







Progressive Transformation of Germinal Centers in Axillary Lymph Nodes Mimicking Metastatic Lymphadenopathy after Breast Cancer Surgery: A Case Report

유방암 수술 후 액와 림프절에 발생한

Progressive Transformation of Germinal Centers: 증례 보고

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Progressive transformation of germinal centers (PTGC) is a rarely diagnosed, benign disease of the lymph nodes that commonly manifests as chronic lymphadenopathy. PTGC may be characterized by single or multiple non-tender lymph nodes, and it commonly involves the cervical, axillary, and inguinal areas. Although PTGC is identified with concurrent lymphoma in some patients, it is not considered as a premalignant entity. Histopathologic diagnosis of PTGC is rarely made, and imaging findings have been reported in very few studies. We present a case of PTGC that occurred at the contralateral axillary lymph nodes and mimicked metastatic lymphadenopathy after breast cancer surgery. We also discuss its imaging findings.

Index terms Progressive Transformation of Germinal Centers; Axilla; Lymphadenopathy; Lymphatic Diseases

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INTRODUCTION

Progressive transformation of germinal centers (PTGC) is one of the benign lymphadenopathy that occurs in the background of reactive follicular hyperplasia. It accounts for 3.5% of chronic lymphadenopathy (1), and is assumed to be underdiagnosed in clinical practice. The imaging features of PTGC have not been reported in the previous literature. We present a case of PTGC in a breast cancer patient which mimicked metastatic axillary lymphadenopathy, and describe the imaging findings.

CASE REPORT

A 32-year-old female presented with a palpable breast mass in right upper outer quadrant. Mammography showed a round hyperdense mass with obscured margin at right breast (not shown). Breast magnetic resonance imaging (MRI) showed an irregular shaped, heterogeneously enhancing mass in right upper outer quadrant (37 mm × 29 mm in size) on subtraction image obtained 2 minutes after contrast administration. Multiple enlarged lymph nodes with cortical thickening were also present in right axilla (Fig. 1A). These imaging findings were highly suggestive of malignancy, and invasive ductal carcinoma was diagnosed by gun biopsy performed at outside hospital. PET-CT scan showed additional hypermetabolism in right supraclavicular lymph node. The patient underwent neoadjuvant chemotherapy and following breast conserving operation with radiation therapy. Histopathology was reported as no residual carcinoma of breast and regional lymph nodes.

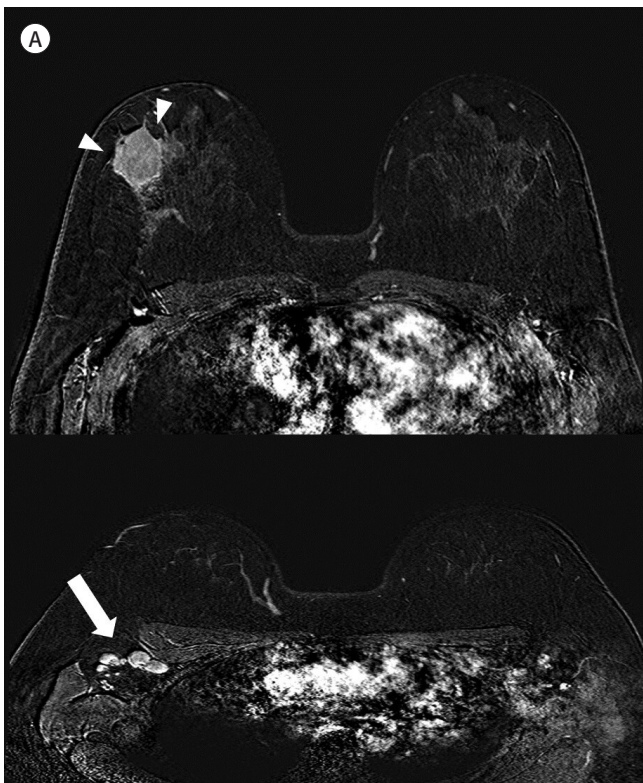


Fig. 1. Progressive transformation of germinal centers in axillary lymphnodes after breast cancer surgery in a 32-year-old female.

A. Preoperative breast MRI: fat-saturated T1-weighted subtraction images obtained 2 minutes after contrast administration reveal an irregular and heterogeneously enhancing mass in the right breast (arrowheads). Right axillary lymph nodes are enlarged with cortical thickening (arrow).

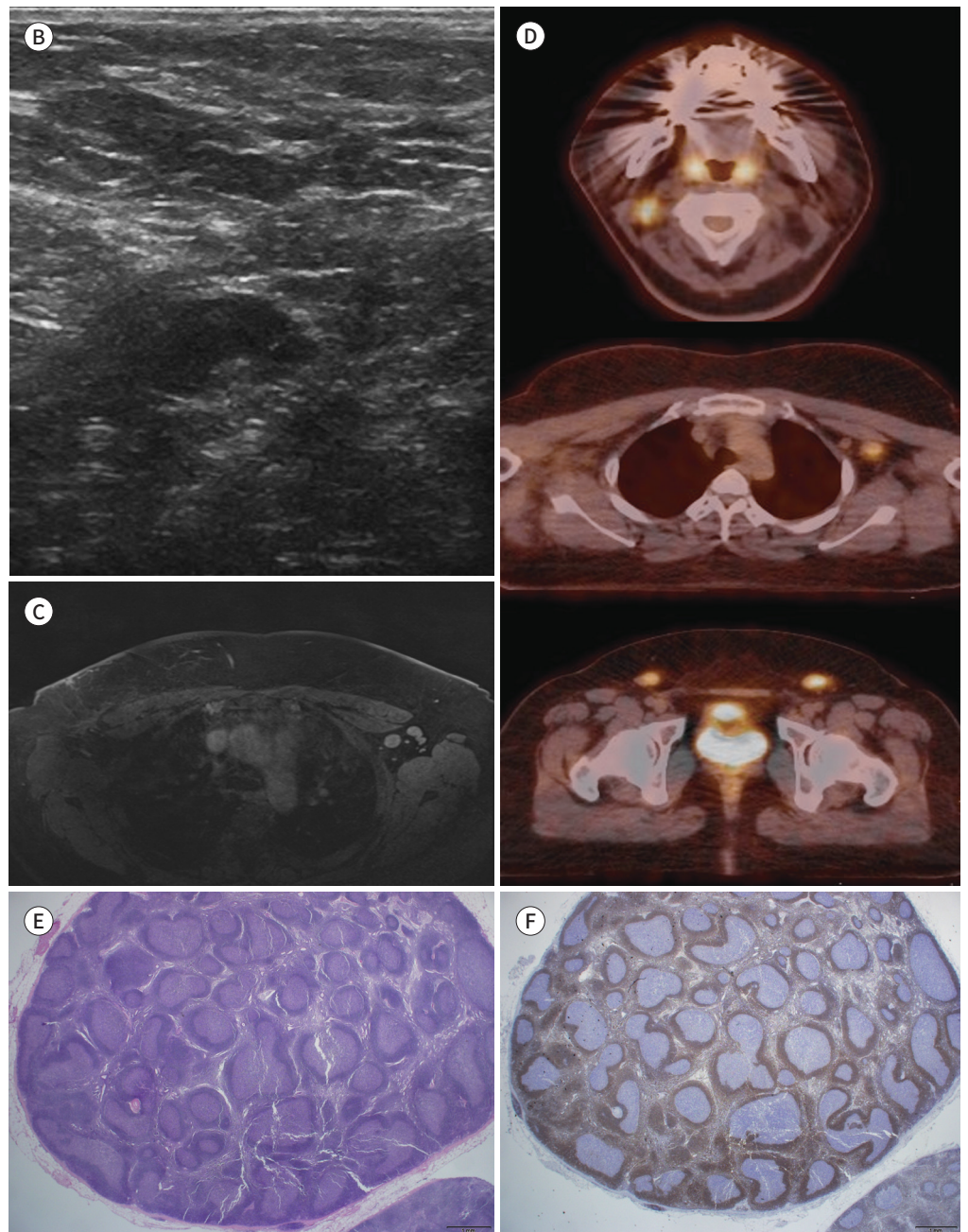
Fig. 1. Progressive transformation of germinal centers in axillary lymphnodes after breast cancer surgery in a 32-year-old female.

B, C. Follow-up axillary sonography (**B**) and MRI image (fat-saturated T1-weighted image obtained 2 minutes after contrast administration) (**C**) at 6 months after conservative surgery of the right breast show multiple enlarged lymph nodes with cortical thickening in the left axillary area.

D. PET-CT scans show multifocal hypermetabolism in the right cervical (SUVmax 5.9), left axillary (SUVmax 3.6), and both inguinal (SUVmax right 4.4, left 5.9) lymph nodes. Metastatic lymphadenopathy is suggested.

E. Microscopic findings (hematoxylin and eosin stain, $\times 12.5$) of excised left axillary lymph nodes shows enlarged lymph nodes with variably sized enlarged lymphoid follicles and frequent secondary germinal centers. Occasionally, coalescent germinal centers are observed.

F. Bcl-2 immunohistochemical staining ($\times 12.5$) shows a negative reaction in germinal centers. SUVmax = maximum standardized uptake value



During clinical follow-up, palpable lymph nodes were detected in her left axilla on physical examination 6 months after the surgery. On the follow-up imaging, lymph nodes with cortical thickening were newly visible at left axilla on sonography, breast MRI (Fig. 1B, C) and chest CT scan (not shown). PET-CT revealed multiple hypermetabolic lymph nodes in left axilla [maximum standardized uptake value (SUVmax) 3.6], right neck (SUVmax 5.9), left external iliac and both inguinal areas (SUVmax; right 4.4, left 5.9) (Fig. 1D). There was no evidence of local tumor recurrence in right breast and axilla. Because metastatic lymphadenopathy was suspected, ultrasound-guided aspiration was done for the lymph node in left axilla. However, cytology was negative for malignancy. Left axillary lymph nodes were surgically excised for the radiologic-pathologic discordance. Microscopically, the section from left axillary area showed four enlarged lymph nodes with florid follicular lymphoid hyperplasia pattern. Germinal centers were distended and occasionally coalescent. Immunostaining for CD3 and CD20 showed reactive zonal pattern. CD21 and Ki-67 immunostains highlighted germinal centers, but Bcl-2 immunostain showed negative reaction in lymphoid follicles. The microscopic and immunohistochemical findings were compatible to PTGC (Fig. 1E, F).

During 4 years of clinical and imaging follow-up, mildly enlarged lymph nodes were persistently noted in left axilla. No interval change was observed in lymph nodes, proving it as a benign etiology.

DISCUSSION

PTGC is a benign reactive pattern identified within a lymph node with reactive follicular hyperplasia. The affected lymphoid follicles are enlarged three to five times greater than the normal follicles, and show expansion of mantle zone. Mantle zone lymphocytes extend into the germinal centers and the distinction between the germinal center and mantle zone is lost (2). In histopathologic examination, PTGC should be differentiated from follicular lymphoma. In cases with confusing morphology, immunostaining is the key for differential diagnosis. Follicular lymphoma shows overexpression of bcl-2, whereas PTGC have only mild focal expression. Previous studies have suggested an association between PTGC and nodular lymphocytes-predominant Hodgkin lymphoma (NLPHL) (3). In some reports, PTGC was more frequently observed in biopsy specimens of patients known to have NLPHL. However, PTGC is not considered as a premalignant entity. The specimen from our patient showed enlarged lymph nodes with large nodules of hyperplastic germinal centers, infiltrated by mantle zone B cells. Negative reaction for Bcl-2 immunostaining confirmed the diagnosis of PTGC.

PTGC is a pattern usually identified focally in a lymph node. The proportion of PTGC component is most commonly less than 5% of total follicles, and only few cases show PTGC in more than 20% of follicles (4). Therefore, complete excision of lymph node is required for the correct pathologic diagnosis of PTGC.

Most common clinical manifestation of PTGC was solitary enlarged lymph node in head and neck area (4). Özkan et al. (5) reported 33 cases of PTGC. The most common sites of lymphadenopathy were neck, axilla, inguinal in order, and other various sites such as intramammary lymph node were reported. Lymph nodes are mostly nontender/asymptomatic and appear as chronic, intermittent lymphadenopathy. Although mean age at diagnosis var-

ied from 43.8 to more than 60 years-old in previous studies (4, 5), quite a few young aged patients are also reported. Patients often undergo multiple biopsies due to persistent lymphadenopathy.

To our knowledge, imaging findings of PTGC are rarely reported. The sonographic feature of PTGC was reported by Tałasiewicz et al. (6) in two cases of cervical lymphadenopathy. Ultrasound showed hypoechoic enlarged lymph nodes without fatty hilum or increased vascularity. The imaging finding of fluoro-deoxy-glucose-PET in PTGC was avid uptake of radio-tracer, as in our case (7, 8). In patients with multiple non-necrotic lymphadenopathy, differential diagnosis may include reactive hyperplasia associated with infectious, inflammatory diseases or lymphoma. It is hard to include PTGC in the differential diagnosis of enlarged lymph nodes, in a patient with underlying malignancy. In our patient, PTGC appeared as enlarged axillary lymph nodes with cortical thickening, mimicking metastatic lymph nodes. However, it was somewhat unusual that metastatic lymphadenopathy occurred in contralateral side of primary breast cancer, without evidence of local tumor recurrence or ipsilateral lymphadenopathy.

We report a case of PTGC that involved axillary, cervical and inguinal lymph nodes after breast cancer surgery. Imaging features in this case were indistinguishable with malignant lymphadenopathy. Although suspicion for malignancy must be raised, PTGC can be included in the differential diagnosis, especially in case of lymph node enlargement in the typical location of PTGC.

Author Contributions

Conceptualization, C.K.R.; investigation, P.S.E.; methodology, C.K.R.; writing—original draft, P.S.E.; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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유방암 수술 후 액와 림프절에 발생한 Progressive Transformation of Germinal Centers: 증례 보고

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Progressive transformation of germinal centers (이하 PTGC)는 드물게 나타나는 양성 림프절 질환으로, 주로 만성적인 림프절 비대의 형태로 나타난다. 주로 한 개 또는 여러 개의 림프절의 무통성 비대로 나타나며, 가장 흔히 침범하는 부위는 경부 림프절, 다음으로 액와부와 서혜부 림프절로 알려져 있다. 일부 환자들에서는 조직병리에서 림프종이 함께 존재하기도 하지만, PTGC 자체는 전암병변으로 인식되지는 않는다. 조직학적으로 PTGC로 진단되는 경우도 적지만, 이에 대한 영상의학적 소견은 거의 보고된 바가 없다. 이에 저자들은 침윤성 유방암 환자에서 수술 후 반대편 액와부 림프절 비대로 나타나 전이성 림프절로 오인한 PTGC 증례의 영상 소견을 보고하고자 한다.

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