

# A Case of Angiocentric Lymphoma Mimicking Behcet's Disease

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We report a case of angiocentric lymphoma in a 41-year-old female who complained chiefly of a genital ulcer and a bulging conjunctiva on the right eye. She had a history of a recurrent oral ulcer over a 5 year period and a genital ulcer over 3 years. The above manifested clinical findings may suggest Behcet's disease. However, a biopsy from the upper vaginal wall and the inferior turbinate showed that atypical small and large lymphocytes with hyperchromatic, elongated and convoluted nuclei had aggregated around the thickened blood vessels, which is consistent with angiocentric lymphoma. Immunophenotypically, the atypical cells were positive for pan T-cell markers not B-cells. Serologically, the patient showed a high titer of EB virus viral capsid antigen(VCA) IgG. (*Ann Dermatol* 9:(1)22~25, 1997).

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Angiocentric immunoproliferative lesions(AILs) are a group of lesions that share histologic, immunophenotypic and clinical features.<sup>1</sup> These exhibit angiocentric and angiodestructive patterns of infiltration of a mature T-cell.<sup>2</sup> Extra-nodal involvements including skin is frequently seen.<sup>1,2</sup> In Korea, AILs have been reported as polymorphic reticulosis by Whang<sup>3</sup> et al. and as lymphomatoid granulomatosis by Chi<sup>4</sup> et al. Herein we report a case of angiocentric lymphoma mimicking Behcet's disease.

## CASE REPORT

A 41-year-old woman was admitted to the department of gynecology because of a genital ulcer

that had developed 1 month ago. She also complained of a bulging conjunctiva on the right eye with pain of 10 days duration. Another symptom was intermittent nasal discharge. She was referred to the department of dermatology for evaluation of Behcet's disease. A physical examination of the vagina showed an ulcer on the upper vaginal wall and the anterior cervix(Fig. 1). Ophthalmological examination showed a hyperemic and bulging conjunctiva and increased intraocular pressure on the right eye(Fig. 2).

Laboratory findings were as follows : a differential white blood cell count was within normal ranges; hemoglobin and hematocrit levels were 9.3gm/dl and 26.9%; the platelet count was normal; the erythrocyte sedimentation rate was 24mm/hr; the GOT/GPT level was 36.0/67.5 IU/L; EKG, electrolytes were normal; routine urinalysis showed hematuria; the EB virus VCA IgG was 1: 160 (normal ; 1:10), the EB virus VCA IgM was 1:10(normal); the platelet antibody was positive. The pathergy test was negative. Orbit and abdomen CT scans showed nasal septal perforation, in-

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**Fig. 1.** Central yellowish ulcer base circumscribed by erythematous plaques on the upper vagina.

**Fig. 2.** Hyperemic and bulging conjunctiva on the right eye.

**Fig. 3.** Orbit CT findings show nasal septal perforation (arrow), inflammation on both maxillary sinuses (arrow heads).

**Fig. 4.** A dense infiltration of atypical lymphoid cells around the thickened blood vessels of the upper vaginal wall (H&E stain,  $\times 200$ ).

inflammation on both maxillary sinuses and enlargement of both adrenal glands and the paraaortic lymph nodes, respectively (Fig. 3). A biopsy from the upper vaginal wall and the inferior turbinate showed that atypical small and large lymphocytes with hyperchromatic, elongated and convoluted nuclei had aggregated around the thickened blood vessels (Fig. 4). On immunohistochemical staining, atypical cells found were pan T-cell markers (UCHL-1:CD45RO)-positive, Pan B-cell markers (L26:CD20)-negative (Fig. 5).

**Fig. 5.** A positive staining reaction with the pan T-cell marker is seen at the inferior turbinate lesion (The immunohistochemical stain with UCHL-1 : CD45RO,  $\times 200$ ).

A diagnosis of angiocentric lymphoma was made and the patient was treated with the chemotherapeutic agents that form the "Promace - Cytabom" regimen. This included cytoxan, adriamycin, etoposide and prednisolone. After the second cycle of chemotherapy was completed, a suppressed bone marrow appeared. Two weeks after that, she died of ARDS(adult respiratory distress syndrome) and sepsis.

## DISCUSSION

The concept of angiocentric immunoproliferative lesions(AILs) was first proposed by Jaffe<sup>5</sup>. The spectrum includes lymphocytic vasculitis, lymphomatoid granulomatosis, polymorphic reticulosis, midline malignant reticulosis and angiocentric lymphoma.<sup>1,6</sup> Angiocentric lymphoma is the end point in the sequence of angiocentric immunoproliferative lesions.<sup>1,7</sup> Since recent reports demonstrated the presence of clonal rearrangements of the T-cell receptor in AILs, the AILs are now thought to represent a continuous spectrum of postthymic T-cell lymphoma.<sup>6,8</sup> The frequent extranodal involvement has been reported in AILs.<sup>2</sup> The favorite involvement sites are the lung, nasal cavity, upper respiratory tract, skin, kidney and central and peripheral nervous systems in frequency.<sup>1</sup> The skin involvement has been reported as high as 50%.<sup>2</sup> It usually presents itself as nodular or ulcerated lesions.<sup>2</sup> Our patient also showed ulcerative lesions of the genital area and nasal cavity. The major histopathological feature is angiocentric and angiodestructive infiltration. The cellular composition is usually polymorphous, with a spectrum of cytologic atypia.<sup>1</sup> Our patient's biopsy specimen also showed that atypical small and large lymphocytes with hyperchromatic, elongated and convoluted nuclei had aggregated and invaded the area around the thickened blood vessels. Therefore, a diagnosis of angiocentric lymphoma was made easily by histopathological findings. However, our initial clinical diagnosis was Behcet's disease because of the long recurrent history of oral and genital ulcers and the presence of genital ulceration and conjunctival lesions. Indeed, the differentiation between AILs and Behcet's disease is easily made by histopathological findings that show angiocentric and angiodestructive infiltration with cytologic atypia. AILs have also been

notorious for their frequent extranodal involvement such as the skin shown by ulcerated lesions on the genital area which is frequently found in Behcet's disease. AILs which are similar to clinical and histological manifestation of Behcet's disease have been reported.<sup>9</sup>

Angiocentric lymphomas are often EBV-positive.<sup>4</sup> This may explain why this disease is seen in increased frequency in parts of the world where EBV infection is prevalent such as Asian countries.<sup>10,11</sup> Our case also showed a high titer of EB virus VCA IgG. On immunophenotypic analysis, the cells infiltrating the blood vessels are usually CD2-positive, CD56-positive and cytoplasmic CD3-positive, but are usually negative for surface CD3.<sup>12</sup> Our case showed that the pan T-cell marker was positive but the pan B-cell marker was negative.

The differential diagnosis includes lymphomatoid granulomatosis, Wegener's granulomatosis (WG) and other aggressive lymphomas. Lymphomatoid granulomatosis is EBV-positive with B-cell proliferation and the most frequent sites are the lung, kidney and central nervous system.<sup>13</sup> WG can be differentiated by the presence of necrosis with abundant cellular and nuclear debris, secondary to the prominent neutrophilic infiltrate. Other aggressive lymphomas show spontaneous necrosis but it does not usually show a vascular distribution.<sup>7</sup> Therapy involves using more aggressive regimes such as ProMACE or COMLA (cyclophosphamide, vincristine, cytosine arabinoside and methotrexate).<sup>2</sup> Prognosis has been thought to be inversely proportional to the number of large, atypical lymphoreticular cells.<sup>14</sup> Recurrent cases for prior therapy are associated with a poor prognosis.<sup>1</sup> Localized upper airway diseases are sensitive to radiation therapy.<sup>1</sup>

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