging to pursue as initial treatment. The use of rituximab with concurrent RT for the management of CD20-positive PTCL with early nodal involvement achieved a rapid response with a reduction of half of the size of the enlarged lymph nodes by two weeks of treatment and its remission by the third week. After completion this dual therapy yielded a complete response after 8 weeks of rituximab and RT.

Developing an individualized alternative treatment plan for patients with CD20-positive PTCL is essential. Further research through clinical trials is needed to reach a consensus and establish an optimal first-line standard regimen for treatment of PTCL and CD20-positive PTCL. For the latter, the use of rituximab and concurrent RT may represent a promising initial combination in the setting of documented early nodal disease.

Declarations

The authors declare that there is no conflict of interest regarding the publication of this paper. All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented. Both authors interpreted the patient data, wrote and approved the final manuscript.

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