Case Report

A Rare Condition with a Common Presentation: NK/T-Cell Lymphoma Presenting as Recurrent Sinusitis and Facial Cellulitis

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Abstract Extranodal natural killer (NK)/T-cell lymphomas are rare tumors that account for 1.5% of all non-Hodgkin-type lymphomas in the United States and almost 7–10% of all non-Hodgkin's lymphomas in Asia and South America. The nasal type commonly presents with facial cellulitis, nasal obstruction or proptosis. Occasionally, local extension from the nasal cavity causes destruction of the hard palate, previously known as “lethal midline granuloma.” We present a case of a 37-year-old male who presented with recurrent right-sided facial swelling, periorbital cellulitis and sinusitis. There was some delay in confirming the diagnosis but he was eventually diagnosed with stage 1e NK/T-cell lymphoma (nasal type). Disease diagnosed at an early stage confers a very favorable curative remission rate. Therefore, clinicians should be aware of the possibility of an NK/T-cell lymphoma when facing a presentation of recurrent sinusitis associated with atypical presentation such as periorbital cellulitis.

Keywords NK/T-cell lymphoma; nasal type; periorbital cellulitis; sinusitis; facial swelling

1. Introduction

Extranodal natural killer (NK)/T-cell lymphomas are rare tumors that account for 1.5% of all non-Hodgkin-type lymphomas in the United States [2] and almost 7–10% of all non-Hodgkin's lymphomas in Asia and South America [2, 5]. The nasal type commonly presents with facial cellulitis, nasal obstruction or proptosis [3,4,5,11]. Occasionally, there may be local invasion into the hard palate that was previously known as “lethal midline granuloma” [5,11]. Disease diagnosed at an early stage confers a favorable outcome [8] therefore clinicians should be aware of this differential diagnosis when faced with an atypical recurrent sinusitis, facial cellulitis or periorbital cellulitis.

2. Case presentation

A 37-year-old otherwise fit and well male presented with a one-month history of right-sided facial swelling and a right 4 cm submandibular neck mass. Past history included a septoplasty and limited endoscopic sinus surgery two years prior.

Initial computerized tomography (CT) scan showed a conglomerate of necrotic nodes around the submandibular

gland and chronic inflammatory changes in the right maxillary sinus (Figure 1). He proceeded to have an ultrasound guided fine-needle aspiration (FNA) of the right neck nodes that revealed nonnecrotizing granulomas, raising the possibility of toxoplasmosis or other exotic infections. A concurrent biopsy from the right middle meatus in the nasal cavity showed acute inflammation. He was treated with antibiotics and was discharged. Cultures and serology (EBV, CMV, and toxoplasmosis) remained negative. The facial swelling and node completely resolved over the next month.

Two months later, he represented to hospital with right-sided facial swelling, right periorbital cellulitis and pansinusitis confirmed on CT scan (Figure 2). He was managed with oral antibiotics, oral steroids, and sinus rinses. He was discharged again and was initially well but was readmitted to hospital one month later with right-sided facial cellulitis and bilateral pansinusitis which was worse on the right. Throughout both these admissions, his cultures and serology remained negative. After his third admission, a semiurgent revision endoscopic sinus surgery with right frontal sinus trephine was performed. Multiple tissue samples were taken from his frontal and ethmoid sinuses intraoperatively. Tissue samples from his previous FNA were also reviewed.

3. Histology

Histology from his sinus biopsies showed dense sheet-like lymphoid infiltrate positive for CD3, CD56, and granzyme (Figure 3). It was negative for CD5 and perforin. Epstein-Barr virus (EBV)-encoded RNAs (EBERs) were positive and Ki 67 was 50–60%. There was no evidence of hemophagocytosis. T-cell receptor gene rearrangement tests were not done as the diagnosis was quite explicit.

Retrospective histological evaluation of the right submandibular lymph showed nonnecrotizing granulomas and positive cell marker studies (CD56 lymphocytes 8%, Ki 67 2%).

Figure 1: Coronal CT of patient with (a) right side submandibular necrotic lymph node and (b) right sided sinusitis on initial presentation.

Figure 2: Coronal CT scan of patient representing with recurrent right sided facial cellulitis and predominantly right sided sinusitis on the 2nd presentation.

4. Investigations

The patient was diagnosed with stage 1e NK/T-cell lymphoma (nasal type). There was no evidence of bone or skin invasion and no evidence of systemic disease on staging body CT scan. Positron emission tomography (PET) CT scan did not detect any other disseminated metabolically active tissues and bone marrow biopsy was clear. There were no high risk features and the patient had a normal performance status. His pretreatment complete blood count and blood chemistry were normal with a normal

Figure 3: Sinus tissue biopsy showing dense sheet like lymphoid infiltrate stained with hematoxylin & eosin (H&E) stain at 400× magnification.

lactate dehydrogenase level (207 U/L), normal hemoglobin count (157 g/L), normal platelet count ($152 \times 10^9/L$), undetectable EBV viral load, and normal liver and renal function. C-reactive protein tests were not available.

5. Treatment

The patient was discussed at the lymphoma multidisciplinary meeting and the decision was made to treat the disease with radiotherapy alone due to its limited stage and low risk. Decision for chemotherapy was deferred until

postradiation EBV viral load was assessed. The patient was subsequently treated with a total of 50 Gy in 25 fractions of involved field radiotherapy. Postradiation PET scan was negative for any local or systemic disease. Postradiation EBV viral load remained undetectable and the patient was deemed to be in complete remission. No chemotherapy treatment was administered.

6. Discussion

Extranodal NK/T-cell lymphomas are classified into two histological categories by the World Health Organization (WHO): (1) NK/T-cell lymphoma, nasal type and (2) aggressive NK-cell leukemia [11]. However, they are conventionally divided into three categories clinically: (1) nasal, (2) nonnasal, and (3) aggressive lymphoma/leukemia subtypes. Each subtype has a different clinical manifestation and associated disease progression and prognosis [8, 11].

6.1. Etiology and diagnosis

The etiology of NK/T-cell lymphomas is not well established, however, there is a strong association with EBV irrespective of ethnicity [6]. The presence of EBV in the neoplastic cells is one of the prerequisites in the WHO classification for NK/T-cell lymphomas [8].

6.2. Clinical features

The two major cutaneous manifestations of extranodal NK/T-cell lymphoma are cellulitis and ulcers [3]. The nasal-type NK/T-cell lymphomas commonly present with facial cellulitis, nasal obstruction or even retro-orbital involvement causing proptosis [3, 4, 5, 11]. Occasionally, local extension from the nasal cavity causes destruction of the hard palate with the characteristic midline perforation, previously referred to as “lethal midline granuloma” [5, 11]. The nasal-type group however is more likely to have localized cutaneous manifestations and presents less aggressively compared to the extranasal and nonnasal groups which are more aggressive and disseminated [3]. The nonnasal group symptoms could include cytopenia, B symptoms, early distant metastasis and hemophagocytic syndrome in approximately 3% of cases [1, 3]. Hemophagocytic syndrome is an often fatal complication which may present with high fevers, maculopapular rash, central nervous system symptoms, multiorgan failure, abnormal liver function tests, hepatosplenomegaly, cytopenias, and coagulopathy [1, 8]. The nonnasal group as the name implies has other sites of manifestation of NK/T-cell lymphomas that include the gastrointestinal tract, salivary glands, spleen, and testis [5].

6.3. Imaging

CT scan has been conventionally utilized to assess the local extent of the disease as well as distant metastases. Magnetic resonance imaging (MRI) has been shown to better define

local soft tissue and bony involvement. PET-CT offers a more accurate definition of the extent of involvement by distinguishing lymphoma involvement from inflammatory masses as NK-cell lymphomas have been shown to be FDG-avid [5, 8].

6.4. Treatment of nasal NK/T-cell lymphoma

In stage I/II nasal NK cell lymphoma, combined chemotherapy and radiotherapy is the treatment of choice [8]. Initially, radiotherapy alone used to be the primary treatment which yielded a complete remission rate of between 40% and 80% [5]. Local relapses occurred at a rate of around 50% [5, 7]. Contributing factors include dosages less than 45 Gy to 50 Gy and radiotherapy planning not assisted by radiological imaging [7]. Systemic relapses with radiotherapy alone occurred in 25–30% of patients, where more than a half were not associated with local recurrence, suggesting that subclinical dissemination of lymphoma has occurred in these apparently early staged patients who were “cured” [5, 8]. The use of chemotherapy alone has been associated with a treatment failure of about 40%. Therefore combined chemotherapy and radiotherapy is the treatment of choice and can be expected to be curative in at least 70–80% of patients with stage I/II nasal NK cell lymphomas [8]. There are however documented relapses more than ten years and up to thirty years in early stage nasal NK cell lymphoma, therefore life-long follow-up is recommended [8].

Chemotherapy is the mainstay of treatment in advanced NK cell lymphomas [8]. A novel regimen “SMILE,” comprising dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide, has been shown in phase I and II studies to be promising. In patients with relapsed or refractory NK cell lymphoma, SMILE treatment resulted in an overall response rate of 74% and a complete remission rate of 35–50% [8]. The commonly used CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) chemotherapy regime is moderately good for stage I/II nasal NK/T-cell lymphomas but has a high rate of disease progression (30–40%) and a high rate of relapse (30–40%) after initial complete remission [5, 10]. It has a poor outcome when used in advanced staged disease with an overall response rate of below 20% [8, 10].

The option of autologous and allogeneic hematopoietic stem cell transplantation (HSCT) as a consolidation therapy following high-dose chemotherapy alone has been considered in patients with advanced stage, relapsed or refractory disease [8]. This is controversial as there are several issues to be considered. There are no prospective trials evaluating the role of autologous HSCT in patients. The largest retrospective trial of 47 patients only showed that HSCT had a survival benefit for patients with stage I/II disease and high risk patients who achieve complete remission [9]. However, patients in these lower stages are likely to have

a complete remission with combined chemotherapy and radiotherapy, so it is doubtful that frontline autologous HSCT is beneficial [5]. As for the high risk patients in complete remission, the recommendation is to carefully consider autologous or allogenic HSCT for consolidation therapy [5,9]. In patients with advanced, relapsed or refractory diseases, the role of HSCT remains poor [9].

7. Conclusion

In our patient, although there was some delay in making the diagnosis, the disease was still detected at an early stage, which confers a very favorable curative remission rate. Clinicians should be aware of the possibility of an NK/T-cell lymphoma when facing a presentation of recurrent sinusitis associated with atypical presentation such as periorbital cellulitis.

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