Dear Editors,

Extranodal NK/T-cell lymphoma (NK/TCL) is a rare, highly malignant non-Hodgkin lymphoma (NHL) that primarily originates from natural killer cells and is frequently associated with Epstein-Barr virus (EBV) infection [1]. While NK/TCL is most common in Asia and Latin America (up to 10 % of all NHL), its incidence is less than 1 % in Europe [2]. Sites of predilection include the nasal cavity and the nasopharynx, less commonly also the skin, soft tissues and the gastrointestinal tract [1, 3, 4]. Conventional treatment approaches with chemotherapy and radiation therapy have not been able to achieve prolonged survival, and the prognosis of NK/TCL is poor even in early stages [4, 5].

A 73-year-old patient presented with a six-month history of an enlarging, partially erosive plaque on the nasal tip (Figure 1a). Other symptoms included difficulties breathing through the nose and mild pruritus. The patient was initially started on topical treatment with tetracyclines and fusidic acid. As there was no improvement, he subsequently underwent a biopsy. Histology revealed an infiltrate of predominantly CD3-positive atypical lymphoid cells (Figure 2a). The ratio of CD4/CD8-positive T lymphocytes was 3 : 2. Approximately 20 % of cells weakly expressed CD20. There was strong expression of CD56 (Figure 2b) as well as of the cytotoxic markers TIA, granzyme B and perforin. The percentage of CD30-positive cells was about 5 %; there was only sporadic expression of CD123. In situ hybridization revealed EBV in the vast majority of neoplastic cells (Figure 2c). Molecular genetic studies showed polyclonal rearrangement of the TCR-gamma locus. Based on the aforementioned findings, the patient was diagnosed with NK/TCL.

CT imaging of the neck, thorax and abdomen showed suspicious lymphadenopathy in the supraclavicular, retroperitoneal and parailiac region. Surprisingly, a biopsy taken from a retroperitoneal lymph node was consistent with diffuse large B-cell lymphoma. The blastic infiltrate was strongly positive for CD20. While there was strong CD3 expression by small T cells, CD30 was expressed only sporadically. Cells were diffusely reactive for BCL-2. There were no CD56-positive infiltrates; neither was there any CD10 expression. Based on the percentage of MIB1-positive cells, the proliferation index was approximately 60 %. In situ hybridization was negative for EBV. The patient was subsequently started on R-CHOP chemotherapy. After eight cycles, imaging studies revealed the B cell lymphoma to be in complete remission. Following initial improvement, the nasal lesion showed progression shortly after chemotherapy had been discontinued. Again, the patient reported difficulties breathing through the

![Figure 1](https://example.com/figure1.png)

**Figure 1** Clinical and CT findings before (a) and 32 months after initiation of immunotherapy (b).
nose, which correlated with soft tissue edema on imaging. Endonasal biopsy showed persistence of the NK/TCL, with more than 90% of cells expressing PD-L1 (Figure 2d). As a result, the patient was now started on the anti-PD-1 antibody pembrolizumab (2 mg/kg every three weeks). As he was considerably bothered by nasal obstruction, we decided to add radiation therapy (2 Gy per day; total dose of 30 Gy) to the treatment regimen in order to speed up symptom relief. After a total of nine cycles of pembrolizumab therapy, the patient has been in complete remission for more than two years (Figure 1b).

Treatment of recurrent or recalcitrant lymphomas continues to pose a challenge. While immune checkpoint inhibitors have been shown to achieve response rates of 60–80% in individuals with Hodgkin’s lymphoma, these figures are lower in patients with NHL (20–40%) [6]. Current treatment options for advanced NK/TCL include anthracycline-based regimens, but the response is usually only short lived. Although asparaginase-based regimens have improved the prognosis of patients with NK/TCL, recurrences are still common [3], thus highlighting the necessity for novel treatment options. Given the rarity of cutaneous lymphomas, there are no large studies and only few case reports; as a consequence, there are no evidence-based treatment recommendations [4, 7]. Chronic EBV infection has been shown to induce PD-L1 expression, which may be seen in 80% of neoplastic cells [8]. Thus, anti-PD-L1/PD-1 therapy is a promising approach for EBV-associated malignancies [9]. In a study published by Kwong et al., seven patients with recalcitrant NK/TCL were treated with pembrolizumab. Five patients showed complete remission; the remaining two patients, partial remission. However, the follow-up period was only six months [10]. Our patient has remained in sustained complete remission for more than two years after treatment with a PD1 inhibitor in combination with radiation therapy. It is conceivable that viral antigens constitute a potential target for anticancer immune responses in this aggressive type of cutaneous lymphoma. In addition, there is some evidence that PD-L1 expression may be a positive predictor of prolonged overall and progression-free

**Figure 2** Hematoxylin-eosin stain shows an atypical lymphoid infiltrate (a); strong CD56 expression by neoplastic cells (b); EBER in situ hybridization reveals EBV in the vast majority of neoplastic cells (c); PD-L1 expression by > 90% of tumor cells (d).
survival, irrespective of previous treatments [11]. This may have contributed to the positive clinical course in our patient.

To the best of our knowledge, this is the first report of a patient with NK/TCL who has been in complete remission for such a long period of time following pembrolizumab and radiation therapy. However, no inferences should be drawn with respect to the use of anti-PD-1 agents in the treatment of ‘classic’ cutaneous T-cell lymphomas. Nevertheless, the present case highlights the versatility and effectiveness of immunotherapy in the treatment of cutaneous malignancies.

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Conflict of interest
None.

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