Infiltrating Lobular Carcinoma: Four Case Illustrations

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CASE 1

Clinical history

A 57 year old female patient presented with abdominal pain, progressive constipation, bowel obstruction and hematuria. On endoscopic examination, there were several protuberating lesions identified in cecum, colon ascendens and the right colonic flexure. There was a circumscribed thickening in the gastric mucosa and in the mucosa of the urinary bladder. On gynaecological examination the uterine cervix appeared thickened and irregular as well. Biopsies were taken from all these lesions.

Histology

Histological examination of the gastric, colonic, urinary bladder and uterine cervix revealed identical pathological changes. The mucosa in all samples was infiltrated with monotonous or moderately polymorphous cells, which showed a diffuse infiltrative pattern or infiltration in single strains. The overlying epithelium was mostly intact. The tumor cells displayed an eccentric or centrally situated nucleus, empty or eosinophilic cytoplasm occasionally with cytoplasmic vacuoles. Mitotic figures were rare.

Immunophenotype

All tumor cells expressed pancytokeratin and cytokeratin 7 strongly and diffusely. Estrogen receptors were focally positive (max 5 % of all cells), progesterone receptors were negative. E-Cadherin was negative in all cells.

Gross cystic disease fluid protein 15 and NY-BR-1 were diffusely positive in the tumor cells. CDX2 was negative. Her2 status (via FISH) was negative.

Histological diagnosis

The tumor infiltration in colon, urinary bladder, stomach and uterine cervix were consistent with manifestations of invasive lobular breast cancer.

Previous histology of the breast

10 years prior to these findings, the patient had undergone mastectomy and axillary dissection of the left breast due to an invasive breast cancer. The archived slides were retrieved and re-evaluated again. The primary tumor was larger than 5 cm in diameter. The histology of the breast cancer corresponded to a moderately differentiated invasive mixed carcinoma with ductal and lobular features. In situ components of either type (LN and DCIS) were identified in the vicinity of the invasive cells. The histology of the lobular component was identical to the cells in the relapsing lesions. 8 axillary lymph nodes had been negative.

Hormone receptors had been determined 10 years ago, both progesterone and estrogen receptors had been strongly and diffusely positive (70–100% of all tumor cells).

Additional immunohistochemistry was carried out on the paraffin blocks to compare immunophenotype of the breast cancer with that seen in the relapsing lesions.
The lobular component of the breast carcinoma was negative for E-Cadherin and showed a diffuse positivity for gross cystic disease fluid protein 15 and NY-BR-1, being congruent with the immunophenotype of the relapsing lesions.

**CASE 2**

**Clinical history**

A 60-year-old female patient was admitted to the clinic of surgery because of persistent abdominal pain.
The clinical symptoms were consistent with cholecystitis and/or cholecystolithiasis. Cholecystectomy was carried out along with hysterectomy and bilateral adnexectomy. The gallbladder appeared thickened, somewhat enlarged intra-operatively, which raised the differential diagnosis of a gallbladder malignancy. The ovaries and the uterine tubes were grossly unremarkable, the uterus showed a thickened polypous endometrium.

**Histology**

Histological examination of the gallbladder revealed a chronic cholecystitis and also a secondary xanthogranulomatous inflammation, however there was no evidence of malignancy in the gallbladder. The uterus displayed a polypous endometrium with simple hyperplasia and an intramural leiomyoma. There was no malignancy in the uterus. Both ovaries and both fallopian
tubes displayed an infiltration of small uniform tumor cells in the outer layers of both organs. The tumor cells lined up in single files or they were identified as single cells. The cells were all cytokeratin positive (Fig. 4).

**Histological diagnosis**

The findings in the adnexal structures were consistent with manifestations of an invasive lobular breast cancer.

**Previous histology of the breast**

History taking found that three years prior to these findings the patient had undergone local wide excision followed by mastectomy and axillary dissection of the left breast for an invasive breast cancer. The archived slides were retrieved and re-evaluated (Fig. 3). The size of the breast cancer was found to be more than 4 cm in diameter. The histology of the breast cancer was diagnosed as moderately differentiated invasive lobular cancer. Metastatic involvement of the axillary lymph nodes was extensive, 14 out of 17 lymph nodes had been positive.

The histology of the infiltrating lobular carcinoma was identical to the tumor cells in the adnexal structures removed.

Hormone receptors of the primary breast cancer were found to be strongly positive for both progesterone and estrogen receptors (70–100% of all tumor cells).

**CASE 3**

**Clinical history**

A 60-year-old female patient was admitted to the clinic of traumatology due to severe cervical pain. Skeletal scintigraphy revealed a diffusely metastatic process involving the skull, lower jaw, several ribs, cervical and upper thoracic vertebral column, the right major trochanter as well as the anterior mediastinum. The imaging findings were consistent with osteolytic bone metastases as well as mediastinal lymph node metastases of an invasive breast cancer. A biopsy was performed on the cervical vertebral column.

**Histology**

Histological examination of bone biopsies revealed partially necrotic lamellar bone tissue as well as fragments of cortical bone. The subcortical tissues revealed small foci of infiltrating tumor cells. The tumor cells were small, uniform, single tumor cells. They were immunohistochemically positive for cytokeratin and showed a partial loss for E-Cadherin. Estrogen receptors were strongly positive, progesterone receptors were negative (Fig. 5, lower row).

**Histological diagnosis**

The findings in the skeletal biopsy were consistent with manifestations of an invasive lobular breast cancer.

**Previous histology of the breast**

Ten years prior to the current symptoms, the patient had undergone local wide excision followed by re-excision and axillary dissection of the right breast for an invasive breast cancer. The archived slides were retrieved and re-evaluated (Figure 1, upper row). There was a multifocal infiltrative lobular carcinoma in the local wide excision specimen, with individual foci measuring 2.4 to 3 cm in diameter, reaching the resection margins. There was a focus of tumor cells in the re-excision specimen. Metastatic involvement of the axillary lymph nodes was extensive, found in 5 of 16 lymph nodes.

The histology of the infiltrating lobular carcinoma was identical to the tumor cells in the bone biopsies.

Hormone receptors were determined on the primary breast cancer, both progesterone and estrogen receptors showing moderate and diffuse positivity (50–60% of all tumor cells).

**CASE 4**

**Metastasing lung carcinoma mimicking breast cancer**

This patient presented clinically with inflammatory changes of the breast consistent with an inflammatory breast cancer stage T4d. She had been diagnosed with non-small cell lung cancer 2 years ago. A core biopsy of the breast was performed revealing a carcinoma built of large cells forming single files. The initial assessment of the core biopsy favoured the diagnosis of pleomorphic lobular carcinoma (Fig. 6). The tumor cells
showed a somewhat different morphology compared with the primary lung carcinoma. However, immunohistochemistry for hormone receptors were negative on the core biopsy. TTF-1 was tested and turned out to be positive thus confirming the diagnosis of metastatic non-small cell lung carcinoma in breast mimicking pleomorphic lobular carcinoma (Fig. 6).