

Nasal extranodal peripheral NK/T-cell lymphoma treated by the protocol NK/T-cell high-dose-methotrexate L-asparaginase dexamethasone

To the Editor: Extranodal NK/T cell lymphoma, a nasal type lymphoma, is a distinct entity by the WHO classification of lymphomas¹ with a frequency of less than 1% of all non-Hodgkin lymphoma (NHL) in the West² and the North Africa³ and an increased incidence in Asia.⁴ Standard treatment is not well established and anthracycline containing combination chemotherapy (CHOP) had less than 30% survival at 5 years in localized disease.⁵ We report a case of extranodal NK/T cell lymphoma, nasal type, treated initially with CHOP as a large cell lymphoma and then with high-dose methotrexate, L-asparaginase and dexamethasone as part of a multicenter phase II clinical trial (GELA-GOELAMS) for extranodal NK/T cell lymphoma.

A 34-year-old man, a welder by profession for 17 years, was seen in September 2008 for a right unilateral nasal obstruction associated with recurrent epistaxis (**Figures 1,2**). There were no associated B symptoms and performance status was 1. Anterior rhinoscopy revealed a right nasal cavity ulcerated mass with bleeding on touch. There was no other abnormal finding on physical examination with no peripheral adenopathy or hepatosplenomegaly. The diagnosis of NHL was established after several attempts at biopsy due to secondary infection and necrosis. The pathology was reported as consistent with large cell NHL and available immunohistochemistry showed lack of expression of CD20, CD3, and cytokeratin. Patient was staged as Ann Arbor stage IEA with no poor prognostic factors according to the International Prognostic Index. The patient was

started on CHOP chemotherapy but after two cycles, he had a poor response with a significant increase of the initial lesion and extension to the right upper lip. A repeat biopsy showed a diagnosis of extranodal NK/T-cell lymphoma, nasal type with EBV+.

The patient was switched to combined treatment with methotrexate 3g/m² on day 1, L-asparaginase 6000U/m² on day 2, 4, 6 and 8 with dexamethasone 40 mg day 1 to day 4 on 21 days cycle for a total of three cycles. The patient responded nicely and the tumor regressed after the first cycle. The patient achieved a complete clinical response after a second cycle (**Figure 3**). One month after the third cycle, he started irradiation, 30 Gy to the initial site of the disease. At the time of last follow up at 24 months, he was in complete remission (**Figure 4**). In conclusion, extranodal NK/T-cell lymphoma nasal type is a rare entity. Diagnosis may be difficult without an appropriate panel of immunohistochemistry that may not be available in all hospitals, especially the detection of cytoplasmic expression (CD3ε), EBV expression and molecular biology techniques. Cases with clinical suspicion of extranodal NK/T-cell lymphoma should have a full panel of immunohistochemistry from a tertiary referral center if needed. Conventional anthracycline-based therapy (CHOP) has a poor outcome. This could be related to the overexpression of PGP (multi-drug resistance) by NK/T tumor cells.⁶ Chemosensitivity to L-asparaginase and high-dose methotrexate has encouraging results and should be tested in future prospective studies.⁷⁻⁸ Our patient had 17 years of occupational exposure to iron dusts and galvanized metals (welding) that may have contributed to the development of this type of NHL. In our patient.



Figure 1. Nasal damage at diagnosis.

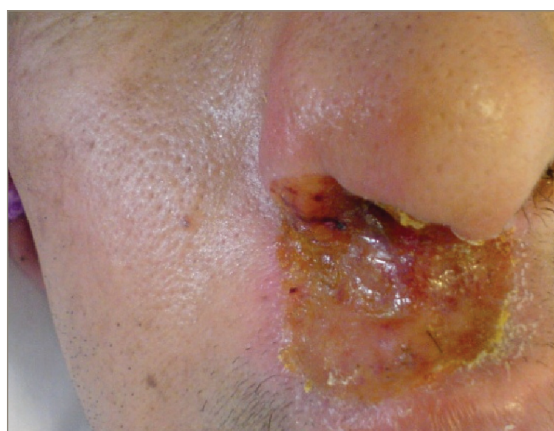


Figure 2. Large nasal damage before treatment.

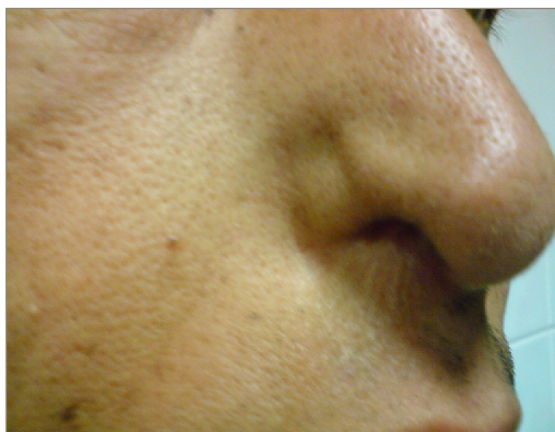


Figure 3. Improvement after treatment with high-dose methotrexate and L-asparaginase.



Figure 4. Complete clinical remission.

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