Unilateral nipple hyperkeratosis

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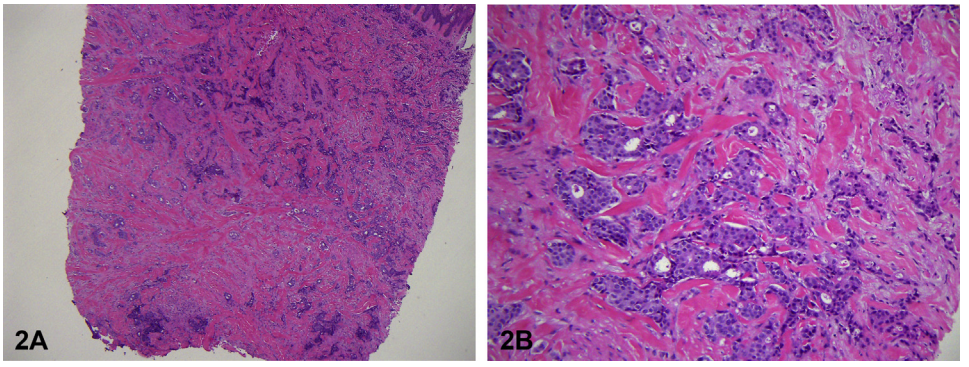

A 63-year-old man with a medical history significant for gynecomastia presented with concern of a new mole on the right nipple, present for approximately 1 year. The patient reported breast fullness and tenderness along with growth of the lesion without nipple discharge. Physical examination found a hyperkeratotic right nipple overlying a tender and indurated erythematous plaque with nipple retraction (Fig 1, *A* and *B*) compared with the uninvolved left nipple (Fig 1, *C*). Subsequent punch biopsy is represented in Fig 2, *A*.

Question 1: What the most likely diagnosis?

A. Nipple eczema

B. Male breast cancer

C. Gynecomastia

D. Pyogenic granuloma

E. Montgomery tubercles

Answers:

A. Nipple eczema — Incorrect. Nipple eczema is a term used to describe an underlying dermal perivascular lymphoid infiltrate localized to the nipple area. It can be caused by irritant/allergic contact dermatitis or a feature of atopic dermatitis. It presents as pruritic erythematous plaques on the nipple and may have scale, crust, oozing, and fissuring. Treatment is directed by the underlying etiology.

B. Male breast cancer — Correct. The most common clinical presentation of male breast cancer is a painless retroareolar mass. Although cutaneous manifestations are uncommon, involvement of the skin may be the first presenting sign. When the malignant cells involve the epidermis, the condition is termed *Paget disease of the breast*. Some early signs and symptoms include nipple retraction, ulceration, discharge, fixation to the skin or muscle, crusting, pruritus, edema, and pain.[1] The punch biopsy also shows invasive adenocarcinoma involving the dermis with perineural invasion.

C. Gynecomastia — Incorrect. Gynecomastia is the most common palpable breast mass, breast enlargement, or breast pain in men. Guidelines for imaging in the evaluation of breast masses in men without symptoms of gynecomastia are published by the American College of Radiology. Men younger than 25 should initially undergo ultrasonography for indeterminate masses on physical examination, followed by mammography for suspicious finding. In contrast, men older than 25 with questionable physical examination findings should undergo mammogram as the initial diagnostic test, with ultrasonography reserved for inconclusive or suspicious findings.[2]

D. Pyogenic granuloma — Incorrect. Pyogenic granuloma, or lobular capillary hemangioma, is an acquired benign vascular lesion that can affect either the skin or mucous membranes. Although the overall etiology is not completely understood, it often occurs in the setting of injury, hormonal factors, or certain medications. Lesions typically are small, glistening, yellow-to-bright-red, friable, dome-shaped papules that can rapidly grow. Treatment is through curettage of the base with removal of all abnormal tissue.

E. Montgomery tubercles — Incorrect. Montgomery tubercles are sebaceous glands that are found around the areola of the nipple. They can become enlarged and appear as flesh-colored papules. These are not a pathologic finding.

Question 2: What is the most accurate test for identifying a cutaneous malignancy of the breast?

A. Wedge biopsy

B. Potassium hydroxide scraping

C. Punch biopsy

D. Shave biopsy

E. Diascopy

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Answers:

A. Wedge biopsy — Correct. Histologic evidence of Paget cells (malignant intraepithelial adenocarcinoma cells) in single or small groups in the epidermis is required to establish a diagnosis of Paget disease. Wedge biopsy is the most sensitive method to establish a definitive diagnosis of Paget disease because the epidermis can be adequately sampled, and the biopsy is likely to include lactiferous ducts.[3] Staging workup is the same for both women and men and classified based on the tumor, node, and metastasis (TNM) staging system developed by the American Joint Committee on Cancer. Treatment options should be discussed between the patient, dermatologists, and oncologists, and can range from broad cytotoxic or targeted drug therapy, radiation, or surgery.

B. Potassium hydroxide scraping — Incorrect. A scraping is typically used to identify either fungal or scabies infections. For fungal infections, following a scraping, a drop of 10% to 20% potassium hydroxide would be added and examined for hyphae, budding yeast, or both under a microscope. For scabies, mineral oil would be added and examined for mites, feces, or eggs. It would not be beneficial in identifying a malignancy.

C. Punch biopsy — Incorrect. Although a punch biopsy will include underlying stroma and possible portions of lactiferous ducts, frequently, it will fail to sample enough epidermis to make a definitive diagnosis.[3]

D. Shave biopsy — Incorrect. Because of potential ulcerations, shave biopsies may not contain enough Paget cells to establish a diagnosis.[3]

E. Diascopy — Incorrect. Diascopy is used to test the vascularity of lesions. Typically, a clear material is pressed against a lesion to test its blanchability.

Question 3: What would be the worst prognostic factor in determining the outcome for this patient?

A. Low levels of MIB-1 expression

B. *HER2*/neu negativity

C. Younger age

D. Sentinel lymph node involvement

E. Overexpression of p27

Answers:

A. Low levels of MIB-1 expression — Incorrect. In female breast cancer, there have been several studies indicating that MIB-1 typically correlates with relapse-free survival, histologic grade, and mitotic figures. In male breast cancer, however, there has not been much literature on the topic, with one study showing that overexpression decreased progression-free survival. In other studies carried out in men, median overall survival was 73 months or 33 months according to whether MIB-1 expression was less than or greater than 23.5%, respectively. Therefore, lower levels of MIB-1 expression may actually be associated with a more favorable outcome.[4]

B. *HER2*/neu negativity — Incorrect. *HER2* negativity has been affiliated with worse prognosis outcomes when diagnosing female breast cancer. In men, however, there have been no definitive data for its overall prognosis. Although studies have found that HER2 positivity leads to an increased overall survival rate, other small studies have found no correlation between *HER2* status and survival. Therefore, this would not be a strong indicator of outcome.[5]

C. Younger age — Incorrect. In multiple studies, no correlation was ever established between young age of patients and clinical outcome.[5]

D. Sentinel lymph node involvement — Correct. Sentinel lymph node involvement is a poor prognosis outcome in both men and women with breast cancer. A sentinel lymph node is one of the first lymph nodes that a tumor with lymphatic involvement will drain into. A sentinel lymph node biopsy is performed to see the involvement of metastasis in regional lymph nodes and can determine if axillary lymph nodes need to be removed during a surgical resection of the tumor.

E. Overexpression of p27 — Incorrect. The expression of p27 protein has been associated with the number of cells that are in the S phase of mitosis. In women, multiple studies have found that that low p27 was a predictor of reduced disease-free survival. Although there have not been any studies of p27 in male breast cancer, a retroactive study found a strong correlation with reduced expression of p27 and lymph node metastasis.[4]

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