



Hepatic resection for breast cancer metastases

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ABSTRACT

INTRODUCTION Hepatic resection is an established modality of treatment for colorectal cancer metastases. Resection of breast cancer liver metastases remains controversial, but has been shown to be an effective treatment in selected cases. This study reports the outcome of 8 patients with liver metastases from breast cancer.

PATIENTS & METHODS 8 patients with liver metastases from previously treated breast cancer were referred for hepatic resection between September 1996 and December 2002. Six were eligible for liver resection. The mean age was 45.8 years. The resections performed included 1 segmentectomy and 5 hemihepatectomies of which one was an extended hemihepatectomy. One patient had a repeat hepatectomy 44 months after the first resection.

RESULTS There were no postoperative deaths or major morbidity. The resectability rate was 75%. Follow-up periods range from 6 to 70 months with a median survival of 31 months following resection. There have been 2 deaths, one died of recurrence in the residual liver at 6 months and one died disease-free from a stroke. Of the remaining 4 patients, 1 has had a further liver resection at 44 months following which she is alive and 'disease-free' at 70 months. The one patient with peritoneal recurrence is alive 49 months after her liver resection with 2 patients remaining disease-free.

CONCLUSION Hepatic resection for breast cancer liver metastases is a safe procedure with low morbidity and mortality.

KEYWORDS

Breast cancer – Hepatic metastases – Hepatic resection

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Hepatic metastases are found in 55–75% of autopsies performed on patients who died from breast cancer.¹ Those patients who develop liver metastases from their treated breast cancer have a poor prognosis.^{2–6} Chemotherapy and hormone and biological therapies are capable of inducing response in some cases but the impact on overall survival remains unclear.^{6–10}

Advances in surgical technique and technology have resulted in a reduction in the mortality and morbidity associated with liver surgery,¹¹ facilitating liver resection in becoming widely accepted as an effective method of treating colorectal liver disease.^{12–15} The role of liver resection for metastases arising from breast cancer remains controversial. There are a growing number of reports from different units which show that mortality and morbidity following liver surgery for breast disease remain low and may provide a survival advantage for some patients.^{16–22} This study reviewed the outcome of 8 patients with liver metastases from previous breast cancer, 6 of whom had surgical excision of their liver deposits.

Patients & Methods

Eight patients with liver metastases from previous breast cancer were referred for consideration of surgical excision between September 1996 and December 2002. Patients were examined and investigated by serum biochemistry (including tumour markers), mammography, skeletal scintigraphy, total body computerised tomography (CT) scanning, upper and lower gastrointestinal endoscopy. Liver imaging included ultrasound (transabdominal and intra-operative), MRI (Tesla enhanced) and spiral CT. Staging laparoscopy to exclude more extensive liver disease than anticipated and/or peritoneal disease preclude liver resection became routine from 2001. Hepatic parenchymal dissection is performed using an ultrasonic dissector and argon-beam coagulator, employing the technique of intermittent hepatic inflow occlusion to minimise blood loss as previously described.¹⁵ Data were collected prospectively.

Results

The mean age at diagnosis of the breast primary was 45.8 years (range, 36–58 years). With the exception of a single patient, all the other 7 patients presented with metachronous liver deposits. The mean duration from the treatment of the primary breast cancer to the diagnosis of liver secondaries was 75 months (range, 24–144 months). In one patient, secondary liver deposits were detected at the time her breast cancer was diagnosed. All patients had received Anthracycline-containing chemotherapy after liver surgery.

Six patients underwent potentially curative liver resections while two patients were found to have inoperable disease (one with extensive superficial bilobar deposits and the other with peritoneal disease) at laparotomy. Two patients had single metastases, two had two, one had three and one had five metastases. The procedures performed are listed in Table 1 and range from a single segmentectomy to an extended hemihepatectomy. None of the patients required peri-operative blood transfusion and there was no mortality or major morbidity. Median hospital stay follow-

ing liver resection was 8.5 days (range, 4–12 days). Microscopic margins were clear in all cases. There have been two deaths, one from a stroke and the other from liver recurrence over a follow-up period ranging from 2–62 months. Of the 4 patients still alive following their 'curative' resection, one developed peritoneal metastases 47 months after hepatic surgery diagnosed at laparoscopy performed for vague abdominal pain associated with rise in serum CA15.3 levels, another developed recurrent liver disease at 36 months, following a 12-month period of observation the recurrence remained isolated and unchanged in size, this was re-resected at 44 months and the patient remains alive and disease-free at 70 months. The last 2 patients are presently disease free. Table 1 summarises the treatment details.

Discussion

Invasive breast cancer is generally thought to be a systemic disease even at the time of presentation and even more so when remote metastases are detected.^{21,23,24} This may, in part, explain why surgical resection of liver metastases for

Table 1 Treatment summary

Patient number	Age at diagnosis of breast cancer (years)	Primary treatment	Tumour pathology (breast)	Interval from primary treatment to diagnosis of liver metastases (months)	Resection (<i>n</i> = number of liver deposits and size of largest deposit)	Survival
1	58	Mx + Ax,	T ₄ G ₂ N _{4/10}	24	R hepatectomy (<i>n</i> = 2, 25 mm)	Died at 30/12 from stroke, no signs of recurrence
2	36	Mx + Ax, Goserelin	T ₂ G ₁ N ₀	54 (pre-op FEC)	Inoperable	Alive at 50/12
3	47	WLE, DXT, TAM	T ₁ G ₁ N ₀	144	Extended R hepatectomy (<i>n</i> = 10, 45 mm) & segmentectomy II (<i>n</i> = 7, 20 mm)	Rec disease at 36/12; re-resected 44/12; alive and disease-free at 70/12
4	53	WLE + Ax, CMF, oophorectomy	T ₁ G ₁ N _{1/15}	48	Inoperable	Alive at 33/12
5	53	Mx + Ax, TAM	T ₁ G ₁ N _{1/14}	60	R hepatectomy (<i>n</i> = 1, 18 mm)	Alive with peritoneal seedlings at 57/12
6	37	WLE + Ax, CMF, DXT, TAM	T ₂ G ₃ N _{4/34}	Synchronous (interval CMF)	L hepatectomy at 10/12 (<i>n</i> = 1, 30 mm)	Recurrent liver disease at 3/12; died at 6/12
7	36	Mx + Ax	T ₃ G ₃ N ₀	120 (<i>n</i> = 2, 35 mm)	R hepatectomy at 15/12	Disease-free
8	47	WLE + Ax, DXT, TAM	T ₃ G ₂ N _{2/18}	80	L hepatectomy + wedge resection x 3 (<i>n</i> = 5, 25 mm)	Disease-free at 10/12

Mx, mastectomy; Ax, axillary dissection; TAM, tamoxifen; WLE, wide local excision; DXT, radiotherapy; CMF, chemotherapy with cyclophosphamide, methotrexate and 5-fluorouracil; FEC, chemotherapy with 5-fluorouracil, epi-doxorubicin and cyclophosphamide; T_x G_x N_x, standard nomenclature for breast tumour size, grade and nodal status.

breast cancer remains controversial. Suppression of growth of putative micrometastases is successful in 10% of patients using a combination of endocrine therapy and chemotherapy in the adjuvant setting.²⁵ When this fails, the mainstay of managing distant metastatic disease relies on further treatment with second-line endocrine and chemotherapy. Hepatic metastases are found in 55–75% of autopsies on patients dying from breast cancer.^{1,26,27} Currently, in most centres, chemotherapy is usually considered the treatment of choice for patients with liver metastases from breast cancer even though the outlook following this form of treatment remains bleak, with median survival ranging from 4 to 15 months.^{16,28,29}

This series analysed the demographics, time and methods of treatment, pathology of the primary breast cancer and survival of 8 patients with liver metastases from a breast primary. The longest survivor is now 70 months following her second liver resection.

The patient in this study who has survived the longest had her liver involvement detected 12 years after treatment of her primary breast cancer. Conversely, the single patient so far to die from recurrence of her liver disease had only a short interval between the diagnosis of her primary breast cancer and liver metastases. This would suggest that the length of time from the diagnosis of breast cancer and the detectable liver metastases influences survival. Pocard *et al.*,¹⁸ in a recent study of 65 cases, found that the prognostic factors important for longer survival were a disease-free interval of more than 48 months and the initial stage of the cancer while Carlini *et al.*²¹ found the only factors of prognostic significance were the control of the primary tumour, the absence of extrahepatic disease and the complete resection of the liver deposits. The limited number of patients in this series precludes statistical analyses. Interestingly, the 2 patients with inoperable disease are still alive 24 and 42 months following open and close laparotomy. This demonstrates that the tumour biology plays an important role in determining survival and it is possible that those patients with synchronous liver metastases or those with a short disease-free interval have a worse prognosis due to the more aggressive and robust nature of the cancer cells.^{30–32}

The impact of liver resection in the treatment of liver metastases arising from breast cancer is slowly becoming recognised. There is a select group of patients who stand to benefit from surgical excision of their liver disease.^{21,16,18,22,26,33,34} The overall reduction in the mortality and morbidity associated with liver surgery in the last decade has made this possible by increasing the impact of liver surgery as a safe and reliable way of treating a wide range of benign and malignant liver conditions.

There is more than ever a need for multicentre prospective randomised studies to demonstrate definitely whether liver resection alone or in combination with adjuvant therapy

improves long-term survival in patients with breast cancer metastases restricted to the liver. Until then, survival data from similar cases collected prospectively possibly on a regional basis remain the next best evidence. The success of such a prospective study will rely on identifying those patients at risk of developing liver metastases preferably at the asymptomatic stage using CA15-3 measurements, liver ultrasound and/or liver computerised tomography. A better understanding of the molecular biology of breast cancer using technology such as tissue microarray (TMA) may, in the future, allow us predict response to therapy. Clinicians may be able to identify those liver tumours that are best treated by either chemotherapy with or without liver resection^{35–39} or radiofrequency ablation^{40–42} or a combination of both.

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