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Short Length of Stay and Rapid Recovery to Normal Function after Surgery for Metastatic Melanoma to Abdominal and Retroperitoneal Viscera

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Abstract

BACKGROUND—Metastatic melanoma to abdominal and retroperitoneal viscera carries a poor prognosis possibly resulting in reluctance to offer surgical management. There is value in defining the morbidity of such surgery.

METHODS—Review of a prospectively maintained database identified patients with metastatic melanoma to abdominal or retroperitoneal viscera who underwent surgery from 9/99-8/06.

RESULTS—Nineteen patients underwent surgery for metastasis to abdominal or retroperitoneal viscera detected by clinical symptoms (80%), or imaging (20%). The median length of stay was 7 days. There was no perioperative mortality. Surgical complications occurred in 4 patients. At initial follow-up, 13 patients (68%) had returned to baseline function, 7 of which reported improvement. Four patients (21%) had minimal symptoms, and only 2 patients (11%) had significantly limited function. Median follow-up was 35 months, at which time 9 of 19 patients (47%) were still alive, with 3 and 5-year Kaplan-Meier survival estimates of 53% (SE 12) and 45% (SE 12), respectively and two of the 19 patients are alive at over 8 years since surgery.

CONCLUSION—In selected cases, surgery may have both palliative benefit and curative potential for patients with visceral metastases of melanoma. Surgical management of such patients should be encouraged in appropriate clinical settings.

Keywords

Melanoma; surgery; metastatic; abdomen; retroperitoneum

INTRODUCTION

Metastatic melanoma to abdominal and retroperitoneal viscera carries a poor prognosis, with median survival for metastatic melanoma reported to be 6-12 months[1-5]. Chemotherapy for metastatic melanoma may be palliative, but long-term response rates are disappointing and reported to be less than 2% of treated patients [6,7] and long-term survival remains in

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the range of 1-5% [8-10]. Furthermore, chemotherapy has no demonstrable role as adjuvant therapy of high-risk resected melanoma.

The lack of effective systemic therapy and poor prognosis can lead to a reluctance to be aggressive in treating patients with a diagnosis of metastatic melanoma. Surgical resection of metastatic disease has traditionally been viewed as a local approach to a systemic disease and outside of specialized centers has largely been limited to palliative indication. Hesitation is heightened in metastatic disease to less surgically accessible areas, including the abdomen and retroperitoneum.

While there are several series in the literature that report improved survival in metastectomies for melanoma[4,11-17], morbidity of surgical resection of abdominal and retroperitoneal metastases has not been well addressed in the recent literature. What is published tends to be from a limited group of institutions and carries an inherent bias based on referral patterns and patient selection. Several review articles, however, support metastectomy in the appropriate clinical setting[18-22].

Decisions to operate weigh the palliative benefit and small chance of survival benefit against the morbidity of surgery itself. Understanding the impact of surgery in this patient population in regards to length of hospital stay and time to return to baseline function would be valuable in counseling treatment decisions.

METHODS

After approval was obtained from the Institutional Review Board (IRB protocol HIC 10803) of the University of Virginia Health Systems, a review of a prospectively maintained database at the UVA Cancer Center was performed to identify patients managed at our institution with metastatic melanoma to abdominal or retroperitoneal viscera. The study population was limited to patients who were operated on with intent to resect all or most disease from September, 1999 to August, 2006. Approximately 2,500 melanoma patients were seen by the melanoma clinic during that time period. The study population was comprised of 13 men (68%) and 6 women (32%). The mean age was 55 years (range 27 – 80). Survival data were supplemented from the Social Security Death Index.

Given the retrospective nature of this study, patient selection was not based on strict inclusion or exclusion criteria. Nevertheless, patients who were resected tended to be symptomatic, to be motivated towards aggressive therapy, and to have isolated metastatic lesions and acceptable surgical risks. Assessment of function was based on a review of our prospectively collected database which includes information regarding postoperative condition, in addition to a complete review of the medical records for the postoperative period. Patients were considered back to their baseline function when they reported return to work or their previous daily activities.

Data were analyzed by chi-square test and two-tailed t-test using Microsoft Excel and MedCalc statistical software. For small data samples, descriptive statistics were used. Survival was calculated from the date of surgery to death or last follow-up. Kaplan-Meier survival curves were generated with MedCalc statistical software package.

RESULTS

Surgical intervention

Nineteen patients underwent surgery for metastasis to small bowel (58%), liver (11%), adrenal (11%), pancreas (5%), stomach (5%), spleen (5%), or rectum (5%). The diagnosis was made as a result of clinical symptoms in fifteen of the nineteen patients (80%). The intent of surgery was curative in 14 of the nineteen patients (74%) and palliative in the remaining 5 (26%). Small bowel resection was the most common procedure (11), followed by partial hepatectomy (2), with the remaining surgical procedures being a splenectomy, bilateral adrenalectomy, gastric resection, pancreatoduodenectomy, bilateral adrenalectomy and a combined adrenalectomy and nephrectomy. Thirteen (68%) patients had R0 resections. Experimental melanoma vaccines were included in management of 16 patients (84%).

Morbidity

The hospital length of stay ranged from 3 to 14 days (median 7 days) for the perioperative admission. There was no perioperative mortality. Surgical complications occurred in only 4 patients: 2 were readmitted for post-operative bleeding, and 2 were treated as outpatients for wound infections. None of these patients required reoperation for management of their surgical morbidity.

Initial follow-up was performed a median of 6 weeks post-operatively, when 13 patients (68%) reported being back to baseline or improved activity and function, 4 patients (21%) experienced only minimal symptoms and post-operative deconditioning, and just 2 patients (11%) were significantly limited by fatigue, anorexia or recurrent distant disease. Of the 13 patients who were back to their baseline, 7 (37%) reported improvement in their condition from their preoperative status. All of these 7 patients were symptomatic prior to surgery and reported relief of these symptoms (obstruction or hemorrhagic symptoms). In addition, 3 of the 7 patients reported improvements that were less closely linked with symptomatic disease, including increased energy level, appetite & weight gain and return to work.

In comparing patients with complete resections (R0) versus incomplete resections (R1 & R2) there was no difference in length of stay (median length of stay for R0 = 7 days versus R1 & R2 = 8.5 days; $p=0.09$). Likewise, occurrence of perioperative complications was equivalent for the two groups ($p=0.71$).

Survival

Median follow-up was 35 months (range 5-110) from the date of surgery, at which time 9 of 19 patients (47%) were still alive, with 3 and 5-year Kaplan-Meier survival estimates of 53% (SE 12) and 45% (SE 12), respectively, and estimated median survival of 4.3 years (lower limit 95% CI 2.4 years). Two of the 19 patients are alive at over 8 years since surgery. For the 14 patients who underwent an R0 resection, the median follow-up was 39 months (range 5-110) from the date of surgery, at which time 9 of the 14 patients were still alive, with 3 year Kaplan-Meier survival estimate of 64% (SE 13). Five are alive more than 5 years after surgery, including the two patients mentioned above who are alive over 8 years since

surgery, and had R0 resections. The 5 patients who had R2 resections all have died of their disease, but lived 8-44 months after surgery (mean 25 months, median 30 months).

DISCUSSION

In melanoma, while there are reports supporting surgical intervention in the symptomatic patient [23,24], the dismal prognosis of Stage IV disease has limited overall enthusiasm for aggressive surgical intervention of visceral disease. Some studies, however, suggest there may be a survival benefit from resection in a select patient population, with reports of 5-year survival ranging from 10-42% [3,4,12-14,25]. Even further, in a study of recurrent stage IV disease, Ollila et al found a 5-year survival rate of 21% when complete resection was possible [26]. Complete resection has also been shown to be an independent variable for survival benefit of resection of Stage IV disease [3,18]. While there is some controversy over whether having multiple metastatic lesions decreases this survival benefit, it is most likely that if these lesions are resectable, the benefit persists [18,19].

The majority of patients in this study population (84%) were also treated with melanoma vaccines at sometime during their disease course. A recently published study by Tagawa et al from University of Southern California reported long-term survival (median of 3.8 years) in select patients with metastatic melanoma treated with metastectomy followed by melanoma vaccine therapy [27]. A recent randomized trial of a melanoma vaccine in patients with resected stage IV melanoma did not show a clinical benefit to vaccination but did show 42% five-year survival in these patients, overall [14]. Potentially the benefits of surgical resection may be greater when combined with adjuvant therapy, by reducing the disease burden surgically and limiting growth of micrometastatic disease systemic therapy. With the demonstration that surgery can be performed with limited morbidity and a short hospital stay, we recommend that surgery be considered a therapeutic option for the management of patients with metastatic melanoma to abdominal and retroperitoneal viscera.

The potential for survival benefit needs to be balanced with the morbidity of surgical intervention. There are no prospective studies and limited retrospective studies in the literature that addresses the specifics of surgical morbidity. Reported morbidity rates range from 1.4-15% [2,3,28] likely reflecting the variability in patient population and definition of morbidity.

An earlier study of metastatic melanoma to any site by Overett et al reports an operative mortality rate of 1.4%, and their data show significant morbidity in cases when complete resection is not possible, stating 13 of 143 patients spent more than 50% of their remaining survival time in the hospital [3]. Major complications in their series included two incidental splenectomies and a fatal pulmonary embolism [3]. Their study included total days in the hospital after surgery and did not separate out the days required for surgical intervention & direct surgical complications from hospital days spent due to disease progression or end of life care. While their data are useful in assessing overall hospital requirements for the patients with Stage IV melanoma, it does not tell us what additional burden is imposed by operating on this patient population. T.F. Wood et al did include complication rates in their study of resection of metastatic melanoma to solid intrabdominal organs and report zero

operative mortalities and a surgical complication rate of approximately 11%[4]. Another study of gastrointestinal metastatic melanoma by Ollila et al reports operative mortality and major post-operative complication rates of just over 1% for 69 patients[2]. In addition, they reported relief of gastrointestinal symptoms in 67/69 (97%) of patients[2].

Our study extends beyond the relief of preexisting gastrointestinal symptoms and addresses factors such as activity level and post-operative functional status. Our data agree with their low mortality and morbidity and demonstrates that patients are out of the hospital quickly and have fast return or improvement in function by their first post-operative visit. In review of the literature, we did not find another study which evaluated patients' recovery of function after surgery for visceral or retroperitoneal metastases. This knowledge will be helpful in counseling patients during decision making processes.

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SYNOPSIS

Metastatic melanoma to abdominal and retroperitoneal viscera carries a poor prognosis. In selected cases, surgery may have both palliative benefit and curative potential. The morbidity can be very low. We recommend that surgical management of such patients be considered.

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Figure 1. Kaplan-Meier 5 year survival curve showing survival following surgery for metastatic melanoma to the abdomen and retroperitoneum. 95% confidence intervals, censored data and the number of patients at risk are shown. Survival data are from the medical record and the social security death index for this study.