An erythematous nodule on the nipple

Joint Session Breast Pathology / Infectious Diseases Pathology

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Disclosures
- None
Patient’s History

• A 49-year-old male
• Stable sexual partner (MSM)
• Past medical history
  • Addison disease
  • Autoimmune thyroiditis
  • Type II diabetes mellitus
  • Dyslipidemia
• Consulted for pruritic nodule on his left nipple
Clinical Differential Diagnoses

- Erosive adenomatosis of the nipple
- Nipple eczema
- Paget disease
- Basal cell carcinoma
- Squamous cell carcinoma
Differential Diagnoses

- Nipple eczema
- Erosive adenomatosis of the nipple
- Paget disease
- Basal cell carcinoma
- Squamous cell carcinoma
- Cutaneous lymphoid hyperplasia
- Leishmaniasis
- Syphilis
Laboratory Studies

- VDRL titer >1:1024

- Fluorescent treponemal antibody absorption (FTA-ABS) IgM test was positive

- Screening for other sexually-transmitted diseases, including HIV infection, was negative
Final Diagnosis

• Primary syphilis of the nipple

Treatment

• 2.4 million units benzathine penicillin intramuscularly
Follow-up

- The nodule rapidly disappeared

- Three months later, the VDRL titer had decreased to 1:4

- His sexual partner had also tested positive for syphilis
Syphilis

- Remains a common disease worldwide
- 10-12 million new infections each year
- Re-emerged in western Europe
- Sexually transmitted disease
- Spirochete bacterium Treponema pallidum
- Humans: natural hosts
- Transmission: direct contact with an infectious mucocutaneous lesion

The Stages of Syphilis

Primary

The chancre lesion is the hallmark of primary syphilis. It may appear 10-90 days after exposure. Common sites include penis and labia. Other sites include anus, oral mucosa. Without treatment, chancre disappears in 2-8 weeks.

Secondary

Rash, pink to brown macules. Involves palms/soles in 50% of cases.

Oral lesions called "mucous patches" resembling snail tracks.

Symptomatic early neurosyphilis, cranial nerve deficits and/or aseptic meningitis presentation.

Ocular syphilis manifestations including anterior or posterior uveitis.

Genito-inguinal rashes, including tinea-mimicker or heaped-up wart-like lesions called condyloma lata.

Latent

Latent syphilis refers to asymptomatic infection after the period of primary and secondary syphilis (noticed or unnoticed) has passed.

Early Latent

Early latent refers to asymptomatic patients with positive testing, in whom history can confirm exposure to or symptoms of primary or secondary syphilis within the last year. This is group may receive single-dose penicillin like primary or secondary.

Late Latent

Late latent patients have positive serology but do not meet criteria for early. Thus, multiple doses of penicillin.

Late (Tertiary)

Late Neurosyphilis, including tabes dorsalis, gait impairments, and dementia. Tabes dorsalis damages the dorsal columns and sensory nerve roots, causing a syndrome of pain and sensory deficits similar to those of B12 deficiency.

Gumma are ulcerating granulomas on skin, bone, and internal organs.

Cardiovascular effects of late syphilis include aortic aneurysm and coronary arteritis.
Primary Syphilis

• Hallmark: The **chancre** lesion

• 9-90 days after exposure

• An indurated and painless genital ulcer

• Common sites include labia, anus, oral mucosa

• Atypical presentation, especially at extragenital locations
# Primary Syphilis of the Nipple

<table>
<thead>
<tr>
<th>Study</th>
<th>Age (Y)</th>
<th>Sexual Orientation</th>
<th>Nipple trauma</th>
<th>Clinical presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al</td>
<td>54</td>
<td>HSM</td>
<td>Yes</td>
<td>Swelling of nipple</td>
</tr>
<tr>
<td>Lee et al</td>
<td>24</td>
<td>HSM</td>
<td>Yes</td>
<td>Erosive change of the nipple</td>
</tr>
<tr>
<td>Oh et al</td>
<td>47</td>
<td>HSM</td>
<td>Yes</td>
<td>Indolent ulcer covered with a crust</td>
</tr>
<tr>
<td>Sim et al</td>
<td>56</td>
<td>HSM</td>
<td>Yes</td>
<td>Erythematous erosive patch with ipsilateral lymphadenopathy</td>
</tr>
<tr>
<td>Chiu et al.</td>
<td>27</td>
<td>HSM</td>
<td>Yes</td>
<td>Asymptomatic crusted plaque</td>
</tr>
<tr>
<td>Yu et al.</td>
<td>36</td>
<td>NA</td>
<td>Yes</td>
<td>Asymptomatic erythematous, crusted and erosive patch with several pustules</td>
</tr>
<tr>
<td>Zheng et al.</td>
<td>36</td>
<td>HSM</td>
<td>Yes</td>
<td>Asymptomatic scaly erythematous patches on both areolas with eroded nipples</td>
</tr>
<tr>
<td>Fukuda et al.</td>
<td>29</td>
<td>MSM</td>
<td>Yes</td>
<td>Indurated, scaly, erythematous lesion with erosion and lymphadenopathy</td>
</tr>
<tr>
<td>Tan; Gan</td>
<td>20</td>
<td>MSM</td>
<td>Yes</td>
<td>Well-demarcated indurated painless ulcer</td>
</tr>
<tr>
<td>Qiao et al</td>
<td>39</td>
<td>NA*</td>
<td>Yes</td>
<td>Asymptomatic ulcer</td>
</tr>
<tr>
<td>Present case</td>
<td>49</td>
<td>MSM</td>
<td>NA</td>
<td>Well-demarcated erythematous eroded nodule</td>
</tr>
</tbody>
</table>

HSM=heterosexual men; MSM=men who have sex with men; NA=not available; *Female
Transmission

• Oral contact (a chancre in the oral mucosa or tongue)

• Active or latent secondary syphilis (minor trauma oral mucous membrane)
Take-home message

• Primary syphilis = solitary nodule of the nipple

• Male

• Morphology
  - Epidermal hyperplasia + Lichenoid reaction pattern with abundant plasma cell (hallmark)
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Thank you
## Table 1. Patients with primary syphilis involving the nipple

<table>
<thead>
<tr>
<th>Study /Year</th>
<th>Patients</th>
<th>Mechanism of contagion</th>
<th>Clinical presentation</th>
<th>Epidermis</th>
<th>Histopathology</th>
<th>Dermis</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al./2006</td>
<td>2</td>
<td>Bitten on the nipple</td>
<td>Patient 1: erosive lesion Patient 2: swelling of nipple</td>
<td>Parakeratosis, infiltration of small lymphocytes, neutrophils and vacuolar alteration of basal cells with scattered necrotic keratinocytes</td>
<td>Dense, superficial and deep perivascular and periadnexal infiltrate of lymphocytes, histiocytes, plasma cell and occasional neutrophils with an angioinvasive pattern</td>
<td>Resolution</td>
<td></td>
</tr>
<tr>
<td>Oh et al./2008</td>
<td>1</td>
<td>Bitten on the nipple</td>
<td>Indolent ulcer covered with a crust</td>
<td>Focal parakeratosis, and partially damaged dermoepidermal junction</td>
<td>Inflammatory infiltrate in the upper part of the dermis and periadnexal area. On high-power view lymphocytes, histiocytes, and many plasma cells around the blood vessels</td>
<td>Resolution</td>
<td></td>
</tr>
<tr>
<td>Sim et al./2010</td>
<td>1</td>
<td>Bitten on the nipple</td>
<td>Erythematous erosive patch with ipsilateral lymphadenopathy</td>
<td>Epidermal hyperplasia</td>
<td>Dense perivascular and periadnexal infiltrate with a slightly nodular pattern. At high power, dense infiltration of lymphocytes and plasma cells</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Chiu et al./2012</td>
<td>1</td>
<td>Bitten on the nipple</td>
<td>Asymptomatic crusted plaque</td>
<td>Epidermal hyperplasia with focal ulceration</td>
<td>Dense lichenoid infiltrate composed of lymphocytes, plasma cells, histiocytes around dermoepidermal junction and perivascular areas</td>
<td>Resolution</td>
<td></td>
</tr>
<tr>
<td>Yu et al./2012</td>
<td>1</td>
<td>Bitten on the nipple</td>
<td>Asymptomatic erythematous, crusted and erosive patch with several pustules</td>
<td>NA</td>
<td>Interstitial inflammatory cell infiltration with prominent endothelial cell swelling, admixture of lymphocytes, histiocytes, neutrophils and plasma cells</td>
<td>Resolution</td>
<td></td>
</tr>
<tr>
<td>Zheng et al./2014</td>
<td>1</td>
<td>Bitten on the nipple</td>
<td>Asymptomatic scaly erythematous patches on both areolas with eroded nipples</td>
<td>Eroded and focally ulcerated epidermis Focal smudged dermoepidermal junction</td>
<td>Diffuse and dense infiltrates composed of lymphocytes, prominent plasma cells and sparse neutrophils</td>
<td>Resolution</td>
<td></td>
</tr>
<tr>
<td>Present case</td>
<td>1</td>
<td>NA</td>
<td>Well-demarcated erythematous eroded nodule</td>
<td>Pseudoepitheliomatous epidermal hyperplasia</td>
<td>Dense inflammatory infiltrate in superficial and reticular dermis, composed by lymphocytes, histiocytes and abundant plasma cells. Prominent endothelial swelling and focally extravasated erythrocytes and hemosiderophages</td>
<td>Resolution</td>
<td></td>
</tr>
</tbody>
</table>
Treponema pallidum

- Coiled, motile spirochaete bacterium
- Humans are its only natural host
- Genome sequenced, very small, circular
- Obligate parasite (limited metabolic capabilities)
- No in vitro culture