AIN SHAMS UNIVERSITY
FACULTY OF MEDICINE

Evaluation of Surgical Treatment of Colorectal Liver metastasis

Thesis

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In general surgery

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Mohammed Abdou Hamoda

Dedication

To

Soul of my mother

Soul of my grandfather

Soul of my consaltant

dr.Awadallah Soliman Baddar

To

My wife Dr. Shaymaa Sherif

My daughters:

Nijar

AL Zahraa

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Introduction

The liver is the most frequent site of blood born metastases, irrespective of whether the primary is drained by systemic or portal veins. It is involved in about a third of all cancers, including half of those of stomach, breast, lung and those arising from the colon. Other frequent primary sites include esophagus, pancreas and those of malignant melanoma. Prostatic and ovarian metastases are exceeding rare.

(***Sherlock and Dooley, 2004*)**

The liver is the most common site of metastases, occurring in about 36% of all cancers and 50% of cancers arising in the portal area. This percentage is higher than that occurring in the lungs, the second most frequent site of metastasis. As might be anticipated, tumors in organs drained by the portal venous system metastasize to the liver more frequently than tumors arising in non-splanchnic organs.

(Altendorf, et al., 2003)

Hepatic metastases are not rare in cirrhotic liver. They are seen, however, less frequently at autopsy in cirrhotic than in non-cirrhotic livers, a phenomenon that is multifactorial in origin. First, portal-systemic shunting permits the portal venous blood to bypass the liver via intra-hepatic and extra-hepatic collateral vessels, presumably carrying malignant cells to other organs. Second the reduction in total hepatic blood flow in cirrhosis decreases the amount of blood that passes through the liver per unit of time. Third hepatic metastases are decreased in cirrhotic patients because the high premature death rate in cirrhosis reduces the risk of developing the metastases. ***(Kokudo, et al., 2001)***

When in the circulation, tumor cells are vulnerable to destruction by the most immune cells. In the bloodstream, some tumor cells form emboli by aggregating and adhering to circulating leukocytes, particularly

platelets, aggregated tumor cells are thus afforded some protection from the antitumor host effector cells. Most tumor cells circulate, however, as single cells. Extravasations of free tumor cells or tumor emboli involves adhesion to the vascular endothelium, followed by egress through the basement membrane by mechanisms similar to those involved in invasion. ***(Webb et al, 2000)***

The site of extravasations and the organ distribution of metastases generally can be predicated by the location of the primary tumor and its vascular or lymphatic drainage,. However, in many cases, the natural pathways of drainage d not readily explain the distribution of metastases. Some tumors tend to involve the adrenals with some regularity but almost never spread to skeletal muscle. Such organ tropism may be related to the expression of adhesion molecules by tumor cells whose ligands are expressed preferentially on the endothelium of target organs, another novel mechanism of site specific homing involves chemokines and their receptors. Chemokines are involved in directed movement (chemotaxis) of leukocytes. On the basis of this fact, it is speculated that blockade of chemokine receptors may limit metastases. ***(Murphy, 2001)***

From the surgical point of view, secondary deposits in the liver can be classified into Colorectal, Neuroendocrine or Non colorectal, non neroendocrine. Adenocarcinoma of the colon and rectum is the third most common site of new cancer cases and deaths in both men and women in the United States. The estimated incidence of new cases in 2002 is 148.300, with 56.600 deaths from the disease. The lifetime risk of developing colorectal cancer in the United States is 6%, with over 90% of cases occurring after the age of 50. The death rate from colorectal cancer decreased by 1.8% per year from 1992 to 1998. ***(Crawford, 2003)***

The liver is the most commonly involved organ as the sole extra colonic site for metastases with approximately 20% of patients having

hepatic metastases at time of diagnosis and of those without apparent metastases at surgery, 50% will develop metastatic liver disease (meta-synchronous). ***(Sherlock and Dooley, 2002)***

Neuroendocrine gastrointestinal tumors are derived from the neuroendocrine cell system. These tumors have widely differing clinical presentations that reflect both their organ of origin and syndromes related to excess hormone production. The neuroendocrine gastrointestinal tumors are divided into two main groups Carcinoid tumors and Endocrine pancreatic tumors. Carcinoid tumors are now described according to their organ of origin, whereas pancreatic endocrine tumors are described according to their main hormone production and related clinical syndrome (insulinomas, gastrinomas, VIPomas, glucagonomas, somatostatinomas and non-functioning endocrine pancreatic tumors).

(Pope and Poston, 2003)

The diffuse neuroendocrine system includes all neuronal and endocrine cells that share a common phenotype characterized by simultaneous expression of general neuroendocrine markers and cell type specific regulatory peptides. It is now recognized that neuroendocrine cells are involved in a wide variety of tumors. The majority occurs as primary tumors of the gastrointestinal tract; however, they can also be found in locations such as the lung, ovary, thymus and kidney.

(Pope and Poston, 2003)

The prognosis depends on the site of the primary and the type of the tumour and its degree of differentiation. In general, patients die within one year of diagnosis of hepatic metastases. Secondaries from tumours of the colon and rectum have the best outlook. The five years survival after resection of the colorectal metastases was 42%. Patients with tumour greater than 5cm. in diameter have a poorer outcome.

(Millward and Whorwell, 2004)

Aim of the work

The Aim of this study is to evaluate the safety of liver resection in treatment of colorectal hepatic metastasis.

PATIENTS AND METHODS

Study Design:

The is prospective study which done in AIN SHAMS University Hospitals throughout 2 years.

Patients:

Inclusion Criteria:

Colorectal liver metastasis which shows:

1- Liver only disease.
2- If lung metastasis is positive we treat lung metastasis at first.
3- Fit for hepatectomy i.e.
    a- Tumors can be resected with at least 1 cm safety margin and residual liver volume of more than 30% in non cirrhotic patients and 50% in cirrhotic patent.
    b- No medical contraindication.

Exclusion Criteria:

1- Patients with significant Portal hypertension i.e spleen > 12 cm or O.V. >grade 1 or platelet count > 100.0000
2- Major vascular invasion.
3- Severe concomitant medical condition such as, congestive heart failure, chronic lung disease, and renal failure.
4- Extra hepatic metastasis. e.g. Bone or C.N.S.

Methods:

Preoperative evaluation:

The Work up to exclude distal metastasis e.g.:

1- Bone Scan if pt. has specific bony aches

2- C T chest.

3- Tumour markers.

4- C T pelvis and abdomen and Portography.

If Patients need major hepatectomy (≥ 3 segments) Volumetry study should be done. If Residual liver volume is less than 30% ; portal vein embolization to ipsilateral lobe should be done then after one month C T Volumetry should be repeated to insure that the residual liver volume is more than 30%.

- **Laboratory:**
  - CBC & PT & PC.
  - Liver function tests and liver enzymes.
  - CEA
  - Kidney function tests.
  - Fasting & post prandial (after 2 hours) blood glucose level.
- **Chest consultation including pulmonary function tests.**
- **Cardiac consultation including echocardiography.**

Operative:

J shape incision or bilateral subcostal incision, start by exploration of the abdomen for any peritoneal deposits or lymph nodes deposits, if +

ve frozen section done and if + ve we stop operation, intra operative U.S. to visualize small hidden deposits (Metastasis).

In anatomical Resection:

Mobilization of the affected lobe, inflow control of the planned resected part, resection using harmonic if coagulation needed check for biliary leak by injection of saline in cystic duct.

In Non anatomical Resection:

Transection with 1 cm safety margin, intermittent use of pringle maneuver if excess bleeding occur with 15 min. clamping followed by 15 min. decamping in cycles after complete hemostasis abdominal drains left routinely.

Post operative:

Patients who undergo major resection must be transfer to I C U but those with minor resection the decision to transfer to I C U or the ward done after discussing with anesthesia team at the end of operation, Oral feeding start once audible intestinal sounds, antibiotic 3rd generation cephalosporin for 5days, Drains removed once output is clear full laboratiories must be done at 1st, 3rd and 7th

Follow up:

Patients should be followed up in outpatient clinic once per week for the 1st month with liver function tests then once per month for three months then every 6 month. Lives function tests then once per month for three months then every 6 month, patients should be reviewed by surgeon and oncologist, tumor markers every 3 month abdominal U.S. and C.T. every 6 month.

Data Analysis:

The patients' parameters will be collected with emphasis on:

A- Pre operatively:

1- Age, Sex, and Lab. investigations. Tumor markers (CEA).Ultrasound report, Helical (triphasic) CT abdomen & pelvis and site ,type of cancer colon .

B- Intra-operative

Operative time (minutes between skin incision and end of skin closure), Intra-operative complications, Estimated blood loss, Need for intra-operative blood transfusion.

C- Postoperative:

Hospital stay: number of days spent in hospital postoperatively, Postoperative complications: hemorrhage, billiary leakage, infections, Period of ileus, Time till resuming complete oral intake, Skin incision related morbidity at 1 week, 1 month, and 3months after discharge during the patient's follow up visit in the outpatient clinic: defined as bleeding, infection, necrosis, skin retraction, incisional hernia, suture dehiscence within the time period allowed for follow up as mentioned above.

All the patient's data will be collected, recorded, tabulated and statistically analyzed.