A Rapidly Progressing Fatal Case of Natural Killer/T-Cell Lymphoma Presenting as Orbital Inflammation

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To the Editor: Natural killer T-cell lymphoma (NKTCL) is a rare form of non-Hodgkin's lymphoma (NHL) that constitutes 1–3% of all cases of orbital NHL. Orbital NKTCL is known as a "masquerade syndrome" with myriad presentations.[1] This case reported a 45-year-old male with primary NKTCL of the orbit initially presenting as orbit inflammation but eventually progressing to systemic aggressive disease.

A 45-year-old male was admitted to the West China Hospital with a 20-day history of progressive and painless redness, reduced vision, and periorbital swelling in the left eye. The patient had no complaint of congestion, fever, chills, or night sweats. He received the treatment for orbital cellulitis in another hospital, but showed no improvement of symptoms. Physical examination revealed proptosed and closed left eye, accompanied by painless periorbital swelling, redness, and exudation [Figure 1a]. Due to the severe periorbital swelling, there was no visual acuity or extraocular movements in the left eye, whereas the right eye had no sign of abnormality. There was no palpable cervical, axillary, or inguinal lymph node. An abdominal examination revealed no enlargement of the spleen or liver. The laboratory test revealed increased C-reactive protein at 26.40 mg/L and elevated procalcitonin at 0.17 ng/ml. The routine blood examination was normal, and the patient was negative for IgA to Epstein-Barr virus (EBV).

A contrast-enhanced computed tomography (CECT) scan of the orbit and paranasal sinuses revealed a soft-tissue mass of 5.8 cm × 5.4 cm in his left superolateral orbit. The soft-tissue mass involved the eyelids, superior ocular rectus, and optic nerve, but there was no bone erosion [Figure 1b]. Due to the fast progressing nature of the initial symptoms, inflammatory diseases were considered as the most possible diagnosis, with suspected inflammatory pseudotumor or cellulitis of particular pathogens. The patient was treated with piperacillin, levofloxacin, and sulfamethoxazole-trimethoprim, but no clinical improvement could be found one week after treatment.

When the patient was receiving antibiotics, additional symptoms including hematemesis and bloody stool developed. A CECT scan of the abdomen revealed a soft-tissue mass of approximately 4.0 cm × 2.0 cm in front of the right kidney and several soft-tissue masses in the cardiophrenic angle and beneath the diaphragm with a slight enhancement. A laboratory test revealed an increased lactate dehydrogenase at 1613 U/L. Flow cytometry (FCM) further confirmed the existence of P1 cells, mature lymphocytes, and myeloid cells in peripheral blood. Flow cytometric immunophenotype (FCI) comprised P1 cells with large forward

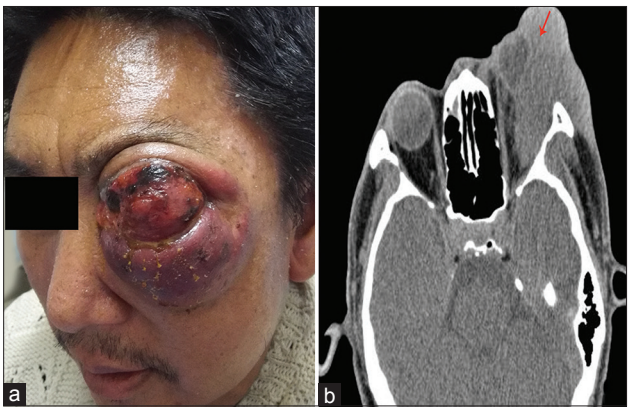

Figure 1: A 45-year-old male presenting with primary natural killer T-cell lymphoma of the orbit. (a) The patient's left eye was proptosed and closed accompanied with painless periorbital swelling, redness, and exudation. No abnormity was observed on the right eye. (b) The contrast-enhanced computed tomography scan of the orbit and paranasal sinuses revealed a soft-tissue mass of approximately 5.8 cm × 5.4 cm in his left superolateral orbit involving the eyelids, superior ocular rectus, and optic nerve, but without bone erosion (red arrow).

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scatter, expressing CD2/CD7, CD38, CD56, CD159a, CD161, and human leukocyte antigen-D related but negative for CD34, TDT, CD45, surface CD3, CDd5 CD138, CD19, and CD20, which indicated extranodal NKTCL. The patient declined the biopsy or any invasive procedure and was soon discharged home without any other treatment. He succumbed to his illness within the next 2-week follow-up.

Extranodal NKTCL is a rare hematological malignancy. The nonnasal/extranasal subtype accounts for approximately 25% of NKTCLs; the tissue mass can develop in multiple locations, such as the skin, gastrointestinal tract, salivary glands, lungs, and testes.[1] Orbital involvement of extranodal NKTCL is rare, and most lesions were found with direct erosion/extension. EBV is suspected to mediate the development of extranodal NKTCL, because of the frequent detection of EBV in the tumor cells. However, a negative EBV load does not exclude NKTCL directly, as in this case.

When NKTCL lymphomas affect the orbit, the initial symptom is always painless eyelid inflammation with swelling and redness and decreased vision. Weight loss, fever, night sweats, and anemia can occur in the late stages. However, the atypical symptoms and myriad presentations can make it easy to be misdiagnosed as orbital inflammation, cavernous sinus thrombosis, IgG4-related disease, or orbital mucosa-associated lymphoid tissue lymphoma. Blood tests, antibiotics, and radiological studies may help distinguish NKTCL from other differential diagnoses at the early stage. A tissue biopsy with pathological morphology is required when there is no clinical improvement with a full course of antibiotics. FCM/FCI analysis of peripheral blood could also be valuable to diagnose NK cell neoplasms.[2,3] A previous study reported that the histological and immunophenotypic hallmarks of NKTCL showed positivity for CD2, CD56, and cytoplasmic CD3e and negative expression of a B cell marker (CD20) and T cell antigen (e.g., CD4, CD5, and surface CD3), which was also noted in this case.[3]

The current treatment strategies for extranodal NKTCL depend on the grade and stage of the disease. The best modality is a combination of radiotherapy and chemotherapy, especially for the early stages. Delayed diagnosis/treatment usually contribute to poor prognosis of NKTCL, while poor response to initial treatment also is indication of dire outcome.[4] The mortality of orbital NKTCL has been reported as high as 87%.[1] Compared with Ely *et al*.,[5] who reported a median survival of 4 months for patients with extranodal NKTCL, our patient experienced much more rapid progression of the tumor without any intervention, indicating the aggressive nature of the tumor.

Several factors contributed to the delayed diagnosis and treatment in this case. The patient refused to undergo a biopsy or receive further treatment, such as routine radiotherapy and chemotherapy, due to the financial burden, which led directly to rapid progression and the eventual mortality. This is a typical challenge in China for rural farmers with poor socioeconomic condition. In addition, the patient's initial atypical symptoms and myriad presentations seemed to lead to the delayed diagnosis. With this report, we highlighted that although NKTCL is an uncommon type of lymphoma and rarely presents as an orbital mass lesion, clinicians need to consider NKTCL as a differential diagnosis when presented with patients of "masquerade syndrome".

In summary, orbital NKTCL is a rare hematological malignancy that has an aggressive course. It can be easily misdiagnosed when presented with orbital lesions. It is important to differentiate a lymphoproliferative disorder from orbital inflammation when initial antibiotic treatment failed to yield notable improvement. Early initiation of proper intervention is critical for the long-term prognosis of patients who are diagnosed with NKTCL.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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