

## Hydronephrosis Complicating Endometriosis in a Case of Infiltrating Lobular Carcinoma of the Breast Treated with Tamoxifen

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### Abstract

Uterine endometrial polyp, hyperplasia and malignant transformation are well known side effects of Tamoxifen use in breast cancer patients. We present a case of hydronephrosis secondary to extra-uterine endometriosis in a female with mixed Invasive Ductal Carcinoma (IDC) and Invasive Lobular Carcinoma (ILC) of the breast on adjuvant tamoxifen.

**Keywords:** Breast carcinoma; Endometriosis; Hydronephrosis; Tamoxifen

### Case History

A 62 years old lady was treated with a left modified radical mastectomy in December 2001 for a multifocal, grade 2, mixed ILC and IDC with one of eight lymph nodes involved by carcinoma. Her past history included total abdominal hysterectomy and bilateral salpingo-oophorectomy for endometriosis. Oestrogen and progesterone receptors were both strongly positive. Adjuvant treatment included adriamycin and cyclophosphamide chemotherapy, chest wall and supraclavicular radiotherapy and tamoxifen 20 mg daily. Routine follow-up included annual breast imaging and examination but no other scans. Her radiotherapy planning CT scan did not image the abdomen. She remained well for 45 months until a routine preoperative chest xray prior to a total knee replacement reported new lung changes which precipitated a computed tomography of the chest and upper abdomen that demonstrated a non-functioning hydro-nephrotic right kidney (Figure 1). Subsequent cystoscopy and ureteroscopy revealed a small polypoid lower ureteral tumour. Biopsy showed atypical cells but no malignancy. A laparoscopic right nephro-ureterectomy was performed. Final histopathology confirmed endometrial polypoid tissue with complex hyperplasia, which appeared to arise from the wall of the ureter (Figure 2). Tamoxifen was ceased and she remains well as of August 2014. The patient did not wish to switch to an aromatase inhibitor in view of her nearly 4 years of tamoxifen and concerns regarding joint symptoms.

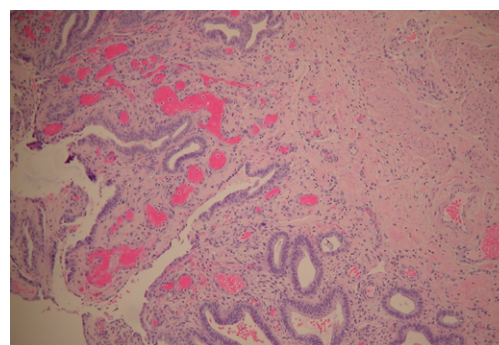


**Figure 1:** Coronal reconstruction CT scan demonstrating right hydronephrosis.

### Discussion

Infiltrating lobular carcinoma constitutes 10-15% of invasive carcinomas of the breast. A number of studies have shown that the pattern of relapse in ILC is different to that of IDC, and includes a predilection for the retroperitoneum. Borst et al. retrospectively analysed 359 cases of ILC and their patterns of spread as compared to IDC [1]. The rates of metastases to the lymph nodes, liver and brain were similar. However the rate of spread to the gastrointestinal system (4.5% vs 0.2%), gynaecologic organs (4.5% vs 0.8%), peritoneum-retroperitoneum (3.1% vs 0.6%), adrenal glands (0.6% vs 0%), and bone marrow (21.2% vs 14.4%) were considerably higher in ILC and statistically significant ( $p < 0.05$ ).

In Lamovec's autopsy study of the metastatic pattern in patients with ILC versus IDC, a statistically highly significant prevalence of ILC metastases to the peritoneum/retroperitoneum, hollow viscera, internal genital organs, leptomeninges, and myocardium was shown [2]. The infiltrates are usually diffuse as in lymphoma or leukaemia, a finding possibly explained by the loss of E-cadherin demonstrated in 95% of ILC. In Kane's series of 153 breast cancer patients undergoing



**Figure 2:** Endometrial polypoid tissue with complex hyperplasia involving lower ureter (x10 magnification).

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serial abdominal computed tomography, 2 developed bilateral hydronephrosis, both due to retroperitoneal metastatic lobular carcinoma [3].

Therefore, the finding of a hydronephrotic kidney in this case raised suspicion for the presence of metastatic disease in the retroperitoneum causing ureteric obstruction. Although Tamoxifen is used to blockade oestrogen receptors, it has a weak agonist effect. One of the relatively rare complications of prolonged tamoxifen use is endometrial polyps, endometrial hyperplasia (with or without atypia) and/or malignant transformation [4]. In the NSABP Breast Cancer Prevention Trial, Tamoxifen, increased the incidence of endometriosis in post-menopausal women from 1.6 to 4.15 per 1000 women per year, although the increased risk seemed to be confined to those without a history of previous estrogen use and a BMI <30 [5]. In addition the analysis was confined to women who had an intact uterus at study entry.

Endometriosis including malignant change after Tamoxifen therapy is the subject of a number of case studies [6]. Endometrial adenocarcinoma presenting as a pelvic mass after tamoxifen therapy in the setting of hysterectomy 13 years prior has been reported [7]. Three previous case reports link ureteric involvement by endometriosis with or without malignancy following tamoxifen, one of which was intrinsic and in the context of long prior hysterectomy [8-10]. Involvement of the urinary tract by endometriosis is rare (<1% of cases), often silent (40%) and over a third of cases with ureteric obstruction are intrinsic, although often also associated with an extrinsic component [11]. Murine models suggest that estrogenic effects leading to endometriosis are modulated by other stromal and vascular factors being modified by tamoxifen, not simply an estrogenic agonist effect on endometrial cells [12]. Aromatase inhibition would be the preferred choice of anti-estrogen adjuvant therapy in the setting of a post-menopausal woman with a history of endometriosis.

## Conclusion

The rarity of hydronephrosis complicating endometriosis or ILC

does not merit routine urinary tract monitoring. However, in patients with a history of partial estrogen agonist exposure such as Tamoxifen and or ILC, the investigation and management of hydronephrosis should consider these as etiologies. A past history of endometriosis is a relative contraindication to tamoxifen for adjuvant therapy.

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