Case Report

Hodgkin's Disease Involving the Breast: A Case Report and Literature Review

Kanita Kayasut, Tuenjai Chuangsuwanich, Chirayu Auewarakul*, Adune Ratanawichitrasin, and Sanya Sukpanichnant.**

*Department of Pathology; *Department of Medicine; **Department of Surgery, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.*

Abstract: *We report a case of Hodgkin's disease (HD) involving the breast as a recurrence of the disease, a rare presentation, in a 39-year-old female patient. She was first diagnosed as nodular sclerosis HD, stage IIA, presenting with left cervical lymph node enlargement at the age of 33 and was treated by combination chemotherapy and radiation. However, she developed a right breast mass 8 months after complete remission. The excisional biopsy of the breast mass was proven to be recurrent HD. The disease was evaluated to be in stage I_E. A literature review of HD involving the breast confirms this rarity.*

Key Words : ● *Hodgkin's disease* ● *Breast*

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Hodgkin's disease (HD) involving the breast, either of primary or secondary nature, is an uncommon lesion. The exact incidence is not known. But, from the compilation of a few series published on this subject, it is estimated to be 0.25 % of all extranodal HD.[1] The first description of HD involving the breast was reported by Kueckens in 1928.[2] Since then a few other cases have been reported in the world literature.[3-7] The present case at Siriraj Hospital, Bangkok, Thailand is an example of HD involving the breast as the only manifestation at the time of recurrence.

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Requests for reprints should be addressed to Dr. Kanita Kayasut, M.D, Department of Pathology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand, 10700. Tel. 419-7000 ext. 6504-5 Fax. 411-4260 E-mail: tekky@mahidol.ac.th

Case Report

A previously healthy 33-year-old Thai

female patient presented at Siriraj Hospital in May 1993 with the enlargement of the lymph nodes at the left side of the neck. Three small discrete inguinal lymph nodes were also detected at each side. She had no constitutional symptoms including fever, loss of appetite, weight loss and night sweat. The liver and spleen were not palpable. The cervical lymph node was biopsied and the diagnosis of nodular sclerosis HD was confirmed by one of the authors (SS). The investigation, including complete blood count, blood chemistry, chest X-ray, computerized tomography of the abdomen and bone marrow aspiration, was performed. Only lactate dehydrogenase was slightly increased at the level of 463 U/L (normal range, 225-450 U/L); the others revealed no abnormality. The clinical stage IIA was thus established according to the Ann Arbor staging. She was given combination chemotherapy including cyclophosphamide, vincristine, prednisolone and procarbazine (COPP) for 1 course. After that, she lost to follow up for 4 years. During this time, she developed bilateral cervical and right axillary lymph node enlargement, measuring up to 17 cm in maximal diameter. She decided to receive treatment at Siriraj Hospital again in April 1997. The clinical stage remained as stage II. The COPP regimen was administered again. After 7 courses of chemotherapy remained a 4 cm matted lymph node at the left side of the neck. The patient then received local irradiation for 2,000 cGy; however, the lymph node was still palpable. The new chemotherapy regimen including monthly cyclophosphamide, vincristine, prednisolone, procarbazine, doxorubicin, bleomycin and vinblastine (COPP/ABV) was administered for 6 courses, the last of which was in October 1998. Complete remission with no lymph node enlargement was achieved after treatment.

No evidence of disease was detected during the 8 month long follow-up, until she noticed a right breast mass in June, 1999. This breast mass had been enlarging slowly for over a few months. She had no pain, fever, weight loss, nipple discharge, or any skin lesion. Physical examination of the breasts revealed a firm movable mass, measuring 3 cm in diameter, located at the lower outer quadrant of the right breast. The nipple-areolar complex was normal and the skin showed no sign of inflammation. The left breast was normal. The axillary and other superficial lymph nodes were not detected. The liver and spleen were not palpable. Routine hematological examination showed no abnormality. Excisional biopsy of this right breast mass was performed and the specimen was submitted to the Department of Pathology.

Gross examination of the breast mass revealed an irregular piece of rubbery grayish white and pale yellow tissue, measuring 3x2.5x 0.5 cm^3 with grayish white and fatty non-homogeneous cut surface. Small vaguely nodular masses were detected. The formalin-fixed specimen was serially sectioned, embedded in paraffin, sectioned for 3 micron thick histologic sections, and stained with hematoxylin and

eosin.

Microscopic examination demonstrated that the breast tissue was replaced by dense lymphoid tissue which was divided by thick collagen bands into multiple vague nodules. (Fig. 1) The classical Reed-Sternberg cell, lacunar cells, and many large mononuclear cell with distinct nucleoli (Hodgkin cells) were found with syncytial growth pattern, rendering a histological diagnosis of nodular sclerosis HD with syncytial growth pattern. (Fig. 2) Paraffin section immunoperoxidase demonstrated that the neoplastic cells were immunoreactive with antibodies to CD15 (LeuM-1) and focally with CD30 (Ki-1). (Fig. 3) But they were negative for antibodies to CD45 (leukocyte common antigen, LCA), CD3, CD20 (L-26), epithelial membrane antigen (EMA), AE_1/AE_3 cytokeratins and S-100 protein. (Fig. 4) These results confirmed the diagnosis of HD. After complete excision of the breast mass, the patient lost to follow up.

Discussion

Extranodal HD is quite rare, especially in the breast.[1] HD involving the breast can occur as a primary or secondary lesion. A review of the literature during 1928 to 1999 discloses only 25 reported cases.[3-7] At Siriraj Hospital, there were 101 cases of HD out of 1,149 malignant lymphomas over a period of 69 months from August 1993 to April 1999.[8,9] No case of breast involvement by HD was identified in that series. This patient is the first case with HD involving the breast in our surgical pathology files.

The pathogenesis of HD involving the breast

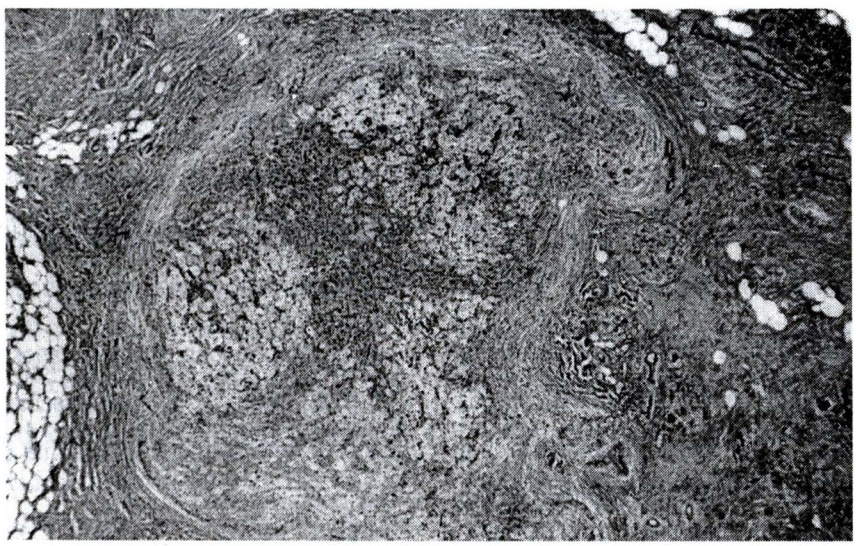

Fig. 1 Nodular sclerosis Hodgkin's disease involving the breast. Note the breast tissue replaced by a dense polymorphous cellular infiltration surrounded by thick collagen bands. (hematoxylin & eosin, X 100)

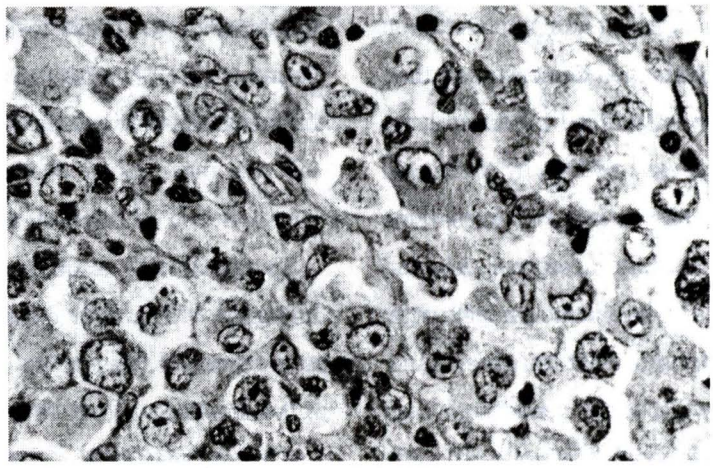

Fig. 2 High magnification of the area showing syncytial growth pattern. Note many large mononuclear cells with distinct nucleoli (Hodgkin cell) and some lacunar cells. (hematoxylin eosin, X 400)

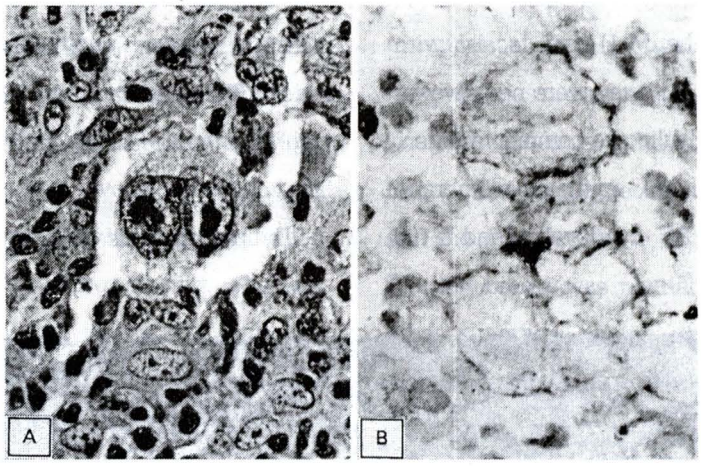

Fig. 3 A) A classical Reed-Sternberg cell amidst the mixed inflammatory background. **B)** Immunoreactivity with antibody to CD15 (LeuM-1) of Reed-Sternberg cells showing a distinct membrane staining. (paraffin section immunoperoxidase for CD15, X 400)

is thought to arise from the internal mammary and intramammary lymph nodes with extranodal extension.[6] The major presentation is a single nodule or a diffuse enlargement of the breast which may or may not be painful. Both unilateral and bilateral involvement of the breast have been described. Most cases occur in young women and rarely occur in male. The age of the previous reported cases ranges from 11 to 63 years.[4,6] A case associated simultaneously with a ductal carcinoma of the breast has been reported.[3]

All the previous reported cases of HD involving the breast that mentioned about the subtype of HD are of nodular sclerosis type. Our patient is also classified as nodular sclerosis

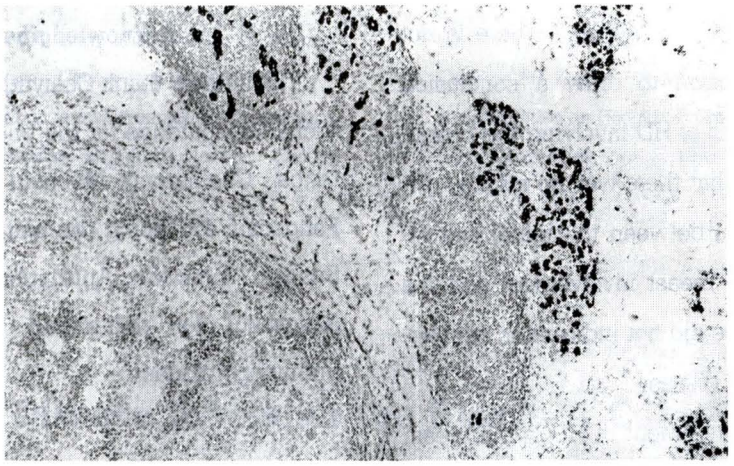

Fig. 4 Low magnification of ductal epithelial cells showing immunoreactivity with antibody to epithelial membrane antigen (EMA) located at the left half of the photomicrograph. Note the negativity in the nodular sclerotic area of Hodgkin's lymphoma at the right half where few residual mammary ducts are discernible. (paraffin section immunoperoxidase for EMA, X 100)

HD with syncytial growth pattern. This pattern is a variant of nodular sclerosis HD revealing sheets and cohesive clusters of numerous Hodgkin cells. Pleomorphic and atypical Hodgkin cells are occasionally seen. This variant has not been demonstrated to have a poorer prognosis than other cases of nodular sclerosis.[10] Importantly, this pattern can simulate carcinoma that requires a careful distinction. Paraffin section immunoperoxidase using markers against HD and carcinoma usually solves this problem.

The Rye Conference on "Obstacles to the control of Hodgkin's disease" in 1965 concluded that all extranodal involvement with HD was to be considered stage IV disease.[11] Then, Musshoff classified the Rye stage IV as stage IVpc (per continuitatem) when extranodal HD was limited and lying in direct continuity with lymph node disease and stage IVpd (per disseminationem) when extranodal disease was unrelated to any lymph node by proximity.[12] He found that stage IVpc showed a survival comparable with stage II disease. Accordingly, the staging system was revised at the Ann Arbor Symposium, 1971.[13] Within each stage, there would be a category for extranodal disease and designated by a subscript letter E after the stage. The present case was classified as stage IIA at the first presentation in 1993 and thereafter as at least stage I_E when recurrence in the breast occurred.

The prognosis in HD depends not only on the stage of the disease but also on its histologic subtype. According to the modified Lukes and Butler classification, lymphocyte predominance and nodular sclerosis subtypes show a better prognosis than do mixed cellularity and

lymphocyte depletion subtypes.[7] There is not sufficient information to draw a conclusion about the prognosis of HD involving the breast. Meis et al. found that there was no marked difference in survival between the initial and recurrent groups of breast involvement and the group of recurrence did not indicate an accelerated phase of the disease.[6]

Basically, the treatment of HD of the breast is similar to that applied to HD elsewhere in the body. It depends upon the extent and distribution of the disease. The therapy used may be surgery, radiation, chemotherapy, or a combination. Bone marrow transplantation, a new therapy for HD, is used only for some selected groups of patients. In recurrent cases, high dose chemotherapy (with or without radiotherapy) with autologous bone marrow transplantation or autologous peripheral blood stem cell transplantation has potential to become the treatment of choice. Three to four years disease-free survival has been reported in 35-50% of cases.[10]

Summary

An additional case of HD involving the breast as a recurrence of the disease is reported in 39-year-old female patient. A concise literature review is present. The breast involvement by HD is such a rare presentation that clinical and pathological recognition is important to prevent delay in diagnosis and treatment.

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บทคัดย่อ: *รายงานการกลับเป็นซ้ำของ Hodgkin's disease (HD) ที่เกิดในเต้านมซึ่งพบได้น้อยในผู้ป่วยหญิงอายุ 39 ปี ผู้ป่วยได้รับการวินิจฉัยครั้งแรกเมื่ออายุ 33 ปี ว่าเป็น nodular sclerosis HD, stage IIA มาด้วยเรื่องต่อมน้ำเหลืองโตที่คอด้านซ้ายและได้รับการรักษาโดยยาเคมีบำบัดและการฉายรังสี แปดเดือนหลังจากโรคสงบ ตรวจพบก้อนที่เต้านมด้านขวา ผลการตัดก้อนดังกล่าว ได้รับการพิสูจน์ว่าเป็นการกลับเป็นซ้ำของ HD โรคถูกประเมินอยู่ใน stage I_E ผลการทบทวนบทความทางวิชาการยืนยันการพบได้น้อยของ HD ที่เกิดในเต้านม*

Key Words : *● Hodgkin's disease ● Breast*

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