The case I will never forget – CASE 6

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Clinical details

- a 54-year-old female patient
- poorly circumscribed palpable tender lump in her left breast
- mammography - stellate lesion, 20 mm
- core-needle biopsy non-diagnostic
- imaging results - patient operated on (lumpectomy)
Gross features

- solid
- firm
- uncircumscribed
- irregularly shaped tumor
- infiltrating into surrounding tissue
- 20 mm in largest diameter
Histological features - summary

- variable cellularity (hypocellular/hyalinized scar-like areas)
- hypercellular areas - spindle shaped cells of fibroblastic appearance
- storiform pattern, infiltration among lobules and into fat tissue
- slight cellular atypia
- no necrosis
- chronic inflammation, germinal centers, numerous plasma cells
- phlebitis of small veins with obliteration of the lumen
**IHC summary**

- **Negative:**
  - cytokeratins (both AE1/3 and HMW), p63, CD34, desmin, S100, beta catenin and ALK

- **Positive:**
  - Ki67 > 30%
  - IgG4 - up to 150 IgG4+ plasma cells/HPF
IgG4-related mastitis
IgG4-related (sclerosing) disease

• first described in pancreas (1995)
• systemic disorded (liver, salivary gland, lymph nodes, mesentery, breast, thyroid)
• increased serum IgG4 levels + mass-forming lesions
• fibrosis and dense lymphoplasmacytic infiltrate
• increased IgG4-positive plasma cells

• in breast - suspicious radiographic features
IgG4 related disease – diagnostic criteria

- tumor-like lesion
- storiform fibrosis
- focal hyalinization, infiltrating into surrounding tissue
- obliterative phlebitis
- lymphoplasmocytic infiltrate
- IgG4:IgG >40%
- IgG4+ plasma cells >50/HPF
- (eosinophils)
<table>
<thead>
<tr>
<th>Case</th>
<th>Age/Sex</th>
<th>Symptoms</th>
<th>Tissue specimen</th>
<th>Other system involvement</th>
<th>Serum IgG4 (normal value)</th>
<th>IgG4+ cells</th>
<th>IgG4/IgG ratio (%)</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zen et al.²</td>
<td>46/F</td>
<td>Painless lump in L breast</td>
<td>Excision biopsy</td>
<td></td>
<td>1.85 g/L (&lt;0.7 g/L)</td>
<td></td>
<td></td>
<td>No recurrence at 1 year</td>
</tr>
<tr>
<td>Cheuk et al.³</td>
<td>48/F</td>
<td>Painless lumps in both breasts</td>
<td>Excision biopsy</td>
<td></td>
<td>350 mg/dL (&lt;135 mg/dL)</td>
<td>272</td>
<td>65</td>
<td>No recurrence at 1 year</td>
</tr>
<tr>
<td></td>
<td>51/F</td>
<td>Two palpable lumps in R breast</td>
<td>Excision biopsy</td>
<td>Eyelid swelling</td>
<td>405</td>
<td>85</td>
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<td>No recurrence at 3 years</td>
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<tr>
<td></td>
<td>37/F</td>
<td>Two palpable lumps in R breast</td>
<td>Needle biopsy</td>
<td>Diffuse lymphadenopathy</td>
<td>383</td>
<td>82</td>
<td></td>
<td>No recurrence at 6 years</td>
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<tr>
<td>Ogiya et al.²²</td>
<td>51/F</td>
<td>Painless mass in R breast</td>
<td>Needle biopsy</td>
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<td>271 mg/dL (&lt;105 mg/dL)</td>
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<td>No recurrence at 7 months</td>
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<td>Ogura et al.⁴</td>
<td>62/F</td>
<td>Painful indurated lump in R breast</td>
<td>Biopsy</td>
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<td>60</td>
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<td>Lost to follow-up</td>
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<tr>
<td></td>
<td>66/F</td>
<td>Tender, indurated lump in R breast</td>
<td>Biopsy</td>
<td></td>
<td>&gt;300</td>
<td></td>
<td></td>
<td>Close follow-up</td>
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<tr>
<td>Dite et al.²³</td>
<td>58/F</td>
<td>Recurrent mastitis</td>
<td>Biopsy</td>
<td>Autoimmune pancreatitis, Mickulicz syndrome</td>
<td>920 mg/L (8–140 mg/L)</td>
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<td>No recurrence of mastitis at 1 year</td>
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<tr>
<td>Present cases</td>
<td>66/F</td>
<td>Painless lump in L breast</td>
<td>Lumpectomy</td>
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<td>179</td>
<td>63.9</td>
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<td>No recurrence at 1.5 years</td>
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<tr>
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<td>45/F</td>
<td>Painless lump in R breast</td>
<td>Excision biopsy</td>
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<td>308</td>
<td>67.3</td>
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<td>No recurrence at 1 year, then lost to follow-up</td>
</tr>
</tbody>
</table>

IgG4 related mastitis

• Less than 30 cases published so far (all but one women)
• No specific criteria for IgG4 quantification
• IgG4:IgG >40%  + IgG4+ plasma cells >50/HPF used

• Differential diagnosis:
  • Fibromatosis-like (metaplastic) carcinoma
  • Inflammatory myofibroblastic tumor
  • Malignant lymphomas
  • Idiopathic granulomatous mastitis
Fibromatosis like carcinoma
Inflammatory myofibroblastic tumor

IgG4-, ALK+
Idiopathic granulomatous mastitis

IgG4- ???
IgG4+ cells – comparison of IgG4-RD and IGM

(a) **
P = 0.061

(b) ***

Follow up of our patient

↑ IgG4
↑ ↑ ↑ AMA

Severe hypothyroidism
Vasospasms
Pain in shoulder and in the hip
Development of systemic sclerosis
Summary

• Rare disorder
• Part of the IgG4-RD syndrome – additional lesions outside the breast
• Complex histopathological criteria – not just IgG4!
• IgG4:IgG >40% + IgG4+ plasma cells >50/HPF reasonably helps
• Correct diagnosis has impact on systemic treatment