

## PRIMARY CUTANEOUS NK/T CELL LYMPHOMA-NASAL TYPE WITH CUTANEOUS ASPERGILLOSIS. A CASE REPORT AND LITERATURE REVIEW

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### comment:

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Very interesting case published in Krishnanand G. et al has touched the problem of lymphoproliferation on many levels. It has illustrated the need to remain vigilant in the diagnosis of both proliferative and infectious skin conditions. Extensive necrosis and purulent inflammation may frequently be dismissed as an infectious or benign inflammatory process in case of lymphoma. Extremely rare coincidence of aspergillosis and NK/T cell lymphoma was described just two times before (pubmed database). Relation to HIV infection was noted in one publication and patient died because of opportunistic infection because of invasive aspergillosis after tumor recurrence [1]. What more, in between described by European Organization for Research and Treatment of Cancer/Mycosis Study Group (EORTC/MSG) 2,821 patients with other hematological malignancies (including 597 who had undergone HSCT) the aspergillosis was diagnosed in 23 cases only (pulmonary one, fatal in the course in most of cases) [2]. The case of Krishnanand G. et al is even more interesting because aspergillosis was probably cut out by wide local excision and there were no recurrence in spite of introduction of metotrexate and lack of antifungal treatment. This need a comment of experienced microbiologist.

Affected by NK/T cell lymphoma, nasal type patients typically present with nonspecific rhinitis or refractory chronic sinusitis. But the location not in upper aerodigestive tract can also happened. Ex. between 73 patients published recently by Li S et al [3] 10 had extranasal disease involving skin, small intestine, epiglottis, testis, adrenal glands, kidney, and breast. That is why flank location should not surprise. A correct NK/T cell lymphoma, nasal type diagnosis requires an experienced pathologist, often taking multiple sets of large biopsies. Histologically, angiocentric and angiodestructive growth pattern is frequently present, with fibrinoid changes within blood vessels even in the absence of angioinvasion. Infarction-like coagulative necrosis and admixed apoptotic bodies are very common findings. The angiocentric and angiodestructive features of the tumor cells can mimic a vasculitis, such as Wegener's granulomatosis, what we

published before [4]. The typical immunophenotype is CD2+, CD 56+, surface CD3-, with cytoplasmic CD3ε+. Cytotoxic molecules are also positive, such as granzyme B, TIA-1, and perforin. EBER in situ hybridization demonstrates virtually all lymphoma cells as positive. But histopathological pattern can be differ, what was revealed by Krishnanand G. et al case. No CD56 antigen expression, as in noted case, is found in 10% cases, no necrosis can be revealed in 8% cases, no angiocentric/angiodestructive growth pattern in more than 30%. But in situ hybridization for Epstein-Barr virus-encoded small RNA should be positive in every case [3]. The etiology of the lymphoma remains not established, however, a strong association with EBV suggests a pathogenic role of the virus [5]. The disease activity can be monitored by measuring circulating levels of EBV DNA, as a high titer of the DNA may suggest extensive disease, unfavorable response to therapy, and poor survival [6]. The use of Fluorine-18 fluorodeoxyglucose positron emission tomography computerized tomography (18-FDG PET-CT) may offer more accurate diagnosis because it may distinguish lymphoma involvement from inflammatory masses [7].

The prognosis in case of NK/T cell lymphomas, nasal type is still poor. It is well known that P-glycoprotein, a product of the multi-drug resistance (MDR1) gene, is expressed on neoplastic cells of that lymphoma. This is a major cause of the refractoriness of the disease to conventional chemotherapeutic regimens containing anthracycline. Some recent studies, however, have identified that L-asparaginase-containing regimens, such as SMILE (steroid, methotrexate, ifosfamide, L-asparaginase and etoposide), are effective for NK/T cell lymphoma, nasal type. Radiotherapy remains effective for the disease [8,9], but is not effective for occult lesion outside the radiation field. The 5-year overall survival (OS) rate using chemotherapy followed by radiotherapy did not exceed 50% [10-12], which was almost the same as that of radiotherapy alone. Radiotherapy followed by chemotherapy was the standard for the limited stage NK/T-cell lymphoma [13,14].

Recently, a strategy of simultaneous chemoradiotherapy was introduced [15,16]. Both studies showed excellent results with 2-year OS of around 80%, but they have not yet shown the advantage over a radiation-first strategy.

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