Disclosures
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Dr. Jeff Simko has disclosed that he receives travel reimbursements and that his institution (UCSF) receives cash and/or equity for his role as consultant, advisor and/or speaker for the following commercial interests: Genomic Health, Inc.; GenomeDX; 3D Biopsy, Inc. and 3 SCan, Inc. The planners have determined that these financial relationships are not relevant to the case being presented and does not present a conflict of interest.

The following planners and faculty had no financial relationships with commercial interests to disclose:

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Activity Planners:  
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Ankur Sangoi, MD
SB 6061

Greg Rumore; Kaiser Walnut Creek
48-year-old woman with history of Hashimoto’s thyroiditis and papillary thyroid carcinoma, discovered left parotid mass 1 month ago. Asymptomatic.
DIAGNOSIS?
Acinic Cell Adenocarcinoma
Acinic Cell Adenocarcinoma

- Malignant neoplasm demonstrating serous acinar differentiation
- 2\textsuperscript{nd} most common salivary gland carcinoma (17%)
- Most frequent bilateral carcinoma
- 80% parotid, 17% minor, 4% submandibular, <1% sublingual
- Women slightly > men
Micro

• Solid, microcystic, papillary-cystic, and follicular patterns
• Large cells with granular, lightly basophilic cytoplasm
• Intercalated duct cells, vacuolated cells may also be seen
Cytology

- Typically cellular smears-large cells with granular cytoplasm resembling normal acini
- Absence of ductal cells or fat
- Nuclei centrally located, usually bland
- Naked nuclei may be confused with lymphocytes
SB 6062

Greg Rumore; Kaiser Walnut Creek

90-year-old female with slow growing left parotid mass for many years.
DIAGNOSIS?
Dx: Basal Cell Adenocarcinoma, Parotid
Basal Cell Adenocarcinoma

• Malignant counterpart of Basal Cell Adenoma
• Separated by infiltrative growth pattern
• 80% parotid gland
• 2 cell types- larger eosinophilic cells with pale nuclei and smaller cells (peripheral) with darker nuclei
• Solid, membranous, trabecular and tubular(rare) patterns
• Squamous differentiation focally
Differential Diagnosis

- Basal Cell Adenoma
- Adenoid Cystic Carcinoma (especially solid type)
- Basaloid Squamous Cell Ca.
### DDX of Basaloid Neoplasms

<table>
<thead>
<tr>
<th></th>
<th>Basal Cell Adenoma</th>
<th>Basal Cell Adenoca</th>
<th>Adenoid Cystic Ca. (solid type)</th>
<th>Basaloid SCCa</th>
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<tbody>
<tr>
<td>Mitoses (&gt;3/10hpf)</td>
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<td>+/-</td>
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<td>Necrosis</td>
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<td>Invasion</td>
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<tr>
<td>Angular Nuclei</td>
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<td>-</td>
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<tr>
<td>Peripheral Palisading of Nuclei</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
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<td>Squamous Differentiation</td>
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<td>-/+</td>
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<td>++</td>
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<tr>
<td>Surface Epithelial Location</td>
<td>-</td>
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</tbody>
</table>
Cytologic Features

- Small cells with scant cytoplasm and round to ovoid nuclei
- Sheets, branching structures, tubules
- Peripheral palisading of nuclei
- Spherical globules surrounded by tumor cells
- Overlap with adenoid cystic carcinoma
Mahendra Ranchod; Good Samaritan Hospital

63-year-old man with cachexia and vague abdominal symptoms. Upper GI performed to r/o malignancy.
DIAGNOSIS?
Why share this case?

- Classical example of a rare disease
- Diagnosis can be made with simple conventional histochemical stains (H&E and PAS-D)
- We can confirm the diagnosis with PCR
- Important to recognize Whipple’s disease and treat promptly
How we made the diagnosis

PAS-positive macrophages in L.P. of duodenum

Clear spaces in L.P.

Stains negative for fungi and AFB

PCR positive for Tropheryma whipplii
Whipple’s disease

• Systemic infection by Gram + coccobacillus
• Major symptoms related to:
  • Small intestine
  • Synovium
  • Heart
  • Brain
Whipple’s disease

- Impaired host reaction to bacterial infection but not reported in HIV patients
- 35% of healthy adults have T. whipplii in saliva
- High mortality when diagnosis delayed
- 2-4 wks I.V antibiotics followed by oral antibiotics for 1 year.
- High relapse rate with short courses of treatment
Liz Treynor; Washington Hospital
55-year-old deceased male with h/o HTN, ESRD, MSSA endocarditis s/p valve replacement, Mycoplasma pneumonia, and C. Difficile colitis in months prior to demise from intracranial bleed. After declared brain dead and donation authorized, Donor Network on screening found Hep B core + Hep C + serology, but Hep B and Hep C PCR negative, and requested frozen section prior to organ recovery.
DIAGNOSIS?
Dx:

<table>
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<td>Arterial Intimal thickening:</td>
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<tr>
<td>Absent</td>
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<tr>
<td>Mild</td>
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<tr>
<td>Moderate</td>
<td>□</td>
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<tr>
<td>Severe</td>
<td>□</td>
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</table>

| Hyaline arteriolosclerosis: | |
| Absent | □ |
| Mild  | □ |
| Moderate | □ |
| Severe | □ |

| Tubulointerstitial area: | |
| Atrophy | Absent | □ |
| Inflammation | Absent | □ |
| Fibrosis | Absent | □ |

| Additional Findings: | |
| Liver Section | |

- Fat droplet filling >1/2 of the cell and/or displaces nucleus, recommendation to estimate % volume on 4 or 10x.
- Small droplet fat—single to several fat droplets each <1/2 of the cell, doesn’t displace nucleus

<table>
<thead>
<tr>
<th>Liver Section</th>
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</thead>
<tbody>
<tr>
<td>% volume</td>
<td>0 %</td>
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<tr>
<td>Est. small droplet fat (% of cells)</td>
<td>0 %</td>
</tr>
<tr>
<td>Estimated total fat</td>
<td>0 %</td>
</tr>
</tbody>
</table>

- Thick band has large vessels so septum not periportal fibrosis in my opinion
- Activity: 0 1 2 3 4
- Is this a frozen section? Yes □ No □
Our Role in Organ Donation

Harvest Frozen is critical, given time constraints:

- Lung expires in 4 hours; liver in 8 hours
- Proper patient allocation takes several hours
- Mismatched organ-- and potentially patient-- may be lost

As hospital-contracted physicians, we are legally obligated to help the Donor Network, as well as protected legally.

Donor Pathologist does not determine suitability; only describes findings
Donor Liver Frozens

Most healthy donors do not need frozen section

Request gross appearance & history

Request background liver if biopsy is a lesion (FNH vs. cirrhosis)

Request fresh, no-gauze, un-soaked tissue to avoid artifacts:

  Gauze/Air Drying:
    Underestimate fat

  Saline droplets in tissue:
    Overestimate fat
    Hide necrosis

Frozen Last Week
Macrovesicular Steatosis
Single fat droplet filling > half of cell and/or displacing nucleus

Usually centrilobular (unless >60%)

*Microvesicular: OK

**Mild <30% : OK

****Moderate 30-60%: ????? (13% primary non-function in one study)

*****Severe >60%: Contraindicated for transplant

High risk of ischemic/reperfusion injury

Lysed fat blocks hepatic microcirculation

MMM--Other Causes for Organ Deferral

• **Malignancy** (but CNS malignancies are ok!)

• **More than Mild:**
  – Necrosis >10%
  – Fibrosis > or = stage 2
  – Activity > or = grade 2
I-OK for Transplant

- **Mic**rovesicular **Steatosis** (common warm ischemic change)

- **Iron** (recipient can metabolize excess)

- **Mononuclear Portal Inflammation**, if viral tests **neg**
  (common ICU change)
Take Home Message

Harvest Frozen is important, given time constraints

As hospital-contracted physicians, we are legally obligated to help the Donor Network, as well as protected legally

Donor Pathologist does not determine suitability; only describes findings
SB 6065

Vanessa Ma/Jeffry Simko; UCSF

57-year-old male with a 0.6cm left parotid mass for 6 months.
DIAGNOSIS?
Intra-ductal carcinoma (IDC), low grade

- First described by Chen 1983
- Pure ductal carcinoma in situ in salivary glands
- May exhibit low, intermediate, or high cytologic grade
- Criteria
  - A tumor resembling mammary intraductal carcinoma with cribriform, micropapillary, solid, comedo, or clinging patterns
- A complete myoepithelial layer around tumor cells
  - Specific to IDC
Low grade cribriform cystadenocarcinoma (LG-CCC)

- Low grade salivary gland carcinoma (LG-SDC), first described by Delgado in 1996
- A variant of cystadenocarcinoma
- Cystic predominant intraductal proliferation and low grade histology
  - Resemble breast from ADH and DCIS
- Architecture
  - Cystically dilated ducts
  - Pseudocribriform /cribriform architecture with "Roman Bridges"
  - Solid areas
- Ductal epithelium
  - Bland with heterogeneous morphology
  - Apocrine-type cytoplasmic microvacuoles
  - Golden brown pigment, PAS+, resemble lipofuscin
- Complete myoepithelial layer around tumor cells
- Ductal phenotype: keratins (+), S100 (+), Her2(-)
Low grade cribriform cystadenocarcinoma (LG-CCC)

- Older patients (mean = 62 yr), F:M=2:1
- Parotid predominantly
  - Superficial and deep lobes
- Other site
  - Palate, submandibular gland, intraparotoid LN, accessory parotid gland
- Slow growing cystic mass
- Tumor size: 0.9 to 4 cm
- Clinical indolent
  - ~20% cases with invasion
  - No perineural or vascular invasion
  - Surgical resection w/o radiation
<table>
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<tr>
<th>No.</th>
<th>Author</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Anatomic location</th>
<th>Size (cm)</th>
<th>Histological type (single cyst / multiple cysts)</th>
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<td>Minor salivary gland in the buccal mucosa</td>
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</table>
• Given that most LG-SDC are non-invasive neoplasms; the terms "cribriform cystadenocarcinoma" and LG-SDC should be replaced by “low-grade intraductal carcinoma" (LG-IDC) of salivary gland” or "low-grade intraductal carcinoma with areas of invasive carcinoma" in those cases with evidence of invasive carcinoma.

Cytology of LGCCC

- Pseudopapillary clusters comprising mucus-producing cells
- Arranged in irregular overlapping clusters
- Inconspicuous nuclear atypia
- Variable-sized and irregular shaped cytoplasmic vacuoles
- MGG stain smears
  - Fine metachromatic cytoplasmic granules
- Background
  - Cystic changes
  - No necrosis or mucin
- DD
  - Acinic cell carcinoma
    - Cytoplasmic vacuoles tend to be uniform
  - Mucoepidermoid carcinoma
    - Squamoid cells and mucous-like vacuolated cytoplasm
Acinic carcinoma

• Esp. papillary cystic variant
• More common microcystic growth pattern
  – No predominant intraductal component
  – No cribriform
• Zymogen granules
  – PAS +/PASD +
• Expressed DOG1 diffusely in a canalicular pattern
• S100 negative
Mammary analog secretory carcinoma (MASC)

- Predominantly an extraductal neoplasm
- Bubbly pink cytoplasm
- Robust expression of mammaglobin and S100
  - MUC-4 +
- Molecular
  - t(12;15) \textit{ETV6-NTRK3} fusion gene
  - ETV6 rearrangement
Take home message

• LG-CCC/LD-SDC/LG-IDC
• Intraductal proliferation
• Bland ductal cells in cribriform
  – Resemble Low grade breast
  – Focal invasion
• Indolent clinical behavior
• No association with conventional SDC
• DD
  – Acinic carcinoma
  – MASC
References


SB 6066

Vanessa Ma/Richard Jordan; UCSF

45-year-old male with a 2.3cm left parotid mass for 3-4 months.
DIAGNOSIS?
Her2
Mammaglobulin
Salivary duct carcinoma, in situ (SDCIS) (high grade intraductal carcinoma of salivary gland, (HG-IDC) with focal invasion

- Duct proliferative architecture
- High nuclear grade
- Presence of necrosis
- AR, HER2, GCDFP positive
- S100 either negative or partial positive
Salivary duct carcinoma (SDC)

- De novo or ex-PA
- Older people over 50 year-old
- M:F =4:1
- High grade
  - Resemble intraductal and infiltrating mammary duct carcinoma
- Comedo necrosis and cribriform proliferation
- Variant
  - Micropapillary, sarcomatoid, mucin-rich and basal-like
- Apocrine morphology
  - AR (+) and GCDFP-15 (+)
  - S100 (-)
- High Ki-67
- Early lymph node metastasis, local recurrence and high mortality
- Surgical resection
  - radiotherapy and/or chemotherapy
  - Anti-ERBB2 antibodies and androgen deprivation therapy
**TABLE 2. Distinctions Between High-Grade Salivary Duct Carcinoma, Low-Grade Salivary Duct Carcinoma, and Papillocystic Acinic Cell Carcinoma**

<table>
<thead>
<tr>
<th></th>
<th>High-Grade Salivary Duct Carcinoma</th>
<th>Low Grade Salivary Duct Carcinoma</th>
<th>Papillocystic Acinic Cell Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Architecture</td>
<td>Cribriforming, with round “stiff” spaces, solid, papillary with psammoma bodies</td>
<td>Pseudocribriform spaces with “floppy” or fenestrated slit-like, solid intraductal sheets of cells, or intraductal papillae with fibrovascular cores</td>
<td>Cystic, with fine papillae also follicular and microcystic</td>
</tr>
<tr>
<td>Necrosis</td>
<td>Yes</td>
<td>Rare</td>
<td>No</td>
</tr>
<tr>
<td>Calicification</td>
<td>Yes</td>
<td>Yes</td>
<td>Occasional</td>
</tr>
<tr>
<td>Mitosis</td>
<td>Frequent</td>
<td>Rare</td>
<td>Variable</td>
</tr>
<tr>
<td>Cellular composition</td>
<td>Monomorphic, epithelioid, squamous, oncocytoid</td>
<td>Heterogeneous ductal, apocrine, vacuolated; myoepithelial cells at periphery</td>
<td>Heterogeneous serous, intercalated ductal, oncocytoid, myoepithelial</td>
</tr>
<tr>
<td>Nuclei</td>
<td>Moderate to high grade, round to oval</td>
<td>Oval, low-grade, condensed chromatin</td>
<td>Peripheral, condensed chromatin, low to moderate grade</td>
</tr>
<tr>
<td>Cytoplasm</td>
<td>Powdery to bright eosinophilic, usually abundant</td>
<td>Pale to bright eosinophilic</td>
<td>“Bubbly,” variable from basophilic to clear to eosinophil</td>
</tr>
</tbody>
</table>

The next WHO classification should abandon “salivary duct carcinoma”

Conventional salivary duct carcinoma should be classified as “high-grade salivary duct carcinoma”

Low-grade salivary duct carcinoma should replace the current nosology of “low-grade cribriform cystadenocarcinoma”

Cystadenocarcinoma should be classified with the descriptor “Not Otherwise Specified” and should be considered an exclusionary diagnostic category

Reference


SB 6067

Chieh-Yu Lin/Megan Troxell; Stanford
47-year-old woman with breast mass.
DIAGNOSIS?
Additional history

• The patient has a lung mass and a positive OctreoScan in the right lower quadrant of the abdomen.

• There are two separate right breast masses, with similar histological features.
Differential diagnosis

• Primary breast neuroendocrine tumor?
• Metastatic neuroendocrine tumor? From lung? From GI tract?
Immunohistochemical stains

Synaptophysin/Chromogranin positive

Neuroendocrine tumor

CK7 positive; CK20 negative

Breast
- ER
- GCDFP-15
- Mammaglobin
- All negative

Lung
- TTF-1 positive
- Napsin negative

GI
- CDX2 negative
# Neuroendocrine: Breast vs. Met

<table>
<thead>
<tr>
<th>Stain</th>
<th>Breast</th>
<th>GI (met)</th>
<th>LUNG (met)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER</td>
<td>54/56 (96%)</td>
<td>1/11 (9%) weak</td>
<td>1/5 (20%) weak</td>
</tr>
<tr>
<td>PR</td>
<td>49/56 (88%)</td>
<td>0/11 (0%)</td>
<td>0/5 (0%)</td>
</tr>
<tr>
<td>GCDFP</td>
<td>24/56 (43%)</td>
<td>0/10 (0%)</td>
<td>0/4 (0%)</td>
</tr>
<tr>
<td>Mamma</td>
<td>26/56 (46%)</td>
<td>0/10 (0%)</td>
<td>0/4 (0%)</td>
</tr>
<tr>
<td>CDX2</td>
<td>0/40 (0%)</td>
<td>11/11 (100%)</td>
<td>0/4 (0%)</td>
</tr>
<tr>
<td>TTF-1^^</td>
<td>0/47(0%)</td>
<td>0/10 (0%)</td>
<td>3/5^ (60%)</td>
</tr>
<tr>
<td>CK7</td>
<td>37/49 (92%)</td>
<td>0/10 (0%)</td>
<td>3/5 (60%)</td>
</tr>
<tr>
<td>CK20</td>
<td>0/40 (0%)</td>
<td>0/10 (0%)</td>
<td>0/5 (0%)</td>
</tr>
</tbody>
</table>

Take Home message

• Panels of immunohistochemical stains to distinguish breast primary vs metastatic neuroendocrine tumor
• History, history, history
SB 6068

Chieh-Yu Lin/Megan Troxell; Stanford

44-year-old woman with biopsy-proven HG DCIS undergoes mastectomy.
DIAGNOSIS?
Myoepithelial markers

- Calponin
- p63
- SMHC
Diagnosis

• Low grade adenosquamous carcinoma
• High-grade DCIS
Low Grade Adenosquamous CA

• Variant of metaplastic carcinoma
• Small round to comma shaped to compressed glands in dense collagenized stroma
  – Low grade cytology, rare mitosis
  – Varying degrees of squamous differentiation
  – May have lymphs/lymphoid aggregates at periphery
  – May infiltrate between normal structures
• May mimic benign sclerosing lesions on core biopsies
• Triple negative but with good prognosis
Low grade adenosquamous carcinoma
Variable myoepithelial staining

- ‘Cuffing’ or lamellar pattern
- Complete, discontinuous or absent around glands
- “Consistently inconsistent”
- Epithelial component may stain with p63 (squamoid, bottom R)

Kawaguchi and Shin. AJSP. 2012; 36:1009-20
Differential diagnosis

- Adenoid cystic carcinoma
- Malignant myoepithelioma
- Malignant adenomyoepithelioma
- Tubular carcinoma
- Radial scar/sclerosing adenosis
- Microglandular adenosis
Take home message

• Low-grade adenosquamous carcinoma, a variant of metaplastic carcinoma, exhibit indolent disease course.

• Recognition of this rare but distinct entity is important for clinical management.
Nabeen Nayak; Sir Ganga Ram Hospital, New Dehli
36-year-old man with abdominal pain and fever x 3 months, honeycomb cystic lesions identified in liver by CT scan. Left hepatectomy performed.
DIAGNOSIS?
Multiple serial sections failed to reveal any additional findings as well as any infective agents including parasites.

Acid Fast Stain, stains for Fungi and for Microbes were all negative.

The CT images shown below along with the clinical data and the gross features of this necrotizing granulomatous lesion, however strongly suggested hepatic Visceral Larva Migrans (VLM) due to Toxocariasis,

Diagnosis: Visceral Larva Migrans – Liver, left lobe
A serodiagnostic ELISA test for antibody against Toxocaris excretory/secretory antigen done subsequently showed fairly strong reactivity.

Confirmatory Western Blot test was however not carried out.

This patient had no peripheral blood Eosinophilia, nor Eosinophilic Abscesses in the liver lesion which are common in VLM and helpful in a histologic diagnosis, as in a second case (16-yr-old girl had abdominal pain).
Visceral Larva Migrans (VML) is an inflammatory tissue lesion caused by migratory larvae of some animal Nemathelminths, humans being a dead end host. This zoonotic infection, mostly by the Toxocara species and generally acquired in early childhood, is globally prevalent with frequencies varying from low 2-16% in developed countries to high 40-80% in the developing countries.

**Infection** being generally mild to moderate and the host being a dead end one, more than 60% cases are asymptomatic and clinically inapparent. The disease therefore appears rare.

**Detection** is either incidental or when the infection is very heavy with large lesions causing significant symptoms.

**Imaging** diagnosis accuracy is about 45% (Trop. Parasitol. 2016, Jan-June;6(1):56-68) – from a Tertiary Liver Center, New Delhi

**Histologic confirmation** can be assisted by IHC for Toxocara Larval Antigen (TCLA) in lesional macrophages.
SB 6070

Nupoor Gajjar; Kaiser Walnut Creek

76-year-old female with new splotchy non-blanching erythema in patient on carboplatin and Taxol for ovarian cancer. Concern for leukocytoclastic vasculitis from chemotherapy versus inflammation of seborrheic keratosis or actinic keratosis with chemotherapy.
DIAGNOSIS?
Case 10

- Ovarian serous carcinoma with metastases to peritoneum, bone, and pleura
- Neoadjuvant chemotherapy carboplatin and paclitaxel
- Week 3 developed non-blanching erythematous macules on bilateral upper and lower extremities and torso
Acute cytotoxic interface dermatitis secondary to chemotherapy

- Histologic alteration caused by chemotherapy or radiation therapy
- Some manifestations can be dose dependent
- May primarily involve palms and soles—acral erythema—more likely dose dependent
- Dyskeratosis or ‘maturation arrest’
Acute cytotoxic interface dermatitis secondary to chemotherapy

- Interface dermatitis with vacuolar change
- Keratinocytes with abundant cytoplasm and enlarged or bizarre nuclei at all levels
- Mitotic arrest with ringed or starburst mitotic figures
- Lack of orderly maturation to granular layer
- Dyskeratotic keratinocytes
Acute cytotoxic interface dermatitis secondary to chemotherapy

- GVHD
  - Lacks cytologic atypia
  - Keratinocytes mature
Acute cytotoxic interface dermatitis secondary to chemotherapy

- Paclitaxel was discontinued
- Patient switched to Carboplatin/Docetaxel
- No new rashes; older lesions resolved after two weeks