ORIGINAL ARTICLE

Surgical therapy for testicular cancer metastatic to the liver

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Abstract
In recent years improved cure rates have been achieved for testicular cancer. A better understanding of the biology of subtypes of testicular cancer and the introduction of surgical intervention has contributed greatly to how we currently approach a young man with testicular cancer. We describe here experience at our institution of the treatment, results and prognostic factors for testicular cancer metastases to the liver. Careful diagnostic work-up and planning of the therapy are required, in cooperation with an experienced team.

Background

Testicular cancer has often been described as 'the model of a curable cancer'. This was not always the case, as prior to the mid-1970s; treatment cured <5% of patients. Given that this was and remains the most common cancer in young men (aged 15–35), there was a great impetus to find better methods of treatment. For two decades, this centered on chemotherapeutic regimens using multiple drugs with non-overlapping toxicity profiles [1]. By 1984, the cure rate for testicular cancer was >80% and experimental protocols began to focus on the refractory cases or 'poor risk' patients. However, chemotherapy alone has not been the only intervention to contribute to this dramatic improvement. A better understanding of the biology of subtypes of testicular cancer and the introduction of surgical intervention has contributed greatly to how we currently approach a young man with testicular cancer [2–4].

Experience and results

Our institution has been a proponent of aggressive medical and surgical management for testicular cancer, including resection of multiple foci of disease that is not eradicated by chemotherapy alone [1]. Hepatic resection for other cancers, like colorectal carcinoma, has been shown to improve survival in selected patients and prognostic variables have been described to predict outcome in these patients [5–7]. Hepatic resection as part of a primary debulking or interval debulking for metastatic ovarian cancer has also shown a survival benefit in patients that can be rendered free of all (or nearly all) measurable disease [8,9]. Although the pattern of spread for testicular cancer is usually lymphatically to retroperitoneal lymph nodes and hematogenously to the pulmonary parenchyma, it may also spread to the liver. We have had encouraging results with hepatic resection of metastatic testicular carcinoma. We published our first series of patients in 1990, having treated 28 patients with disseminated germ cell carcinoma [10]. The lessons learned from this series include: (1) it can be done safely, without a significant increase in morbidity and mortality (we observed no deaths and 28% of patients experienced complications), and (2) survival was predicted by histopathologic characteristics of the specimen(s) as we would have predicted based on extrahepatic metastatectomy series.

Our most recent series of 57 patients treated with hepatic resection for metastatic testicular cancer highlights our current treatment algorithm and prognostic indicators [11]. Patients receive at least three cycles of cisplatin-based chemotherapy, after which tumor marker levels of human chorionic gonadotropin (B-HCG) and alpha-fetoprotein (AFP) are reassessed. Patients are then stratified into three groups: (a) those with normalization of their serum markers and no radiographic evidence of disease, (b) patients with normalization of serum markers with evidence of

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persistent disease on follow-up imaging, and (3) patients with elevated serum markers and persistent disease. The first group is followed closely with serum marker analysis and imaging for evidence of relapse. Patients with normalized serum markers and radiographic evidence of disease are candidates for surgical resection. Patients with elevated serum markers are usually treated with salvage chemotherapy. These latter two groups make up the cohort of 57 patients who underwent a total of 60 hepatic resections at our institution. Concomitant procedures were performed in 87% of patients and included: (a) retroperitoneal lymph node dissections (RPLND, $n = 37$), (b) RPLND with pulmonary or mediastinal resection ($n = 10$), (c) nephrectomy ($n = 5$), IVC resection ($n = 3$), and orchiectomy ($n = 1$). Postoperatively, hepatic specimens were evaluated and patients were again stratified into groups based on histopathologic characteristics: group 1 had no evidence of cancer (i.e. necrosis or fibrosis) in the resected specimen(s), group 2 had histopathologic evidence of teratoma, group 3a had persistent germ cell cancer in the face of normal preoperative serum markers, and group 3b had active disease and persistent elevation of serum markers preoperatively. With a median followup of 47.1 months, eight of nine (89%) patients in group 1 were alive with no evidence of disease at last followup. With a median follow-up of 56.9 months, 21 of 29 (72%) patients in group 2 had no evidence of disease. Despite the presence of persistent cancer in the resected hepatic metastases, 6 of 14 patients in group 3a and 2 of 5 patients in group 3b remain alive and disease-free, with a median follow-up period of 20.4 months. Overall, 37 of 57 patients continue to remain disease-free. Favorable prognostic variables included: (1) no histopathologic evidence of cancer within the liver specimen and (2) normalization of preoperative serum markers in 'poor risk' patients with histopathologic evidence of active disease in their resected specimen(s).

The vast majority of patients diagnosed with metastatic testicular cancer are cured with chemotherapy alone. Our ability to establish treatment expectations has a lot to do with the development of staging systems that effectively discriminate 'good risk' from 'poor risk' disease. Patients with hepatic metastases fall into the 'advanced' or 'poor risk' category in the current International Staging System [12]. This group also includes other nonpulmonary visceral metastases and markedly elevated serum b-HCG and/or AFP. These patients have a 40–60% cure rate with standard therapy [12]. High dose chemotherapy with peripheral stem cells has been used effectively as salvage therapy in these high risk patients with improvement in survival [1].

Conclusion

Our success in the treatment of metastatic germ cell tumors is achieved by multidisciplinary efforts. In some cases complete excision requires multivisceral radical resections as a last attempt to cure patients who have exhausted all other therapeutic options. Complete surgical resection of all measurable disease is the gold standard and correlates with improvement in both relapse-free and overall survival after hepatectomy with actuarial survival rates of 78% at 3 years in other tumor types [13]. This requires careful diagnostic work-up and planning of the procedure in cooperation with an experienced team.

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