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CASE REPORT

Sinonasal Extranodal NK/T-cell Lymphoma Presenting with Torrential Epistaxis

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ABSTRACT

Extranodal sinonasal natural killer/T-cell lymphoma is known for its locally destructive nature at the midface region. The initial presentations are related to the localized granulomatous-like lesion usually in the nasal cavity that may lead to symptoms of nasal obstruction, discharge, hyposmia and epistaxis. Advanced disease may present with a rapid dissemination of disease to the liver, spleen, skin, lymph nodes, and bone marrow hence poorer prognosis. We report a case of a young lady with rapid progression of extranodal sinonasal NK/T cell lymphoma with torrential tumour bleeding from the oral and nasal cavities compromising the upper airway patency, which warranted an emergency tracheostomy and arterial embolization.

KEYWORDS: Extranodal NK/T-cell lymphoma, non-Hodgkin lymphoma, bleeding, radiotherapy, embolization, granulomatous

INTRODUCTION

Extranodal (sinonasal) natural killer/T-cell lymphoma (ENKTL) is an aggressive non-Hodgkin lymphoma (NHL) characterized by locally progressive destruction of the midface, particularly the nasal/paranasal region [1]. Historically it was grouped in granulomatous nasal disease and termed as midline lethal granuloma, which leads relentlessly to death [2]. ENKTL is commonly seen among residents of South-East Asia, accounting for 7-10% of all NHL cases, although it may occur in populations from all geographical regions worldwide, albeit with lower prevalence [3]. In Malaysia, Chinese descendants are commonly affected followed by Malay and Indian ethnic groups. That may indicate an association of the disease prevalence with genetic background [4]. Etiologically, it appears to be caused by the Epstein-Barr virus (EBV) [4, 5]. All age groups can be affected but it is commonly seen in the fifth and sixth decades of life with a male preponderance [1].

ENKTL classically presents with nasal obstruction, discharge, hyposmia and bleeding. As the disease progresses, swelling of midface arises that is followed by the formation of deep necrotic ulceration affecting midline structures of the nasal skeleton and palate, and consequently involving adjacent structures including the orbit, oral cavity, skin and paranasal sinuses [2].

We present a case of a young lady with rapid progression of ENKTL with torrential tumour bleeding from the oral and nasal cavities compromising upper airway patency.

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CASE PRESENTATION

A 33-year-old lady, newly diagnosed with extranodal NK/T-cell lymphoma, presented with progressively worsening unilateral left sided nasal blockage for 2 weeks, which later became bilateral requiring mouth breathing. The blocked nose was associated with rhinorrhea, postnasal drip and hyposmia. At that time, she sought medical attention at a private hospital where an endoscopic removal of the nasal mass was performed. Post-operatively, she started to experience bilateral painful cervical lymphadenopathy. She also had throat pain that was associated with foreign body sensation, dysphagia and odynophagia to solid food. Despite antibiotic and analgesic treatment, the symptoms were not resolved. She had poor oral intake with significant weight loss of 5 kilograms. A month after the initial presentation, she started to develop recurrent unprovoked bleeding from the oral and nasal cavity. This made her afraid to fall asleep, as she could not breath if the bleeding occurs when she dozes off.

On examination, she looked pale, was not tachypneic and was sitting in an upright position. There was no facial dysmorphism. Misting of bilateral nostril was absent on cold spatula test. Anterior rhinoscopy showed pinkish irregular mass occupying both nostrils with the presence of blood-stained mucoid discharge. Intraoral examination revealed a soft palate mass that narrowed the oropharyngeal inlet and obscured the posterior oropharyngeal wall. There were some ulcers and necrotic patches over the hard palate (Figure 1). Laryngoscopy showed normal supraglottic region. However, the postnasal space was difficult to visualize. Neck examination revealed bilateral firm and rubbery jugulodigastric nodes, which were larger on the left side measuring 4 x 4 cm. There was hepatomegaly, and lung examination was unremarkable**.** The diagnosis was confirmed histologically where the nasal tissue biopsy showed atypical lymphoid cells with positive immunophenotyping of CD3, CD56 and CD30. The disease course was rapid within the one-month presentation.

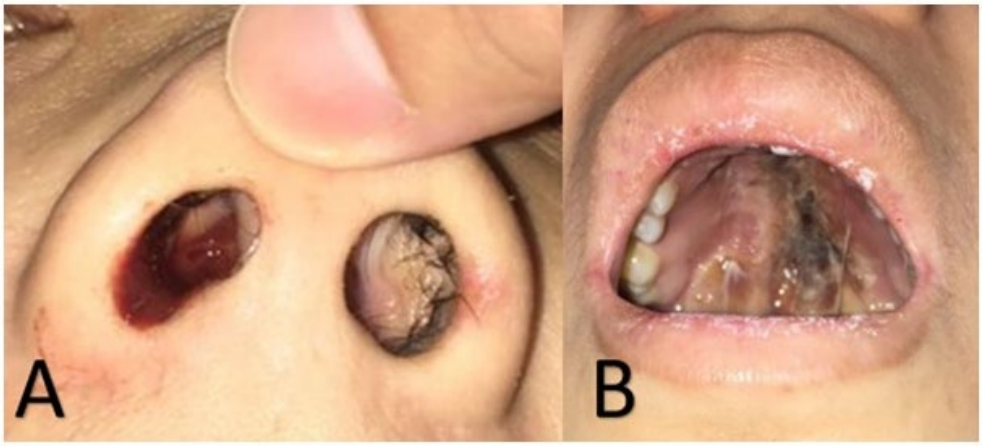

Figure 1 Intranasal mass occupying both nostrils covered by mucoid blood-stained discharge (A) and ulcer at hard palate with necrotic area in the midline where bleeding had ceased (B)

Due to the mass within the nasal region obscuring the nasopharynx and the oropharynx, the patient had difficulty in breathing when lying supine. She also experienced chocking episodes and became breathless during sleep. Therefore, an emergency tracheostomy under local anesthesia was performed while the patient was in a sitting position in the operating theatre. Considering the impending airway obstruction, this helped secure the airway prior to definitive treatment of the tumour. There was no attempt at endotracheal intubation or use of laryngeal mask airway due to the risk of losing the airway control secondary to bleeding from the tumour.

The initial computed tomography of the nasal/paranasal sinus that was done while she was admitted to a private hospital, a week prior to admission to our centre showed homogenous mass in the left nasal cavity and left maxillary sinus that extended posteriorly to the left nasopharynx. There was mucosal thickening on the right maxillary sinus and early involvement of

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the cartilaginous part of the nasal septum. When she was admitted to our centre, repeat CT for staging and embolization revealed a homogeneous mass that involved the nasal cavity, maxillary and ethmoidal sinuses bilaterally and the entire nasopharynx with more significant septal destruction seen anteriorly. The was an eight-day gap between the two imaging. When comparing the latest and initial CT imaging, there was a remarkable disease progression seen in the nasal and paranasal region (Figure 2). CT abdomen showed diffuse lymphomatous infiltration of the liver.

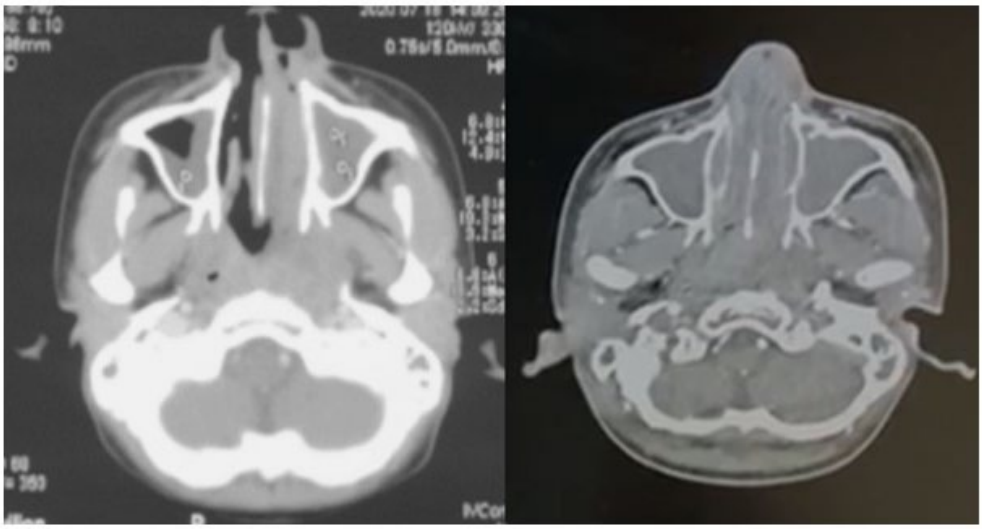

Figure 2 CT images of the paranasal sinus of the patient taken eight day apart showed rapid disease progression from the initial presentation (left) compared with the current disease status (right) where the homogenous mass occupies the whole nasal cavity, nasopharynx and bilateral maxillary sinuses. Note the bony and cartilaginous erosion of the nasal septum.

While in the ward, she experienced multiple torrential bleedings from the mass in the oral and nasal cavities requiring multiple packed cell transfusion. Compression gauze packing with adrenaline of the intraoral and nasal cavity regions failed to stop the bleeding. The blood parameter showed normal platelet count and coagulation profile. The lowest haemoglobin level following this massive bleeding was 6.9g/dL**.** She underwent haemostatic radiotherapy as well as bilateral internal maxillary artery embolization to control the bleeding from the tumour mass.

Despite four daily fractions of haemostatic radiotherapy and the above-mentioned measures including dexamethasone, the patient continued to experience significant intraoral bleeding requiring daily red cell transfusion to sustain the hemoglobin at 8g/dL. On the fifth day, she was hemodynamically unstable requiring vasopressor support and deemed unsafe to be transported for radiotherapy. She was eventually sedated and ventilated. In view of these and with radiotherapy treatment interrupted, the treatment plan was changed to chemotherapy, using CHOP-L regime (cyclophosphamide, adriamycin, vincristine, prednisolone and L-asparaginase). The bleeding was no longer evident 24 hours after the commencement of this regime. The tumour showed a rapid reduction in size where she was eventually weaned off to tracheostomy oxygen mask, and was able to sit-up and at one-point oral feeding was attempted where she was able to tolerate minimal amount of clear fluid.

Her L-asparaginase was stopped early on day 5 over concerns of myelosuppresion. On day 10 post-initiation of chemotherapy, she developed refractory hypoglycaemia and septicaemic shock attributed to extended resistance (XDR) *Acinetobacter baumanii* bacteremia. Her condition deteriorated into multi-organ failure despite combination of broad-spectrum antibiotic of polymyxin, carbapenem and penicillin-type antibiotic with addition of granulocyte stimulating factor and Factor VIIA recombinant as well as the ventilatory support. Unfortunately, she succumbed to the sepsis two days later.

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DISCUSSION

Extranodal (sinonasal) natural killer/T-cell non-Hodgkin lymphoma or nasal NK/T-cell non-Hodgkin lymphoma is a rare subtype of lymphoma with an aggressive course characterized by angioinvasion, angio-destruction and necrosis of midfacial region [1,2].

Histologically, ENKTL is characterised by a lymphoproliferative process consisting of a mixture of polymorphic and atypical cells along with non-neoplastic inflammatory cells including plasma cell, small lymphocytes and histiocytes [1]. As a result, there is an intense inflammatory reaction complicating the histologic finding of ENKTL. The tumour shows a tendency of angiocentric distribution with angio-invasive and angio-destructive growth pattern with associated ulceration and necrosis leading to progressive destruction of cartilage and soft tissues [2]. ENKTL typically causes vascular damage and tissue destruction that may contribute to the torrential massive bleeding as seen in this patient. The bleeding from the tumour is becomes more deleterious due to the inflammatory background induced by the neoplastic cell that in turn mediates tissue hypoxia and cellular injury.

The clinical course of ENKTL is staged according to TNM (Tumor-Node-Metastasis) staging as proposed by Yan et.al. [6]. The majority of patients (70%) has localized disease mainly in the nasal cavity or surrounding structures at initial presentation but some may present with a rapidly progressive disseminated disease with infiltration of the liver, spleen, skin, lymph nodes, and bone marrow, hence carrying a poorer prognosis [7].

In this case, securing a patent airway was a very crucial step as there is a high risk of aspirating blood into the lungs and upper airway obstruction due to enlarging tumour size or tissue oedema secondary to chemotherapy. However, endotracheal intubation was not permissible because of the risk of precipitating tumour bleeding from soft palate mass while manipulating the laryngoscope during intubation. Tracheostomy under local anaesthesia was the best option for this patient, though it was very challenging to perform tracheostomy while the patient was in a sitting position. With a tracheostomy tube in situ, the patient was able to lie supine for CT staging and simulation as well as undergo radiotherapy treatment.

Managing bleeding from the tumour mass is the major challenge owing to tumour ango-invasive and angio-destructive behaviour leading to failure of the local healing pathway. A multidisciplinary team approach involving otorhinolaryngologists, histopathologists, haemato-oncologists, intensive care unit physicians as well as an interventional radiologist is prudent. Approximately 10% of patients with advanced cancer may experience bleeding from the tumor [8]. Haemostatic compression dressing and agents are primary action to be taken at the bedside. Concurrent restoration of blood volume loss and close monitoring are crucial when dealing with tumour bleeds, hence intensive care admission is critical. Haemostatic radiotherapy provides a practical and potential treatment option in controlling the local tumour bleeding at various anatomic sites when local therapies fail to do so [8]. In fact, radiotherapy may be utilised as the primary modality to control active tumour bleeding when there is significant blood loss requiring intensive management and repeated blood transfusion. A retrospective study by Sapienza et. al (2018) reported the use of short-course radiation resulting in 88% bleeding control in head and neck tumours with prescription of either 20 Gray (Gy) in 5 fractions, 30 Gy in 10 fractions, and 8 Gy in a single fraction [9].

Besides that, embolization of internal maxillary artery (IMAX) bilaterally by interventional radiologist via transcutaneous femoral artery further augments bleeding control. The major fears from embolization of IMAX include monocular blindness, facial nerve paralysis, skin necrosis and cerebrovascular accident. Fortunately, none occurred in this case [10]. The role of endoscopic nasal surgery is limited to diagnostic purposes and in most occasions, surgery is performed due to a diagnostic dilemma of the presenting nasal mass mimicking chronic rhinosinusitis or fungal sinusitis [11].

SMILE (steroid (dexamethasone), methotrexate, ifosfamide, L-asparaginase, and etoposide) protocol has been routinely used as an institutional cytotoxic intervention against NK/T cell

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lymphoma [12]. When haemostatic radiotherapy failed to arrest severe bleeding beyond 48 hours CHOP-L was chosen above SMILE as it was perceived to be more cytotoxically dense upfront. Majority of its cytotoxic activity is packed in one day compared to the latter, where it is extended to over 5 days [13]. This anecdotal experience implies that cytotoxic chemotherapy was able to immediately arrest tumour bleeding in NK-cell lymphoma, outperforming radiotherapy in achieving haemostasis. Nevertheless, it may still be argued that the haemostasis following chemotherapy was partially contributed by the preceding radiotherapy.

CONCLUSION

Extranodal (sinonasal) natural killer/T-cell lymphoma is an aggressive NHL characterized by locally progressive destruction of the midface, particularly the nasal/paranasal region and may present with torrential massive bleeding from the tumour due to its angio-destructive nature. Prompt airway assessment and securing a patent airway, as well as control of the bleeding were critically important in this case. A multidisciplinary team approach is the cornerstone of the patient's management. A combination of chemotherapy of CHOP-L showed immediate favourable outcome in our patient. If we are to experience a similar situation again, we will opt to deliver cytotoxic chemotherapy upfront rather than radiotherapy to control haemostasis.

Conflict of Interest

Authors declare none.

Author's Contribution

1. SNAJ – Drafting the article
2. SM – Data collection
3. CN – Interpretation of data
4. ADA – Critical revision
5. NML - Critical revision
6. IM – Final approval

REFERENCES

1. Metgud RS, Doshi JJ, Gaurkhede S, Dongre R, Karle R. Extranodal NK/T-cell lymphoma, nasal type (angiocentric T-cell lymphoma): A review about the terminology. Journal of Oral and Maxillofacial Pathology 2011; 15(1):96–100.
2. Al-Hakeem DL, Fedele S, Carlos R, Porter S. Extranodal NK/T-cell lymphoma, nasal type. Oral Oncology 2007;43(1):4-14.
3. Gill H, Liang RHS, Tse E. Extranodal natural-Killer/T-Cell lymphoma, nasal type. Advances in Hematology 2010; 2010: 1–5.
4. Tai YC, Kim LH, Peh SC. High frequency of EBV association and 30-bp deletion in the LMP-1 gene in CD56+ lymphomas of the upper aerodigestive tract. Pathology International 2004;54(3):158–166.
5. Harabuchi Y, Takahara M, Kishibe K, Nagato T, Kumai T. Extranodal natural Killer/T-Cell lymphoma, nasal type: Basic science and clinical progress. Frontiers In Pediatrics 2019;7:141.
6. Yan Z, Huang H, Wang X, Gao Y, Zhang Y, Bai B et al. A TNM Staging System for Nasal NK/T-Cell Lymphoma. Plos One 2015;10(6): e0130984.
7. Yamaguchi M, Suzuki R. JSH practical guidelines for hematological malignancies, 2018: II. Lymphoma-9. Extranodal NK/T-cell lymphoma, nasal type (ENKL). International Journal of Hematology. 2019; 109(4): 371-6.
8. Rasool MT, Manzoor NA, Mustafa SA, Maqbool LM, Afroz F. Hypofractionated radiotherapy as local hemostatic agent in advanced cancer. Indian Journal of Palliative Care 2011;17(3):219–221.
9. Sapienza LG, Ning MS, Jhingran A, Lin LL, Leão CR, da Silva,BB, de Assis Pellizzon AC, Gomes MJ, Baiocchi G. . Short-course palliative radiation therapy leads to excellent bleeding control: a single centre retrospective study. Clinical and Translational Radiation Oncology 2018;14:40-46.
10. Dubel GJ, Ahn SH, Soares GM. Transcatheter embolization in the management of epistaxis. Seminars in Interventional Radiology 2013;30(3):249–262.
11. Selvamalar V, Thamby SP, Al-Hatamleh MAI, Rohimah M, Baharudin A. A diagnostic dilemma of sinonasal T cell lymphoma: Report of a unique case and literature review. The Gulf Journal of Oncology. 2019;1:83-89.
12. Kwong YL, Kim WS, Lim ST, Kim SJ, Tang T, Tse E, Leung AY, Chim CS. SMILE for natural killer/T-cell lymphoma: analysis of safety and efficacy from the Asia Lymphoma Study Group.

Blood, The Journal of the American Society of Hematology. 2012;120(15):2973-80.

13. Johnstone C, Rich SE. Bleeding in cancer patients and its treatment: a review. Annals of Palliative Medicine 2017; 7:265-273–273.

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