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Is Metastasectomy for Urothelial Carcinoma Worthwhile?

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Three decades ago, I saw a man with a large groin mass that proved on biopsy to be urothelial carcinoma. Six years earlier, I had done a radical cystectomy and pelvic lymph node dissection for organ-confined bladder cancer. As this was the only site of disease, I performed a radical groin dissection, encouraged by the fact that surgeons at my institution operated regularly to remove metastatic cancers of the colon, breast, lung, kidney, and bone as well as sarcomas. Why not metastatic bladder cancer?

In 1983, when methotrexate, vinblastine, doxorubicin (Adriamycin), and cisplatin (M-VAC) was established as effective chemotherapy against urothelial cancer, we began, where possible, to surgically resect all metastatic sites of disease [1]. In our original M-VAC series of 25 patients, 13 had complete resection of viable tumor (4 survived 5 yr), and postchemotherapy surgery evolved to become routine for unresectable or metastatic bladder cancer. Of 276 patients who received cisplatin-based chemotherapy, 89 (32%) underwent postchemotherapy surgery (8 patients were unresectable). Most patients had resection of metastatic pelvic and retroperitoneal lymph nodes or soft tissue masses, but some had resection of visceral metastases involving liver, lung, or bone. Thirty patients (34%) survived 3–5 yr after postchemotherapy surgery. In 27 patients (33%), no viable tumor was found, pathologically confirming a complete response to chemotherapy. In 54 patients (67%), residual, viable cancer was completely resected; 18 patients (33%) remained alive at 5 yr, similar to survival of patients having complete responses to chemotherapy (41%). Of 14 patients who refused postchemotherapy surgery, only 1 (7%) survived, suggesting that surgical resection benefits patients who achieve either partial or complete clinical response to chemotherapy [2].

In this issue of European Urology, the wisdom of this approach is confirmed by Lehmann and his colleagues from Germany [3]. What makes the German experience remarkable is that it involved many expert surgeons operating in multiple centers, making their data more robust than data reported from single institutions. The data show an overall 5-yr survival rate of 28% among 44 patients undergoing complete metastasectomy for urothelial carcinoma. Most had resection of retroperitoneal or distant lymph nodes, but a few survived after resection of lung or bone metastases. Almost all the survivors received chemotherapy. Only 18% had necrosis or fibrosis in resected specimens, and these patients, similar to our results, had no survival advantage over patients having residual vital urothelial cancer resected. As the authors discuss, their experience, combined with that of others, provides a strong argument in favor of postchemotherapy surgery for urothelial carcinoma.

The authors do not state how many patients they evaluated over 15 yr to select their 44 cases for surgery. We know from our data that only a third of patients were deemed to be candidates for postchemotherapy surgery, and of these, about a third...
survived. This means that postchemotherapy surgery may save about 1 or 2 out of every 10 treated patients. Some of these patients had only scar in the specimen, but we believe surgery was still worthwhile because negative pathology for tumor can also mean that residual nests of microscopic tumor were simply not detected among a large fibrotic specimen.

The rationale for surgery of metastatic disease is that few patients are cured, even if they respond completely to chemotherapy, owing to high incidence of relapse at responding sites of disease. The question is patient selection: Who should be operated on? Although the authors were unable to identify which patients were most likely to benefit from an aggressive surgical approach, they suggest that surgical removal of urothelial cancer metastases should only be performed in patients with small-volume disease and in the context of systemic chemotherapy. I agree; however, currently available postchemotherapy surgery experience in urothelial cancer is now sufficiently mature to permit some guidelines regarding patient selection:

- Patients with metastatic urothelial cancer should receive systemic chemotherapy first because that will help to determine the indication and the extent of surgical resection for metastatic disease.
- A major clinical response (complete or partial) to chemotherapy portends the best chance for long-term survival with postchemotherapy surgery. In any of the published series, no patient survived who failed to respond to chemotherapy. Postchemotherapy radiographs and scans are unable to distinguish patients who have no evidence of residual pathologic disease from those who do not. Positron emission tomography (PET) scans may help to identify viable cancer, providing a firmer indication for surgery; however, PET in urothelial carcinoma is currently investigational.
- An occasional anecdotal patient with a solitary metastasis, like my patient presented above, can be salvaged without receiving chemotherapy; however, they are rare indeed.

- Limited nodal or a solitary visceral or lung lesion is most likely to benefit from surgical resection.
- Multiple liver metastases or metastases involving more than one visceral site or abdominal organ have a poor outcome, despite complete surgical resection of all viable disease. Bone metastases, especially involving the pelvis or axial skeleton, also have a poor prognosis. Although we have had isolated successes in resecting sacral metastasis, complete surgical resection of bone metastases usually fails, owing to more extensive bone and adjacent soft disease than is often appreciated on conventional x-rays. Furthermore, the dismal results achieved with surgery for most visceral or bone metastasis stand in stark contrast to the more favorable results in patients with locally advanced pelvic regional or distant nodal disease.
- Surgical resection has to be technically feasible, and the number of metastatic sites has to be limited (one or two, in the case of nodes) or only one site (in cases with visceral metastasis).
- A patient who is motivated to undergo aggressive treatment and who has a performance status to withstand a major operation certainly helps.

As Lehmann et al convincingly show, by combining sound clinical judgment with expert surgical skill, up to a third of patients with metastatic urothelial cancers may survive their disease with aggressive surgery integrated with effective chemotherapy.

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References