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Primary Non-Hodgkin's Malignant Lymphoma of the Vulva

—A Case Report—

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A case of primary non-Hodgkin's malignant lymphoma of the vulva which occured in a 68-year-old woman is presented. Non-Hodgkin's malignant lymphoma is infrequently involved in the female genital tract. Moreover, primary vulvar involvement of this tumor is very rare. To date only 6 cases have been reported in the literature. To our knowledge this is the first reported case of a non-Hodgkin's malignant lymphoma of the vulva in Korea.

Key Words: *Malignant lymphoma, Vulva*

INTRODUCTION

Malignant lymphomas originating in the pelvis are relatively rare. More than 80% of them involve the ovaries and uterus. Vulvar primary involvement comprises only 4% of them (Lathrop, 1967). A review of the literature reveals only six reported cases of non-Hodgkin's lymphoma primarily arising from the vulva (Taussig, 1937, Lathrop, 1967, Schiller and Hadge, 1970, Wishart, 1973, Shinohara et al., 1988, Bagella et al., 1990) and one case from Bartholin's gland (Plouffe et al., 1984). This represents the first reported case of primary vulvar involvement of non-Hodgkin's malignant lymphoma in Korea.

CASE REPORT

A 68-year-old multiparous Korean female presented with a 1-year history of a mass in the right upper labium of the vulva in early March, 1991. Initially, she felt the mass of about 3cm in diameter without any discomfort. As it slowly enlarged, she suffered from dull pain for 2 months prior to admission. Examination revealed a hen's egg sized firm mass with irregular margins involving the upper lateral portion of the right major labium. It was movable and non-tender. The uterus and the cervix were in senile involution and the ovaries were not palpable. The vagina was atrophic. There was no inguinal adenopathy and the remainder of the physical examination was normal. Routine preoperative laboratory and radiologic studies were all normal apart from a slight increase of liver enzymes because of chronic persistent hepatitis. Wide local excision, with 1-cm peripheral margins, was performed. The mass was 5×4.5×2.5-cm in size and the cut surface showed a multilobular soft mass of yellow white color with central confluent necrosis and hemorrhage (Fig. 1). Frozen section was reported as malignant tumor, probable malignant lymphoma with clear resection margins. Permanent section revealed that the tumor was composed of solid sheets of large, monomorphic, and atypical cells containing round vesicular nuclei with one to four prominent nucleoli. The cytoplasm was moderate in amount and acidophilic. Occasional multinucleated or mononucleated giant cells with bizarre nuclei were present and atypical mitoses were frequently seen. A nodular pattern was not present (Fig. 2 and 3). Immunohistochemical stains using avidin-biotin-peroxidase complex (ABC, DAKO, Santa Barbara, CA) on paraffin blocks revealed strong positive reactions on leukocyte common antigen (1:30, DAKO, Santa Barbara, CA) and L26 (marker for pan-peripheral B cell, 1:100, DAKO, Santa Barbara, CA). Other specific antibodies against UCHL1 antigen (marker for T cell, 1:150, DAKO, Santa Barbara, CA), Ki-1

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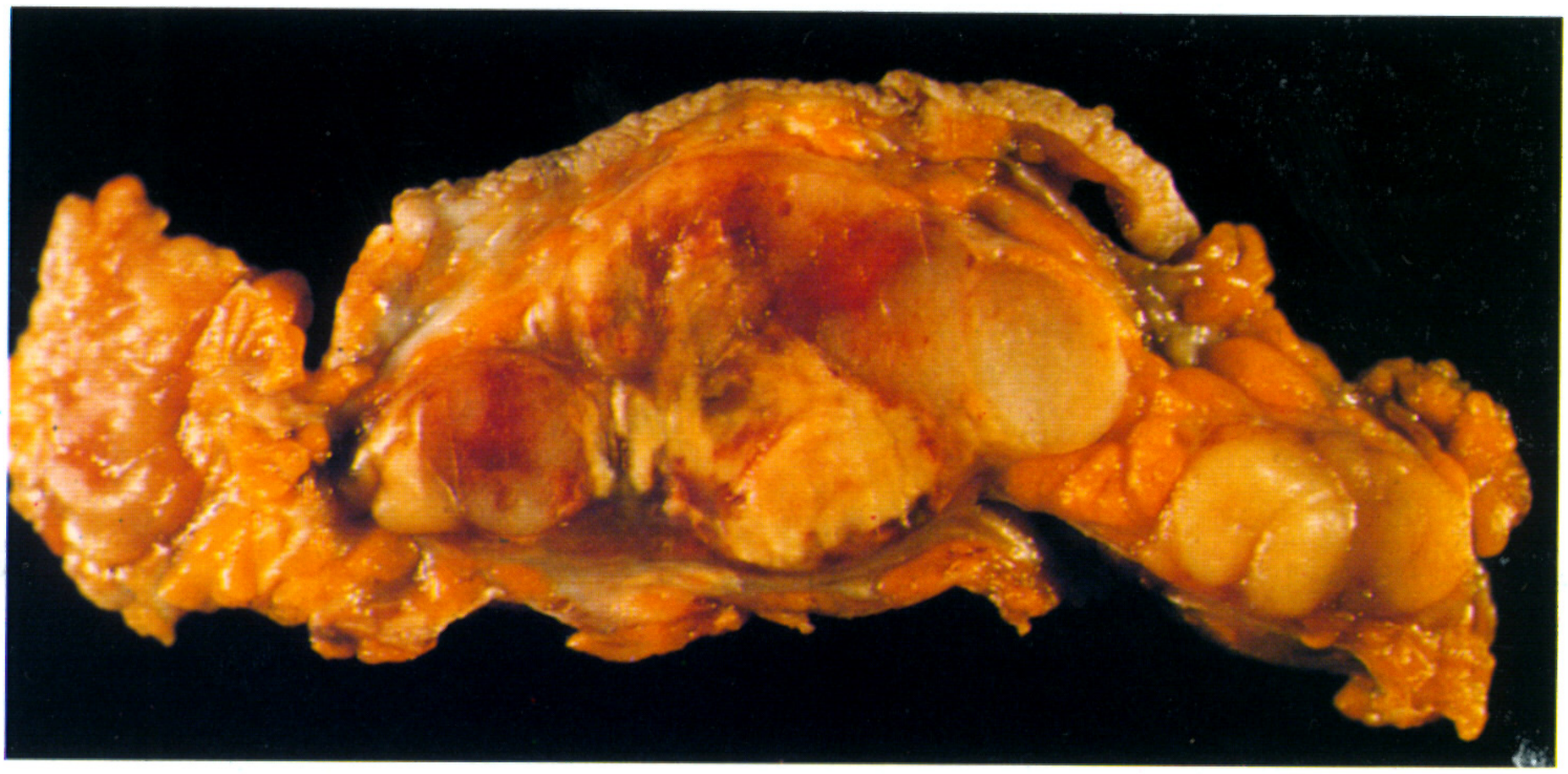

Fig. 1 Cut surface of resected specimen reveals multinodular firm mass of yellow-white color, with multifocal hemorrhages and necroses. Covering skin is intact.

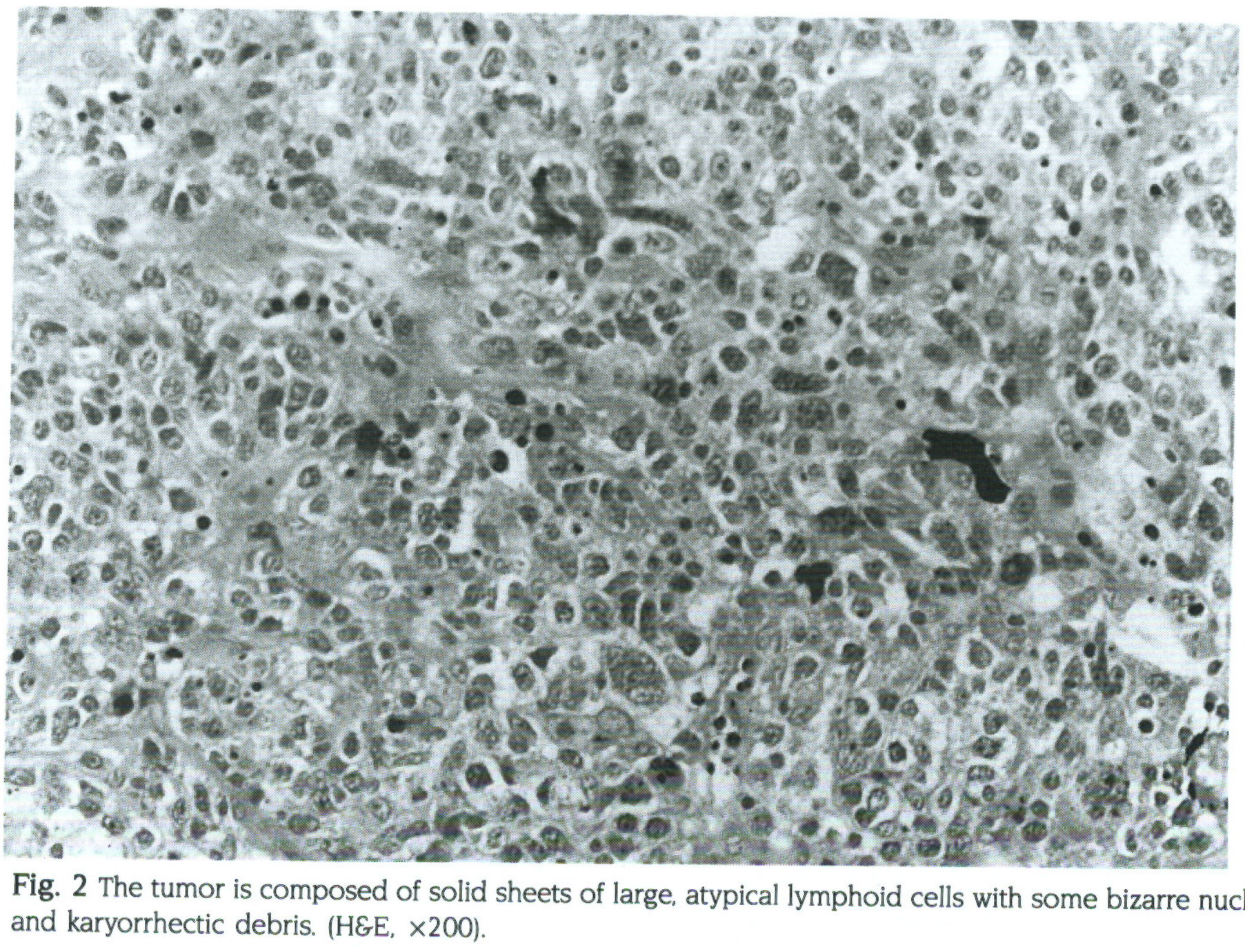

Fig. 2 The tumor is composed of solid sheets of large, atypical lymphoid cells with some bizarre nuclei and karyorrhectic debris. (H&E, ×200).

antigen (1:20, DAKO, Santa Barbara, CA), S-100 protein (1:200, DAKO, Santa Barbara, CA), and melanoma antigen (1:5, SANBIO, Holland) were all negative. Diagnosis of malignant lymphoma of high grade, diffuse, large cell, anaplastic type on working formulation and B cell lineage on functional classification was rendered.

The patient underwent clinical, noninvasive staging including computerized tomographic scan and bone marrow study, all of which were proved to be normal. Based on the study, the patient was classified as stage IE according to the Ann Arbor classification. We recommended postoperative adjuvant chemotherapy,

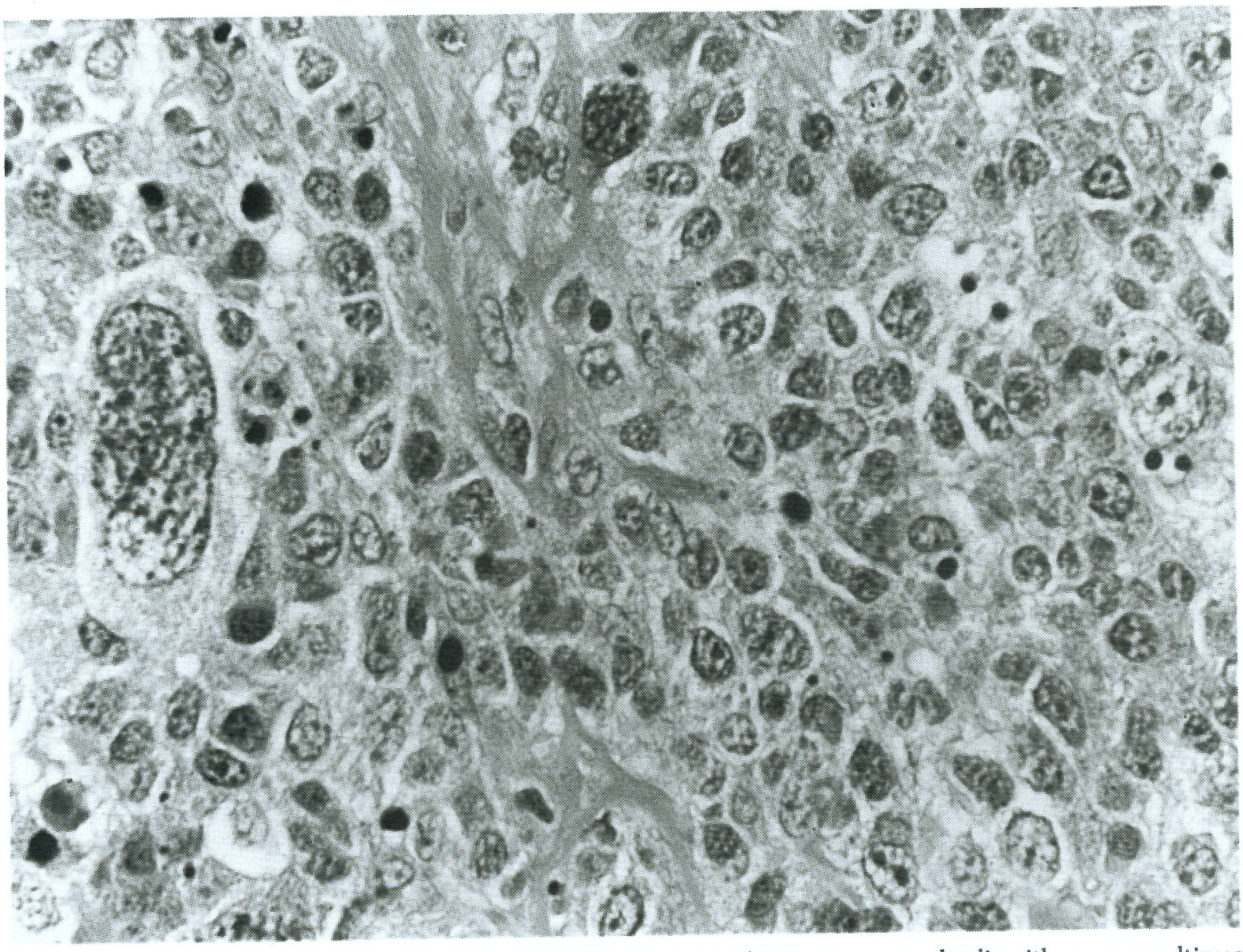

Fig. 3. Tumor cells contain large, round, vesicular nuclei and prominent nucleoli, with some multinucleation. (H&E, ×400).

however the patient refused it.

The postoperative course was uneventful and she was discharged on the 8th postoperative day. The patient has been clinically free of disease for 14 months following the surgery.

DISCUSSION

Patients with malignant lymphoma who present with gynecologic symptoms are very rare. However, autopsy studies have shown that about 40% of women dying of non-Hodgkin's lymphoma had involvement of the uterus or ovaries (Rosenberg et al., 1961, Lucia et al., 1952). The incidence is even higher if, as in Lathrop's report, the denominator includes only those with an intact reproductive system. Recently, the incidence of lymphoma is increasing in women so that the gynecologist should have more interest in this disease, particularly since the initial diagnosis is often missed as undifferentiated carcinoma by the pathologist (Crisp et al., 1982).

Non-Hodgkin's malignant lymphoma is an extremely heterogeneous disease varying from a relatively indolent course to a fulminating fatal course. The development of immunologic and cytochemical techniques can specifically identify the subpopulations of tumor cells-B cell (bone marrow), T cell (thymus) and true histiocytic cells. The majority of non-Hodgkin's malignant lymphomas are of B cell lineage as in this case and these are generally more responsive to treatment (Crisp et al., 1982). This type of non-Hodgkin's lymphoma often occurs as a localized mass, which usually arises from peripheral lymph nodes. Uncommon sites are extranodal locations such as the gastrointestinal system, bone, skin, central nervous system, breast, thyroid and, rarely the genital tract (Bagella et al., 1990). In Korea,53% of 457 non-Hodgkin's lymphomas were extranodal judged by the biopsy site. The common sites were gastrointestinal tract, tonsil and oronasal cavity. In that study, 4 case of gynecologic lymphomas were reported in the ovary and the vagina (Chi et al., 1987).

In an attempt to resolve confusion and controversy of variable classification schemes-Rappaport, Kiel, Luckes and Collins, Dorfman etc.-the National Cancer Institute developed a working formulation of non-Hodgkin's lymphoma for clinical use. This formulation was proposed as a common language that might be used by all clinical investigators to translate from one classification scheme to another (Rosenberg et al., 1982). In those classifications, two distinct patterns of

nodal involvement by malignant lymphomas-follicular and diffuse-are defined. Diffuse lymphomas are more common and have a more unfavorable prognosis. In general, the larger the cell type, whether follicular or diffuse, the poorer the prognosis (Crisp et al., 1982). The survival of malignant pelvic lymphoma is poor in comparison with that of patients having lymphomas in other sites. Woodruff et al. (1967) reported on 35 patients with ovarian involvement of lymphoma, their survival was about 6% at 5 years. Charlton et al. (1974) reported similarly poor survival in the series from the Armed Forces Institute of Pathology. The median survival of reported cases with vulvar lymphoma, even in the presence of a unicentric nodal or extranodal localization, was not reaching one-year.

Clinical and instrumental evaluation of the patient should be done for staging. Basic workup with special interest in the laboratory evaluation of liver and kidney function and computerised tomographic scan to assess the involvement of abdominal lymph nodes are needed. A bone marrow biopsy is required because of the high incidence of marrow involvement in some subtypes. Staging laparotomy is usually not considered expedient, because of the old age of the patients and associated diseases which contraindicate an invasive staging.

Therapeutic modalities depend both on the histologic subtype of the disease and on the clinical stage. Surgical excision of localized nodal and extrandodal disease is usually performed for diagnostic purposes. Surgical treatment is not curative because of the frequent hematogeneous spreading. Radical debulking surgery is not indicated in extranodal disease except in large cell and undifferentiated types. Surgically evaluated, early stage, low grade, follicular lymphomas have had good cure rates with limited-field external beam radiation therapy. Completely evaluated Stage IE patients with the more aggressive diffuse and large cell follicular lymphomas can also achieve excellent cure rates with appropriate radiation therapy. Although the lower-grade follicular lymphomas can be treated with doses of 3500 to 4000 cGy, the moreaggressive lymphomas require higher doses, probably because of their larger bulk, with a significant number of local relapses noticed at 5000 cGy (Muntz et al., 1991). Disadvantages of radiation therapy are its inability to treat occult disseminated disease and, for young women with genital tract lymphoma, its destruction of reproductive and gonadal function. Chemotherapy is the treatment of choice in the higher-grade diffuse large cell and undifferentiated lymphoma. The few cases of vulvar lymphoma reported in the literature have been treated by systemic chemotherapy or sometimes radiotherapy following local excision. However, chemotherapy has been adopted more. Chemotherapeutic regimens generally accepted for use include CHOP (cyclophosphamide, adriamycin, vincristine, prednisone) for diffuse pattern and CVP (cyclophosphamide, vincristine, prednisone) for nodular pattern lymphoma (Crisp et al., 1982). Chemotherapy produces about a 70-80% remission rate and an anticipated cure rate is approximately 35%. Relapse of disease, even after complete remission, is not unusual in these highly malignant forms, especially in the central nervous system where involvement is fatal. The use of intrathecal administration of methotrexate has been suggested to prevent meningeal and cerebral involvement. New therapeutic modalities such as various combination chemotherapys, possibly associated with systemic use of interferon and monoclonal antibodies are in experimental protocol.

In conclusion, a case of a 68-year-old woman with primary vulvar involvement of non-Hodgkin's lymphoma is presented. Though such a rarity is known, primary extranodal or secondary lymphomatous process should be included in its differential diagnosis for vulvar masses.

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