Interesting Case

Mantle Cell Lymphoma of Waldeyer’s Ring Misdiagnosed as Tuberculosis

A 59-year-old male patient was firstly referred to dermatologist because he had erythematous tender papules on both hands and arms. The dermatologist observed that he had history of significant weight loss, voice change and enlargement of both tonsils, then he was referred to Otolaryngology department for evaluation. In the first visit at Otolaryngology department, the history and clinical examination were taken. He works as a gardener. He has diabetes mellitus type II, hypertension and dyslipidemia. He lost his weight from 76 kilograms to 59 kilograms in 6 months but he had neither fever nor drenching night sweat. Muffled and hyponasality voice was noted. He had profuse enlargement of nasopharyngeal lymphoid and asymmetrical enlarged tonsils. His base of tongue, supra-glottis, glottis and hypopharynx were normal. There were multiple discrete bullous lesions with central dimple on both arms and hands (figure 1).

First attempted biopsy was done under local anesthesia on his right nasopharyngeal mucosa. The pathology report revealed that there is a small granuloma composed of epitheloid cells in respiratory epithelium with lymphoid follicles. So the initial pathological diagnosis was granulomatous inflammation suggestive of tuberculosis. The researchers also sent the tissue of nasopharynx for imprint. The hematologist reported that there were mixed small and large lymphocytes which may be compatible with reactive hyperplasia of nasopharynx. On the second ENT visit, we suggested him to repeat a biopsy on his nasopharynx and his tonsils. The second pathology report showed chronic inflammation on nasopharyngeal mucosa and unremarkable squamous cells on the tonsil. There was some pulmonary infiltration on his left lower lung. We decided to referred him to a pulmonologist for evaluation. He had negative AFB smear of his sputum in three consecutive days, and also had negative result of Anti-HIV, c-ANCA and p-ANCA. The pulmonologist suggested him to start anti-Tuberculosis drugs with standard regimen: Isoniazid, Rifampicin, Pyrazinamide and Ethambutol in first eight weeks. During these 8 weeks, he was worked up about the skin lesion at the Institute of Dermatology. He was done skin biopsy on his forearm and the histopathology revealed that there were basal vacuolization, necrotic keratinocyte, papillary dermal edema, extravasation of red blood cells and generalized lymphocytic with histiocytic infiltrations. The direct immunofluorescence was negative for IgG, IgM C3 and fibrinogen but special immunohistochemistry was positive for CD 68. The dermatologist continually worked up the cause of Erythema Multiforme which they found all negative result on tuberculin skin test, PCR for mycobacterium tuberculosis and mycobacterium species, PCR for Mycoplasma species but positive result on mul-
tiplex PCR for HSV-2. The dermatologist stopped to work up and he was diagnosed **Herpes simplex virus-associated Erythema Multiforme**. He was gotten 1,000 milligrams per day oral form acyclovir for first 5 days and then 800 milligrams per day for next 26 weeks. After starting treatment of TB for 8 weeks, we found that his skin lesion was improved but his nasopharynx and the tonsils still be unchanged. He complained about new lymph nodes on his right epitrochlear region. We referred him to surgery department for taking a biopsy. The pathology report of two lymph nodes; 1x0.8x0.7 and 1.5x1x0.7 cm. was reactive hyperplasia and negative for malignancy or granuloma. After starting treatment of TB for 3 months, finally he had been undergone tonsillectomy and nasopharyngeal curettage under general anesthesia for definitive diagnosis. The final pathology report stated that all of specimens infiltrate with atypical small lymphoid cells in mantle zone and parafollicular area. These cells are reactive with CD20, CD5, Bcl-2, CD43 and Cyclin-D1 but to be negative with CD3, CD10, CD23, Kappa and Lambda. The final diagnosis in this patient is **Mantle cell lymphoma**. We referred him to hematologist for proper treatment. He underwent bone marrow biopsy aspiration and whole body computer tomography scan. The result of bone marrow biopsy showed that there was 15-20% cellularity, M:E ratio was 1:5 and megakaryocytes are increase. We did not find abnormality of his chest and abdomen imaging. After evaluating cardiac status, he was started R-CHOP regimen. Recently he still underwent chemotherapy with seventh course of R-CHOP regimen.

Approximately a quarter of lymphomas of head and neck are extranodal type and more than half of extranodal lymphomas of head and neck present in the Waldeyer’s ring. So lymphoma should always be included in the differential diagnosis of patient with mass in Waldeyer’s ring.1-2. Because of his skin manifestation and the first pathology report of the nasopharynx; granulomatous inflammation, he was delayed the diagnosis of Mantle cell lymphoma for 3 months after the first visit. Granulomatous diseases can be due to various aetiologies: infection, reaction to the haematological diseases, vasculitis, or systemic sarcoidosis. The definitive diagnosis of these conditions, especially lymphoma, is an important for clinicians.2-3. About the diagnosis step, the researchers tried more than one attempt to get large pieces of his nasopharynx and tonsils for pathological diagnosis, but the results were shown only the inflammation process. Joshua et al recommended to perform tonsillectomy which provided about 30% chance of identify occult tonsil malignancy. Furthermore, they mentioned that the excisional tonsillectomy has higher yield of detecting primary tumor location than the random deep biopsies tonsils.4

For the skin lesion, Erythema Multiforme (EM) can be a hypersensitivity reaction, Infection such as Mycoplasma virus, Herpes simplex virus or Tuberculosis and also lymphoma. His investigations were almost negative except the PCR for HSV. So the dermatologist believed that the HSV was the cause. But this patient had multiple systemic problems, so we cannot exclude the EM which associated underlying neoplasms, especially lymphoreticular malignancies. However, the researchers cannot conclude the exact cause of EM in this patient.5-6

**Mantle cell lymphoma** is now recognized as a subtype of B-cell lymphoma and it has aggressive clinical behavior. Earlier diagnosis and more aggressive approaches resulted in improved outcomes for patients with MCL. Fisher RI et al proposed that MCL is responsive to doxorubicin-containing chemotherapy, but the complete remission rates are only 30% to 40% and the median survival is 3 to 4 years. This patient was given chemotherapy R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone). Foran revealed that Rituximab alone produces a 38% response rate in patients with untreated MCL and the other studies suggested that Rituximab improves the response and duration of response when combined in the frontline setting.8-9 Even though the chemotherapy in this patient does not complete, the researchers hope that the tumor reduction by tonsillectomy will enhance the result of his treatment.

Finally, the researchers highlight that **granulomatous inflammation is not always associated with chronic infection such as tuberculosis but also with hematologic malignancies**. Nevertheless, to exclude tuberculosis or other infections in a patient who was suspected to be lymphoma is considerable. Because the treatment of choice is chemotherapy with other immunosuppressive agents, it is necessary to find out and treat concomitant infection.
References


