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OLGU SUNUMU

Two cases of nasal natural killer T-cell lymphoma

İki olguda nazal natural killer T-hücreli lenfoma

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Nasal natural killer T-cell lymphoma is a very aggressive and destructive disease with a poor prognosis. We hereby present two male patients in whom diagnostic problems and a mortal course were encountered. One patient (age 31 years) had progressive ulceration in the nasal area. Two biopsies that had been taken elsewhere were inconclusive. The other patient (age 40 years) was referred with a previous histopathologic diagnosis of squamous cell carcinoma. He complained of an unhealing wound in the hard palate. Biopsies were repeated in each case. Diagnosis was made by immunohistochemical examination. Both patients died shortly after the diagnosis. The importance of obtaining an adequate and deep biopsy sample and employing sophisticated immunohistochemical examination is emphasized for accurate diagnosis.

Key Words: Granuloma, lethal midline/pathology/diagnosis; killer cells, natural; lymphoma, T-cell/pathology/mortality; nose neoplasms/pathology.

Nazal natural killer T-hücreli lenfoma kötü prognozu olan agresif ve destrüktif bir hastalıktır. Burada hastalığın tanıda zorluklar gösterdiği ve ölümcül süreç izlediği iki olgu sunuldu. İlk olgunun (yaş 31, erkek) burun bölgesinde ilerleyici ülserasyon vardı. Daha önce başka merkezlerde lezyon bölgesinden alınan iki biyopsi sonuç vermemişti. İkinci hasta (yaş 40, erkek) skuamöz hücreli karsinom histopatolojik tanısıyla merkezimize gönderilmişti. Hasta sert damağındaki iyileşmeyen yaradan şikayetçiydi. Her iki olguda da biyopsiler tekrarlandı. Alınan örneklerin immünhistokimyasal yöntemlerle incelenmesiyle tanı konabildi. İki hasta da tanıdan kısa bir süre sonra yaşamını yitirdi. Bu yazıda, doğru tanı için yeterli büyüklükte, derin biyopsi örneği alımının ve modern immünhistokimyasal çalışmaların önemi vurgulandı.

Anahtar Sözcükler: Granülom, ölümcül orta hat/patoloji/tanı; öldürücü hücre, doğal; lenfoma, T-hücreli/patoloji/mortalite; burun neoplazmları/patoloji.

Nasal natural killer (NK) T-cell lymphoma is a recently described clinicopathologic entity. It is an aggressive, angioinvasive disease that progressively destroys the nose, paranasal sinuses, and other regions of the midface. A small number of NK T-cell lymphomas have been reported following the recent advances in immunohistochemistry. The prognosis and treatment modalities of these lesions have yet to be well-clarified.

CASE REPORTS

Case 1– A thirty-one-year-old man presented with a large defect in the nasal area. He had a history of nasal obstruction, purulent rhinorrhea, and

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unpleasant nasal odor for about 1.5 years. He had been suffering from nasal swelling, pain, and general malaise for two months, with progressive ulceration in the nasal area over the last 20 days (Fig. 1). Two biopsies that had been taken elsewhere from the lesion were inconclusive. Laboratory tests demonstrated moderate anemia (hemoglobin 10.9 g/dl, erythrocyte sedimentation rate 124 mm/h). Magnetic resonance imaging revealed an irregular solid mass filling the entire nasal cavity, and erosion of the nasal septum, nasal cartilages, and the nasal skin (Fig. 2). A deep biopsy was performed and the specimen was submitted to the surgical pathology laboratory fresh and unfixed. Sections of the biopsy fragments demonstrated a polymorphous lymphocyte population associated with large areas of necrosis. The unit lesion appeared to be an angiocentric and angiodestructive infiltrate, with both small and large atypical lymphocytes and reactive inflammatory cells (Fig. 3). Atypical lymphocytic cells were stained immunocytochemically for CD45, CD43, CD56, and CD3 antibodies, but not for CD20. A histopathologic diagnosis of NK T-cell lymphoma was made. The patient developed paralysis of the seventh and ninth nerves a few days after the diagnosis. He was referred for radiotherapy; however, he died of multiorgan failure shortly after the initiation of radiotherapy.

Case 2– A forty-year-old man with a previous histopathologic diagnosis of squamous cell carcinoma was referred to the ENT Department. He had a complaint of an unhealing wound in the hard palate for three months. Examination revealed a papillary lesion confined to the hard and soft palates and surrounded by friable mucosa (Fig. 4). Magnetic resonance imaging indicated an irregular mass covering the right posterior hard palate and extending to the soft palate (Fig. 5). Computed tomography scans of the lungs and the whole abdomen were uneventful.

Another biopsy was performed. The sections of the specimen demonstrated overlying benign squamous epithelium, with a polymorphous lymphocytic infiltration underneath. Atypical lymphocytes showed an angioinvasive and angiodestructive pattern. Atypical cells were small to medium in size, ranging from 15 to 20 microns in diameter.

Fig. 1 – *Destructive lesion involving two-thirds of the nose.*

Fig. 2 – *Contrast-enhanced T1-weighted image showing an irregular isointense mass filling the entire nasal cavity.*

Fig. 3 – *Infiltration and destruction to the vascular wall by polymorphous atypical lymphocytes (H-E x 200).*

Immunocytochemically, the atypical lymphocytes stained for CD45, CD43, CD3, and CD56. No staining was obtained for CD20. Histopathologic diagnosis was NK T-cell lymphoma (Fig. 6). Biopsy specimens were negative for Epstein-Barr virus latent membrane protein.

The patient was administered three cycles of chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone. Although a complete remission was observed at the beginning, he developed local recurrence three months later, for which he received radiotherapy. He developed metastasis to the skin, testes, and the lungs and died of systemic disease eight months after the initiation of treatment.

DISCUSSION

Over the years, various confusing terms have been used to describe locally destructive lesions, including lethal midline granuloma, lethal granulomatous ulceration, rhinitis gangrenosa progressiva, polymorphic reticulosis, and Stewart's granuloma.[1,2] With advances in immunohistochemical studies, these lesions were shown to be lymphoid in nature.[1] These extranodal lymphoproliferative lesions are classified as B-cell, T-cell, and natural killer T-cell phenotypes.[3] The latter, which is defined as angiocentric lymphoma in the European American Lymphoma classification system, are further divided into three subtypes depending on the involved site: nasal NK T-cell lymphoma, involving the nose and the upper aerodigestive system, non-nasal type NK T-cell lymphoma, and those associated with leukemia, NK T-cell lymphoma/leukemia.[1,4]

T-cell and NK T-cell lymphomas have many similarities both in clinical and histological aspects; however, the latter tends to have a more aggressive course with progressive ulceration and necrosis.[3] Destruction of the facial midline structures is also more common.[3] T-cell lymphocytes which show immunoreactivity for CD56, but not for several T-

Fig. 4 – *Irregular polypoid mass extending from the right posterior hard palate to the soft palate.*

Fig. 5 – *Contrast-enhanced T1-weighted image showing an irregular hyperintense mass extending from the posterior hard palate to the soft palate.*

Fig. 6 – *Diffuse polymorphous atypical lymphocytic infiltration (H-E x 200).*

cell markers are considered NK T-cell lymphomas.[3] CD56 is a cell-adhesion molecule and a correlation between CD56 positivity and angiotropism has been suggested.[3,4] Its presence may mediate cellular adhesion to blood vessels.[3]

Patients usually complain of discomfort with a duration of a month to a year prior to the diagnosis.[3] Duration of the symptoms was 1.5 years and three months in our patients, respectively. The nasal cavity is the most frequent localization.[1,5] The nasopharynx, palates, paranasal sinuses, alveolar bones, and the larynx are other reported sites.[1,5] Nasal obstruction, purulent rhinorrhea, unpleasant nasal odor, and crusting are the most common symptoms.[1,5] Cutaneous lesions composed of indurated nodules and annular plaques have been reported in the extremities of a patient with palatal NK T-cell lymphoma.[2] Fever, malaise, and weight loss are systemic manifestations of advanced lesions.[2] Unhealing ulcers and cranial nerve involvement are other features.[3] The earliest clinical sign is usually friable mucosa[5] which was observed on the hard and soft palates in the latter case. Unilateral aggressive ulceration is the most frequent late presentation suggesting unfavorable prognosis.[5]

Radiologic examination usually demonstrates soft tissue involvement with or without bony erosion.[1] The medial wall of the maxilla, nasal septum, and lamina paprycea have been reported as the most common sites of bone erosion.[1]

The diagnosis was made with the aid of histopathologic examination and immunohistochemical studies in our patients. Biopsies may fail to demonstrate atypical lymphoid population, so multiple biopsies may be required.[2,3] Wide areas of necrosis in addition to the presence of pleomorphic infiltrates may mask the subepithelial atypical lymphocytes in NK T-cell lymphoma.[3] Superficial sampling may be inconclusive and sometimes misleading; therefore, the need for attempts to obtain deep biopsy specimens has been emphasized.[3] Another important point for a precise diagnosis is the implementation of an adequate immunohistochemical study.

The initial biopsy specimens of the first patient showed indefinite granulation, very few giant cells and necrosis. Since these findings were interpreted as suggestive of, but not diagnostic for, Wegener's granulomatosis, a subsequent biopsy was performed. Immunohistochemical studies indicated immunoreactivity for CD56, CD45, CD43, CD3, but not for CD20. Histomorphologic and immunohistochemical findings enabled a correct diagnosis of NK T-cell lymphoma in the first patient.

Diffuse atypic lymphoid infiltration, significant aberrant mitotic activity, and squamous epithelization were histopathologically demonstrated in the second case. Immunohistochemical studies which showed staining for CD56, CD45, CD43, and CD3, in the absence of immunoreactivity for CD20, corroborated the diagnosis.

Differential diagnosis of NK T-cell lymphoma includes fungal and bacterial infections, sarcoidosis, carcinomas, other types of lymphomas and Wegener's granulomatosis.[5] Histopathologically, Wegener's granulomatosis exhibits c-ANCA positivity and distinct histopathologic features including the presence of vasculitis, necrosis, granulomatous infiltration, and giant cells.[6]

Natural killer T-cell lymphoma may respond to local radiotherapy and systemic chemotherapy.[5] Combination of radiotherapy and chemotherapy seems to be more effective.[5] It usually has a dismal prognosis regardless of the treatment modality used. Advanced disease and age are the most significant factors associated with a poor prognosis.[3] One-year and five-year survival rates have been reported as 45% and 22%, respectively.[2] Bone marrow transplantation may be considered if the disease is encountered at a relatively young age.[2,5] Some encouraging results have been reported regarding bone marrow transplantation.[3]

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