

DISCUSSION

DR. RONALD BUSUTTIL (Los Angeles, California): I feel that it is very clear from the material that has been presented by Dr. Adson that there is, indeed, a small subset of patients with hepatic metastases who respond quite favorably to hepatic resection, and that this resection, if feasible may be as extensive as a trisegmentectomy, with very acceptable operative mortality.

However, I feel that I must also point out that, although we are on very firm footing in recommending resection for smaller, isolated metastases, we must have some reservation on recommending such extensive hepatic resection, which at the present time should be considered investigational.

As has been pointed out by the authors, if only 20–30% of patients with large lesions are benefited, and the risk of operation is in the neighborhood of 10%, then the risk–benefit ratio is only about 0.3–0.5, which is really not that beneficial. However, regarding the overall, collective experience, which has accumulated with hepatic resection for colon metastases, the favorable results that have been presented by Dr. Adson have been indeed substantiated.

(slide) This is a collective review of a large series of hepatic resections for colorectal metastases that was presented by Drs. Foster and Berman in 1977; and as you can see, out of 164 cases, the number of patients that were alive at two years was approximately 50%, and the number of those that were alive at five years was approximately 25%. This is all cases taken into consideration.

If, now, one looks at only the colon and rectum primaries, the results are very similar with approximately 50% alive after two years, and approximately 25% alive after five years.

In our own experience at UCLA, we have treated approximately 25 patients with hepatic resection that has ranged from wedging out a small, isolated solitary metastasis to several trisegmentectomies. Our results at the present time have been quite favorable, and confirm the authors' experience of not only prolonged survival, but also improved quality of life following surgery in this very select subset of patients.

Unfortunately, this type of patient with a solitary liver metastasis which is amenable to surgery only comprises approximately 5% of the patients that we see with metastatic adenocarcinoma.

Well, what about the other 95% that we see? I think that it is this majority of patients which really presents us with the most difficult therapeutic dilemmas. As you know, the standard current treatment has been systemic chemotherapy, but the results have really been fairly disappointing.

(slide) This slide summarizes the most effective, if you will, combination chemotherapy that has been used to date, and that is the combination of 5-fluorouracil, in combination with methyl-CCNU.

As you can see, the initial results presented by Meertel in 1975 were very encouraging; he reported a response rate of about 44%. However, as additional studies were performed the overall results indicated a lesser response of only 14%, which really is only about the same response rate that we can expect with systemic 5-fluorouracil alone.

Because of the poor results we see with systemic chemotherapy, the Division of Oncology at UCLA has been using an experimental multimodality protocol, using hepatic artery ligation and intrahepatic infusion of 5-fluorouracil to treat those patients who have already failed the conventional systemic chemotherapy.

(slide) In a group of 25 patients, using this multimodality therapy, a mean survival of nine months has been achieved in those patients who have already been tried on systemic chemotherapy and then been converted to this modality of hepatic artery ligation with intrahepatic infusion of 5-fluorouracil.

Let me conclude by asking the authors two questions. How do you rule out in those patients occult metastases that would preclude hepatic resection? Do you feel that this same aggressive surgical approach with solitary hepatic metastases from colon carcinoma should be extended to apply to other visceral neoplasms? And if so, what are your criteria for resection?

DR. JOHN L. CAMERON (Baltimore, Maryland): I would like to discuss primarily the paper presented by Dr. Jones.

Over the past four years we have followed six patients who have been diagnosed as having hepatic hemangiomas, the smallest one being 6 cm in diameter. None of these patients have been operated on. They have all been diagnosed by having the characteristic defect on technetium scan, a CAT scan which showed a homogeneous lesion that totally and completely enhanced after i.v. contrast material, and an arteriogram which showed a uniform blush with no abnormal feeding vessels.

We have been confident enough that these could be diagnosed as hepatic hemangiomas that none of these patients have been operated on. They were all asymptomatic at presentation, and they have all remained asymptomatic.

It's quite clear from the literature that small hepatic hemangiomas remain, by and large, asymptomatic, do not have to be operated on, and we're not at all certain that the same doesn't apply to many hepatic hemangiomas.

I'd like to know from Dr. Scott if there were specific indications for hepatic resection in their four patients with hepatic hemangiomas, other than just an asymptomatic liver mass; and secondly, whether they feel or not that a large hepatic hemangioma that is asymptomatic needs currently to be resected.

Finally, I'd like to ask both Dr. Adson and Dr. Jones whether they feel that their controls are really adequate concerning liver resections for colon metastases. When we do a major hepatic resection on a patient with a colorectal tumor that is metastatic to the liver, are we really influencing the disease, or have we just selected out those patients with biologically low-grade tumors, and are just watching the natural behavior of the disease?

DR. FRED W. RUSHTON (Jackson, Mississippi): Our overall experience in Jackson with hepatic masses has fairly closely paralleled that presented by Dr. Jones' group. Between the years 1961 and the present, 95 primary liver tumors, including those that were not resected, included 61 hepatomas, 16 hemangiomas, seven hepatoblastomas.

I rise, first of all, to congratulate Dr. Jones on an excellent paper, and secondly to call special attention to a clinical entity that has arisen as, perhaps, a complication of progress in medicine.

(slide) This is the case of a young woman who presented to our emergency room with a three-day history of right upper quadrant abdominal pain, nausea, and vomiting. Examination revealed a tender, ill-defined right upper quadrant mass. Laboratory screening was essentially unrevealing. A sonogram was done, which showed the gallbladder to be normal. As one moves toward the umbilicus on the sonogram, there was a large mass that had internal echoes, and was felt to be separate from the liver and from the gallbladder, as well as from the kidney.

A liver scan was done, as well as a barium enema, which were both within normal limits, and following this she developed an increase in her abdominal pain, with a falling hematocrit, and was taken forthwith to the operating room.

(slide) At operation, she was found to have a large, pedunculated tumor arising from the edge of the liver, which had ruptured into the peritoneal cavity, with intra-abdominal bleeding. It was removed by simple excision and drainage.

(slide) On cut section, it was found to contain blood clot.

We feel that, in addition to the entities described by Dr. Jones, benign hepatic adenoma will continue to be seen with increasing frequency in association with widespread use of oral contraceptives, and we feel that it should deserve significant consideration in the differential diagnosis of right upper quadrant masses in female patients.

DR. WISHARD S. LORIMER, JR. (Fort Worth, Texas): In this day and time of informed consent, I think one needs to discuss with the patient the possibility of surgical excision of hepatic tumors, if one intends to do this concomitantly with colon resection. I'd like to ask Dr. Adson if he does this. Also, if you have a large metastatic

tumor that you can't do concomitantly, how do you time the second operation?

The second point I'd like to make is that I think it's very important, when we encounter a resectable metastasis that we do not resect initially, we should at least find out what the histopathology is.

In a recent experience of two cases, one that I planned to go back in turned out to be an oat cell carcinoma, occult, from the lung; and the second is a case in which the surgeon was not prepared to do a wedge resection of a deeply-seated 2-cm lesion, and he very wisely took a needle biopsy. The pathology report was a hemangiosarcoma. The patient declined to have anything done about this. The surgeon brought the case to me last January, and at that time he had a huge mass occupying his right upper quadrant.

(slide) This turned out to be the end result of that hemangiosarcoma. It required an extended right hepatic lobectomy, and it also had infiltrated the cupola of the right hemidiaphragm, which also required resection.

The patient had an uneventful convalescence following this, but here again, a lesion which was initially thought by the surgeon to be metastatic colorectal carcinoma turned out to be something else.

DR. MARTIN A. ADSON (Closing discussion): I really have two things to do. One is to discuss Dr. Scott's paper, and then close mine; and I want to do a third thing that I've deferred.

You said, Dr. Carter, that you hadn't acknowledged my new membership, and I didn't either; but I did not purposely. I didn't want to break up while I was making my formal presentation. Let me tell of my appreciation in a roundabout way.

(slide) Twenty years ago, having never seen a major hepatic resection, I had to decide whether or not to remove this tumor. Reflecting on that decision, I recalled a slide that Dr. P. G. Arnold, a transplanted Southern surgeon who's now with us, gave to me, and it must not go unused: "Two roads diverged into a wood and I—I took the one less traveled by—and that has made all the difference." Robert Frost.

I did resect that tumor. The patient lived for 11 years, and justified other resections.

That road has led, for me, to membership in the Southern Surgical Association, and that has made all the difference.

Dr. Jones' experience is not small, and his associates and he deserve congratulations. They have shown again that the risk of major hepatic resection is acceptable, and benefits significant. They referred, and he did tonight, to a report of mine published in 1973, and quoted a 50% five-year survival rate following resection of malignant hepatomas.

I want to revise that report, for some of those "malignant hepatomas" were, in fact, huge hepatocytic adenomas, misclassified by our pathologists. Dr. Louis Weiland has reclassified those tumors: 34 were malignant hepatomas, and 12 benign.

My personal series with primary solid tumors as of a year ago is represented on this slide, (slide) one postoperative death for the 46 patients, and the five-year survival for the malignant lesions of 36%.

The slide outlining the complications of this group of 46 resections I could not find to bring along, but I can tell you of the postoperative progress of 27 patients that I reported earlier with major resection of metastases done since 1973. There was the one operative death during that period of time. Only six of those 27 patients were in hospital more than 12 days after operation. The longest hospital stay was 18 days, and the average stay in hospital for that group was 11 days.

One other question: What of the diagnostic methods which Dr. Jones made reference to in his manuscript?

(slide) This is a malignant hepatoma, of great size. (slide) It was not seen on this CT scan, for it was isodense with the normal liver. However, metastatic tumors are more likely to be seen, (slide) as was this solitary lesion. And when multiple lesions such as these are seen by computed tomography, the patient may be spared an operation.

(slide) Drs. Fortner and Starzl have little use for angiography, but for me it provides a map for safer travel. This shows a trisegmental lesion—these would be the feedback vessels to the medial

segment of the left lobe; and for me to have this and a venous phase portogram which shows the portal venous bifurcation is helpful.

(slide) This is a tumor of similar size involving the left hepatic lobe that required a total left lobectomy.

I want to ask Dr. Jones about his use of angiography, and have two other questions for him. One is: What incision does he favor for right lobectomy? Again, Drs. Fortner and Starzl try to avoid thoracic extension of abdominal incisions. I feel I do not have safe control or flexibility without this large, thoracoabdominal incision when resecting large lesions. (slide)

The final question Dr. Cameron has already asked: What can he tell of the natural history of cavernous hemangiomas? (slide) This is one that contained an infected hematoma, (slide) and this one was taken from a man who didn't want to give up riding his motorcycle. Those decisions were easy, but I'm unsure about the indications for resection of the medium-size lesions and, as Dr. Cameron has asked, some of the very large asymptomatic lesions.

Now, to close the other paper, if I can find my hasty notes about those questions.

(slide) Dr. Cameron asked a planted question. It had to do with: What about our controls? I have had deep concern that we had some kind of divine guidance in selecting our patients, and, therefore, we used the control curve from our retrospective study. And then Dr. Charles Moertel, a medical oncologist who is realistic about the limitations of chemotherapy, and also sympathetic with our goals, gave to me two weeks ago this group of 58 patients that were seen between 1950 and 1960. They were consecutive controls that had only hepatic metastases and were untreated.

We were looking for biologic oddities, to see if there were some people who had spontaneous remission, or quiescent cancer, or very long survivals; and we did not find any. This gives me more confidence that what we're doing surgically is a function of our surgery, more than the natural history of the disease.

I agree with Dr. Busutil that what we are working with is a very, very, very small proportion of patients. I did not have this slide made up since he asked the question; it's usually part of my presentation. (slide) Twenty per cent of patients with colorectal cancer do have hepatic metastases. Only 25% of these lesions are solitary or unilobar, and, therefore, 5% of patients have resectable lesions that would tempt the surgeon, but, as we see, only 20–30% of those are benefited.

Dr. Busutil, you did mention a risk-benefit equation that exaggerated the operative risk. My operative risk for major resections of 46 primary lesions and 30 metastatic lesions is 4%. It is that I compare with a 20–30% benefit.

I agree with your goal at UCLA with infusion chemotherapy, but would like to look at that harder. I noticed the mean survival of nine months, but I saw nothing about controls; and I would like to know how much is done to the patient—how much hospitalization; how much is done that is noxious to the patient; and what about quality of life?

I think it's very important that we do not make our efforts to palliate people noxious. As John Bucan, Lord Tweedsmuir, said, "We must have the grace to let a sick man die in peace."

How do we rule out other metastases? We can't rule them out completely, but the CT scan, particularly two-second scanner, is very likely to pick up 1–½ cm metastases in the opposite lobe.

In regard to removal of metastatic liver tumors from other visceral cancers, I'm guided by, pretty much, the cellular differentiation. There are some grade 2 stomach cancers. There are islet cell tumors of the pancreas, and other neoplasms that are biologically lazy enough to be treated by hepatic resection with similar results as those seen with colorectal metastases.

Dr. Lorimer has asked about informed consent. I know little of that but can tell you what I do. We do not have consent forms in our institution. I do spend enough time talking with patients before operation, getting to know them, that I think that we are brothers by the time they come to operation. The lawyer who leads a patient who could have had a small metastasis removed safely at the initial operation to have a second operation should be sued.

If we can find a small metastasis at the time of the primary re-

section, that's small enough to be done with negligible risk, we take it out, because we consider the cost of going back. If it's a larger metastasis, I will then defer the major resection, and wait for the patient to get off his knees, have a little holiday, and come back in four to six weeks.

I have mixed feelings about biopsy of the lesion, because biopsy may cause seeding; it would take another five minutes to discuss the pros and cons of that, and I'm already overtime. Dr. Lorimer, I see your point. Let's visit about that some time.

DR. J. B. HANKS (Closing discussion): Concerning our experience with hemangioma, all four of our patients underwent resection for large, 14 cm average, symptomatic lesions. One of these patients had a fever of unknown origin, and was worked up for a possible abscess, which turned out, in fact, to be a hemangioma.

Six years ago, Dr. Longmire presented before this society his results with major resection, which included eight large hemangiomas, and stated that the rare large hemangioma may be symptomatic by virtue of its size, and the possibility of spontaneous rupture could justify resection. He also stated that the asymptomatic hemangioma did not require treatment, and we have certainly agreed with that approach. While at Duke we are not following any small hemangiomas—we have none that we know of at this point—I would like to emphasize that all our hemangiomas were indeed symptomatic.

Concerning Dr. Adson's question about arteriograms and radionuclide scans, 21 of our 32 patients had arteriography. Five of the seven hepatomas had arteriography, and all five were positive. Of the three pediatric hepatoblastomas, two received arteriography, both of which were positive. Of our 12 metastatic lesions, 11 had arteriography of which nine were positive. Of the two that were negative, one was a small 3.4 cm lesion, and the other was a leiomyosarcoma. Three of the hemangiomas had arteriography, and all three were positive.

Twenty-three of our 32 patients underwent radionuclide scanning; 22 of these were positive. Therefore, we feel that the use of arteriography, and radionuclide scans gives a very high yield of information.

Concerning Dr. Adson's question about our surgical approach, in the pediatric population we have employed the abdominal incisions for hepatic resection. In adults with left lobectomy, or partial left lobectomy, the principal approach has been through a midline incision. For right lobectomy, we have classically employed a right subcostal incision, through which the initial assessment of operative resectability has been performed by manual abdominal exploration. When this has been confirmed, a thoracic extension has been done in the majority of the patients for enhanced exposure.

Recently, with the last patient in this series, and with a patient who underwent a right lobectomy by Dr. Jones last week, who was not included in this data, we have performed right lobectomy through entirely abdominal right subcostal margin incision.