31st European Congress of Pathology, Nice, 2019

**Slide seminar joint session** of the Working group for infectious diseases and the Breast Working Group

**Infections of the breast, case 6**

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50-year old woman.
- Asymptomatic.

Clinical history:
- M. Bechterew adequate treatment.
- Varicella
- Borrelia.
- In 2017 suspicion of TBE (tick borne encephalitis) was raised but could not be proved.
Mammography routine screening July 2017
Mammography routine screening November 2018
Breast MRI showed numerous 2-3 mm masses in both breasts.
At this stage suspicion of hematogenous spread was raised.

Core needle biopsy was performed via ultrasound.
Ultrasound guided core-needle biopsy
ECP Slide Seminar: Infections of the breast, case 6

Three core biopsies examined with H-E.
The core needle biopsy showed tightly packed epithelioid granulomas.
- High power view showed densely packed epithelioid granulomas without necrosis.
- Multinucleated giant cells were present.
- No neutrophils could be seen.
Granulomas can be seen in many different diseases in the breast

- Rheumatic disorders.
- Infectious diseases.
- Granulomatous lobular mastitis.
- Foreign body reaction.
- Associated with carcinoma.
- Cause masses mimicking cancer.
Special stains to exclude fungal infection and bacterial infection.

- PAS
- GIEMSA
Negative staining: PAS and Giemsa

Ziehl Neelsen control slide

Ziehl Neelsen negative staining
Clinical history:
Suspicion for TBE (tick borne encephalitis) by Rickettsia had been raised but could not be proved.
Detection of rickettsia with immunohistochemistry, **specific anti-rickettsial rabbit antiserum**


The authors thank prof Kenneth Nilsson for microbiological confirmation of the findings
Anti Rickettsia immunohistochemistry
The etiology of the lesions was further confirmed with DNA-extraction and PCR.

DNA from de-paraffinized tissue sections, using the QIAamp DNA Mini Kit (Qiagen GmbH, Hilden, Germany), and DNA was eluted into a final volume of 50 μl, according to the manufacturer’s instructions. The real-time PCR assay was performed in a Rotor-Gene 3000 (Corbett Research, Sydney, Australia) using LC Taqman Master kit (Roche, France) using a for spotted-fever-Rickettsia genus-specific realtime PCR with probe and primers targeting the gltA-gene, as previously described.

Rickettsia DNA was identified in 4 of 7 tissue sections with cycle threshold (Ct) values ranging between 35-39. Sequencing was attempted but failed on all four samples.

Reference:
- All known Rickettsia are zoonotic being transmitted to humans via an animal vector.

**Arthropods:**
- Ticks, lice, fleas and mites.
- Belong to Rickettsia family and are obligate intracellular.
- Gramnegative bacteria.
History
- Rickettsia first described by Howard Ricketts.
- 3 larger groups:
  - Tick borne Rickettsia with more than 20 types.
  - Epidemic spotted fever group with 2 species (R. typhi, R prowazeckii.)
  - Ancestor group R. Canadensis and R. bellii.
Tick borne diseases are increasing. Newest summary of Center of Disease Control indicates that tickborne infections have doubled in US between 2004 and 2016 from 22527 to 48610.
<table>
<thead>
<tr>
<th>Reported Tickborne Diseases, US</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lyme disease (confirmed and probable)</td>
<td>36429</td>
<td>42743</td>
</tr>
<tr>
<td>Anaplasmosis and ehrlichiosis</td>
<td>5750</td>
<td>7718</td>
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<tr>
<td>Spotted fever rickettsiosis&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4269</td>
<td>6248</td>
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<tr>
<td>Babesiosis</td>
<td>1910</td>
<td>2368</td>
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<tr>
<td>Tularemia</td>
<td>230</td>
<td>239</td>
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<tr>
<td>Powassan virus</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>48610</td>
<td>59349</td>
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</tbody>
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<sup>a</sup> Includes *Rickettsia rickettsii*, *R parkeri*, *R species 364D*.

Patient underwent a full course of antibiotic medicine with Tetracycline.
Follow-up mammography in February 2019: effect of tetracycline therapy
Follow-up in July 2019: No abnormality in the breasts and axilla
16 months earlier

November 2018

Control 3 months later
Corebiopsy after treatment was performed.

New core biopsy showed only normal breast tissue.

New PCR for sequencing and subtyping for the agent.
A single case report of tsutsugamushi disease in south western Shikoku. A 64-year-old male with fever and headache and an eschar on the right anterior side of the breast and an enlargement of the right axillary lymph node. The causative agent was *Rickettsia tsutugamushi*. (Article in Japanese, Yamauchi H et al. Kansenshogaku Zasshi. 1995 Jul;69(7):840-3)

Occasional positivity of the specific serum-agglutination for the Rickettsia Q18 (2 cases out of 11) was mentioned in connection to Mondor’s disease (Article in French, Bartolo M et al. J Mal Vasc. 1983;8(3):253-6.)
Core biopsy after treatment was performed.
- Numerous 2-3 mm lesions spread throughout both breasts.
- Predominantly located in subcutaneous tissue.
- Slightly enlarged lymphnodes more likely to present reactive changes.
- ”De novo finding” since previous mammography screening.
Corebiopsi after treatment was performed

- New core biopsies showed only normal breast tissue.
- New PCR for sequencing and subtyping of the agent.