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Original article

Treatment of peritoneal carcinomatosis from breast cancer by maximal cytoreduction and HIPEC: A preliminary report on 5 cases☆

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ABSTRACT

Although peritoneal carcinomatosis from breast cancer is a rare event it frequently causes morbidity and mortality. Current literature provides scarce information on its management. We report outcomes in 5 patients (mean age 59.4 years) with peritoneal carcinomatosis from breast cancer treated with maximal cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC) by the closed technique, at 40 °C for 1 h with cisplatin 75 mg/m^2. The primary breast cancer was a ductal carcinoma in 3 patients and a lobular carcinoma in 2. Mean peritoneal cancer index was 20.2. In 4 of the 5 patients surgery achieved macroscopic complete cytoreduction. One patient died of disease at 56 months, 4 are alive and disease-free at 13, 45, 74 and 128 months.

These encouraging outcomes suggest that cytoreduction and HIPEC is a promising approach to offer to highly selected patients with peritoneal carcinomatosis from breast cancer and that this approach merit investigation in a larger series.

Introduction

Breast cancer (BC) remains among the most frequent malignancies in western countries.[1,2] The most common sites of haematogenous metastases include bone, lung liver and brain.[3–5] As local and systemic treatments improve, breast cancer metastasis patterns change so that metastatic disease now manifests at unusual sites. Among them, peritoneal carcinomatosis is a rare event but one that carries high morbidity and mortality.[6–8]

No clear guidelines are available regarding the role of cytoreduction with or without hyperthermic intraperitoneal chemotherapy (HIPEC) in peritoneal carcinomatosis from BC,[1,9] nor does the literature provide reliable information on these patients' prognosis, most papers being case reports.[6,10–17]

Patients and methods

From a series of 221 consecutive patients admitted to our Institution from November 2000 to December 2011 with a diagnosis of peritoneal carcinomatosis from various primary tumours and treated by maximal cytoreduction[18] and HIPEC we selected for this retrospective review 5 patients who gave informed written consent, had a clear histological diagnosis of peritoneal carcinomatosis from BC, performance status 0–2,[19] adequate cardiac, hepatic, renal and bone marrow function, and resectable disease.[20] Exclusion criteria were progressive and unresponsive disease, extraperitoneal spread, other malignancies, unresectable disease and active infection or severe associated medical conditions. To rule out the differential diagnosis with a primary ovarian tumour, samples from peritoneal carcinomatosis and primary BC were assayed with an immunohistochemical panel consisting of human epidermal growth factor receptor-2 (HER-2), Wilms's tumour 1 suppressor gene (WT1), cancer antigen 125 (Ca 125), cytokeratin-7 (CK7), cytokeratin-20 (CK20), oestrogen receptor (ER),

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Table 1
Clinical characteristics related to the primary breast cancer.

Patient	Age (years)	Histology	Stage	Surgery	Radiotherapy	Adjuvant chemotherapy
Pt 1	58	IDC	T2 N1	Radical mastectomy	No	CMF
Pt 2	54	ILC	T2N3	Quadrantectomy	Yes	Refused
Pt 3	55	ILC	T2 N1 M1 (bone)	Radical mastectomy	No	CMF
Pt 4	77	IDC	T2 N1	Radical mastectomy	No	Refused
Pt 5	53	IDC	T1 N0	Radical mastectomy	No	None

IDC: infiltrating ductal carcinoma.
ILC: infiltrating lobular carcinoma.
CMF: cyclophosphamide/methotrexate/5-fluorouracil regimen.

progesterone receptor (PR) and gross cystic disease fluid protein (GCDFP-15). Nuclear staining for WT1 and cytoplasmic staining with the other markers was graded as negative or positive on a scale ranging from 1 to 4+, according to the percentage of reactive cells (<1%: negative; 1–25%: 1+; 25–50%: 2+; 50–75%: 3+; >75%: 4+). Tumours in Grade 1+ or more were considered positive. In all cases the histopathological samples allowed us to compare histological features in the primary and secondary tumours. At laparotomy, the extent of peritoneal carcinomatosis was recorded using the peritoneal cancer index (PCI) according to Sugarbaker's criteria.[21] Surgical cytoreduction was then undertaken with the aim to leave the patient with no macroscopically visible residual disease. Depending on the extent of peritoneal carcinomatosis one or more peritonectomy procedures were required.[18] Small nodules of scattered peritoneal implants were ablated or excised with high-voltage electrocautery, Tissue-link (BPS 6.0, Dover NH) or an argon-beam coagulator. The completeness of cytoreduction (CC) score was calculated according to Sugarbaker's criteria (CC0: no visible residual disease; CC1: residual nodules measuring less than 2.5 mm; CC2: between 2.5 mm and 2.5 cm; CC3: larger than 2.5 cm).[22] HIPEC was then given by the closed technique.[20] Four surgical drains were positioned for inflow/outflow and temperature monitoring and connected to a sterile closed extra-peritoneal circuit with up to 6 L of perfusate circulating by means of a peristaltic pump at a flow rate of 500 ml/min. HIPEC was given at 40 °C (outflow temperature) for 60 min with cisplatin at a dose of 75 mg/m^2. Trendelenburg/anti-Trendelenburg and latero-lateral inclinations were changed every 5 min to guarantee that the whole peritoneal surface was perfused. As a final step, the abdomen was rinsed with 3–4 L of sterile saline at 37 °C.

After surgery the patients were admitted to the ICU for at least 24 h. Chemotherapy toxicity was recorded using WHO toxicity grades for chemotherapy.[23] Treatment-related morbidity and mortality were classified from grade I to V according to National Cancer Institute Common Toxicity Criteria[24] as follows: Grade I/II: minor complications requiring no treatment or medical treatment; Grade III: major complications requiring interventional radiology; Grade IV: reoperation or ICU admission; grade V: in-hospital mortality. Quality of Life (QOL) was assessed using the QOL-CS according to Ferrel.[25]

The patients were referred to the medical oncologist staff to plan eventual systemic adjuvant chemotherapy. A total body computed tomographic (CT) scan was acquired to evaluate eventual measurable residual disease. Patients with residual disease (CC > 0), were advised to undergo adjuvant systemic treatment, according to tumour biological features (ER, PR and HER-2 expression) and patients' clinical conditions. Aromatase inhibitors were used for postmenopausal ER- or PR-positive peritoneal disease or both and patients with HER-2-positive tumour expression at histology underwent combination therapy with trastuzumab. Patients with no residual disease (CC0), were advised to undergo adjuvant systemic treatment as a precautional option. Every 6 months patients attended follow-up to assess clinical conditions, serum markers, and CT scan findings as well as other diagnostic or laboratory measures if needed on clinical grounds.

Results

Of the 221 patients who underwent maximal cytoreduction and HIPEC for various primary cancers, 5 had a histological diagnosis of peritoneal carcinomatosis from BC. Their mean age at cytoreduction and HIPEC was 59.4 years (range 53–77). The clinical characteristics and related treatments are reported in Table 1.

Table 2
Immunohistochemical panel findings in the 5 patients at primary diagnosis and at peritoneal relapse.

Patient	BRCA carrier status	ER PR Her-2		WT1		GCDFP-15		CK7 CK20 Ca-125	
		Primary	Relapse	Primary	Relapse	Primary	Relapse	Primary	Relapse
Pt 1	Neg	+	+++					Pos	Pos
		+	Neg	Neg	Neg	Neg	+	Neg	Neg
		Neg	Neg					Pos	Neg
Pt 2	Neg	+	+					Pos	Pos
		Neg	Neg	Neg	Neg	Neg	+	Pos	Neg
		+	++					Neg	Neg
Pt 3	Neg	+	++					Pos	Pos
		Neg	Neg	Neg	Neg	Neg	++	Neg	Neg
		Neg	++					Pos	Neg
Pt 4	Neg	Neg	Neg					Pos	Pos
		Neg	Neg	Neg	Neg	Neg	++	Neg	Neg
		Neg	Neg					Neg	Neg
Pt 5	Neg	Neg	++					Pos	Pos
		Neg	+	Neg	Neg	Neg	+++	Neg	Neg
		Neg	Neg					Neg	Neg

BRCA: breast cancer gene; ER: oestrogen receptors; PR: progesterone receptors; HER-2: human epidermal growth factor receptor-2; WT1: wilms's tumour 1 suppressor gene; GCDFP-15: gross cystic disease fluid protein; CK7: cytokeratin-7; CK20: cytokeratin-20.