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AN OVERVIEW ON DIAGNOSIS AND SURGICAL MANAGEMENT OF GALLBLADDER CANCER

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ABSTRACT

Gallbladder cancer is among the most deadly cancers, and it continues to present surgeons with numerous challenges. Cholelithiasis, an abnormal pancreaticobiliary junction, and focal mucosal microcalcifications are all known risk factors for gallbladder carcinoma. The most common histologic type in most patients is adenocarcinoma, which is frequently associated with Kras and p53 mutations. Endoscopic ultrasonography, magnetic resonance cholangiopancreatography, as well as helical computed tomography, as well as radiologic or endoscopic improvements in endoscopic ultrasonography as well as magnetic resonance cholangialpancratia, have improved preoperative staging. Cholecystectomy (subsegmental surgical excision of segments IVB but instead V plus a hepatoduodenal ligament lymphadenectomy) for advanced disease without indications of distant metastasis (T2-4/N0-N2) or a radical cholecystectomy (subsegmental resection of segments IVB as well as V plus a hepatoduodenal musculotendinous lymphadenectomy) for severe stages without indications of distant metastasis More extensive hepatic resection, such as extended right hepatectomy or central segmentectomy with caudate lobectomy, has been recommended by certain surgeons. Patients who underwent a pancreaticoduodenectomy to enhance distal ductal margins as well as lymphadenectomy for T3 or T4 malignancies were studied by Japanese surgeons. These patients had a reduced incidence of tumor recurrence but no benefit in terms of survival. Adjuvant treatment options are still restricted. The most frequent postoperative treatment is radiation therapy with fluorouracil radio sensitization. Capecitabine, oxaliplatin, & bevacizumab are now being studied in the treatment of gallbladder cancer in clinical studies.

KEYWORDS: *Biliary, Cancer, Cholecystectomy, Endoscopic, Gallbladder.*

1. INTRODUCTION

Gallbladder cancer (GBC), the most frequent malignant tumor of the biliary system and the sixth most common gastrointestinal cancer, is a rare and extremely deadly illness. In the United States in 2005, it was projected that 7,480 instances of biliary tract cancer, the majority of which sprang from the gallbladder, were identified, with 3,340 people expected to die from the illness. GBC usually appears at an advanced stage in most patients, typically at the time of cholecystectomy for suspected chronic cholecystitis. GBC presents a challenge to both clinicians and surgeons in terms of improving results[1].

1.1.GBC affects

Women more often than men in all populations, with prevalence's three to five times greater for females in certain studies.4 Gallstones are more common in women over 65 who have a lengthy history of gallstones. GBC has a global geographic distribution that corresponds with the incidence of gallstone disease, according to our experience at Mayo Clinic Rochester. Bolivia has the greatest frequency of GBC in the world, although it is also found in Chile, Northern India, or Central Europe. The incidence of GBC varies by ethnic group in the United States, with Native Americans as well as Mexican Americans having the greatest rates. With a frequency of 1/100,000, African Americans have the lowest rate of GBC[2].

1.2.Pathogenesis and Risk Factors:

The pathophysiology of GBC is poorly understood, and the illness is presently thought to have a complex origin. Obesity, a high fat and carbohydrate diet, numerous pregnancies, and the use of estrogens are all linked to an increased risk of gallstone disease. The most well-known risk factor for GBC is cholelithiasis. Chile, which has the highest GBC mortality rate in the world, also has one of the highest rates of cholelithiasis. Gallstones affect the overwhelming majority of individuals with gallbladder neoplasms. Patients with gallstones have a four to five times greater risk of GBC than those who are acalculous.

In a survey of 2,583 Rochester, Minnesota residents with cholelithiasis, researchers discovered a threefold increase among the incidence of GBC in males with stones. Surprisingly, women's risk was not raised. The mechanism that causes cholelithiasis to predispose to GBC is unknown. Gallbladder neoplasia has been linked to a big stone size and the length of time that gallstone symptoms have been present. In other investigations, the risk of GBC was related to the size of the stones. Because gall bladder size is linked to the age of the calculus, the length of time the stone has indeed been present in the pathogenesis of GBC is likely the most important component. Gallstones may cause chronic inflammation of the gallbladder mucosa, which can lead to malignant transformation in the form of atypia, dysplasia, carcinoma in situ, and ultimately invasive cancer. The p53 gene mutations may play a significant role in this chain of events[3].

The majority of asymptomatic gallbladder polyps are benign lesions that do not develop to malignancy. Neoplastic polyps are a risk factor for GBC because they may contain carcinoma foci. Polyp diameter larger than 10 mm, patient aging greater than 50 years, existence of gallstones, solitary polyps, and symptomatic polyps are all linked with an increased risk of cancer. Polyps greater than 10 mm should be treated by cholecystectomy, while polyps less than 10 mm may be monitored with serial ultrasonography in individuals without additional risk factors. Xantho granulomatous cholecystitis, persistent typhoid infection, gallbladder adenomyomas, as well as inflammatory bowel illness are all linked to an elevated incidence of GBC[4].

1.3. Pathology:

In the literature, the dysplasia–carcinoma sequence for GBC has been suggested. In most specimens with invasive GBC, black revealed regions of cancer in situ. 29 It is predicted that it will take 10 to 15 years to develop from dysplasia to cancer. 30 GBC is characterized by a background of persistent mucosal inflammation rather than adenomatous polyps. The common incidence of an adenoma–carcinoma sequence, as observed in colon cancer, has yet to be validated in GBC[5].

Papillary carcinomas develop into the gallbladder's lumen are much less aggressive. They are less likely to infiltrate the liver and become less likely to spread to lymph nodes. The gallbladder may be the location of distant metastasis from other cancers, with lung or melanoma being the most frequent. Studies looking at the molecular changes in GBC have shown that p53 and K-ras mutations are common. The frequency of GBC with p53 mutations has been found to vary from 35 to 92 percent. GBC has been linked to K-ras and p53 mutations in AJPBD patients, indicating that pancreatic juice reflux may contribute to a carcinogenic environment. 36 The identification of a K-ras mutation may be helpful in the early diagnosis of GBC in patients with AJPBD[6].

1.4.Clinical Significance:

The delayed clinical manifestations of GBC in most patients, owing to a lack of specific symptoms as well as low clinical suspicion, is a major obstacle to improving GBC outcomes. So because symptoms of GBC are often vague, at least 20% of patients are identified with biliary colic and cholelithiasis after cholecystectomy for biliary colic and cholelithiasis. The most frequent symptom of GBC is abdominal discomfort (73%) followed by nausea and vomiting (43%), jaundice (37%), anorexia (35%), as well as weight loss (35%). (35 percent). Ascites, a palpable tumor, and constitutional symptoms are all signs of advanced illness with a dismal prognosis. Duodenal blockage, gastrointestinal bleeding, or hematobilia owing to invasion of neighboring intestines or arteries are less frequent presentations[7].

1.5. Staging:

Because the degree of penetration through the gallbladder wall and the amount of lymph node metastases determine surgical treatment and correlate with prognosis, GBC staging is an important part of the complete management and reporting of this tumor. GBC is also divided into grades according on the degree of differentiation, with grade 1 being the most differentiated and grade 10 being the least differentiated. The most frequent malignancies are those of grade 3. GBC grading has no bearing on prognosis. GBC has a number of different staging categories. Newer categorization methods have superseded the Nevin–Moran classification system, which was first published in 1976 and was widely used in the past[8].

The Japanese Biliary Surgeons Society staging system, the customized Nevin–Moran classification, the TNM system developed by the International Union Against Cancer as well as the American Joint Committee on Cancer (AJCC), and the TNM system developed by the International Union Against Cancer as well as the American Joint Committee on Cancer (AJCC), and also the TNM system developed by the International Confederation Against Cancer and the American Working Group on Cancer (AJCC), and the TNM system developed by the International Union Against Cancer as well as the American Joint Committee on While there is still debate over whether method is better for predicting survival, the TNM system is the most often utilized[9].

1.6. Surgical Intervention:

The aim of GBC treatment is to achieve a R0 resection. Only a third of patients are surgical candidates due to their advanced stage upon presentation. The liver parenchyma, hepatoduodenal ligament structures, and surrounding organs are the primary targets of GBC (duodenum, transverse colon, stomach, and small bowel). The patient is not suitable for surgical resection if preoperative imaging shows hepatic metastases, encasement of the main portal vein or appropriate hepatic artery, or extensive celiac or para-aortic lymphadenopathy. Because of the

high incidence of undetected metastatic GBC, staging laparoscopy should be done regularly before to celiotomy.

If laparoscopy reveals metastatic illness, tissue biopsy may be used to prevent a nontherapeutic laparotomy. Gross vascular invasion including encasement of major vessels (T4), ascites, widespread hepatic participation, distant metastases, as well as poor functional status are all contraindications to surgical removal. Despite these dismal statistics, surgical resection remains the sole chance for a cure. Only 38% of GBC patients treated in their hospital during the past 20 years were suitable for resection, according to Ito and colleagues. In comparison to 13 percent, the group that had full resection (all phases considered) rather than palliative surgery had a better overall survival rate. 59 Patients who did not have surgery had a 0% 5-year survival rate, according to the same study

1.7.GBC and PD:

When it comes to GBC surgical treatment, western doctors are often less aggressive than their Japanese colleagues. The usage of PD for GBC is one such example. The possibility of preforming a PD for certain T3 and T4 GBCs has been documented in many Japanese research. Infiltration of malignancy into the pancreatic head and metastasis to peri-pancreatic lymph nodes are the most frequent reasons for PD. Araida's series of PD (n=93) for GBC was the biggest. 75 T2–T4 lesions were seen in all PD patients.

If there was no hepatoduodenal ligament invasion or microscopic lymph node metastases, there was no survival advantage for individuals who had extensive (N2, N3) lymphadenectomy alone. Patients with PD who had microscopic lymph node metastases, on the other hand, had a reduced recurrence rate. According to this research, PD may assist a small group of patients, but for the vast majority of GBC patients, a complete lymph node excision of the N1 and N2 nodes will be more beneficial for long-term survival and lower recurrence rates.

1.8. Treatment for Palliative Care:

Palliative treatments may be considered if the patient's GBC is determined to be unresectable after surgical investigation. Biliary blockage affects more than 60% of individuals with GBC. The treatment is personalized, although in certain individuals, a Roux-en-Y hepaticojejunostomy at the proximal common hepatic duct or hilum may be necessary. Gastric blockage occurs in about half of all GBC patients who also have biliary obstruction. In this patient group, a gastrojejunostomy is often done to relieve or prevent this disease. In patients with low functional status, short life expectancy, or severe comorbidities, nonoperative alternatives such as percutaneous or endoscopic end biliary stents, as well as endoscopic enteric stenting as well as feeding tubes, may be utilized.

In this patient group, no controlled studies have evaluated the use of stents vs surgical bypass. Patients who were palliated with a biliary-enteric bypass had fewer septic sequelae than those who were palliated with a biliary stent, according to a tiny research published around ten years ago. Given the significant morbidity associated with stents, it is preferable to conduct a biliary enteric bypass on patients who are determined to have locally advanced, unresectable illness during abdominal exploration. Nonoperative treatment of biliary and intestinal blockage generally offers a superior method of palliation for patients with metastatic illness who have a short life expectancy[10].

1.9. Adjuvant Therapy is a kind of treatment that is used to help:

For GBC, no pharmacological treatment has been shown to be effective. Fluorouracil has traditionally been included in adjuvant chemotherapy regimens. External beam radiation is often employed in fluorouracil chemo sensitization, although there is little evidence to back up its effectiveness. Over a 12-year period, Mayo Clinic gave adjuvant radiation (54 Gy) with concomitant 5-fluorouracil (5-FU) to 21 consecutive patients. The overall 5-year survival rate was 33%, with stage I–III illness having a 65 percent 5-year survival rate and stage IV disease having a 0% 5-year survival rate. Patients with large residual disease (R2), micro residual tumor (R1), and no residual disease (R0) had median survivals of 0.6, 1.4, &5.1 years, respectively. This research found that the survival rate was higher than that of historical controls.

2. DISCUSSION

Gallbladder cancer is one of the most lethal tumors, and it continues to provide a number of challenges for surgeons. Gallbladder cancer is linked to cholelithiasis, an aberrant pancreaticobiliary junction, and localized mucosal microcalcifications. Adenocarcinoma is the most frequent histologic type in most people, and it's commonly related to Kras and p53 mutations. Preoperative staging has improved thanks to advances in endoscopic ultrasonography, magnetic resonance cholangiopancreatography, including helical computed tomography, as well as radiologic and endoscopic advancements in endoscopic ultrasonography and magnetic resonance cholangiopancreatography.

Cholecystectomy (subsegmental resection of segments IVB and V plus a hepatoduodenal ligament lymphadenectomy) or radical cholecystectomy (subsegmental surgical excision of sections IVB as well as V plus an effective and efficient ligament lymphadenectomy) for advanced disease without signs of distant metastasis (T2-4/N0-N2) If a Tis or T1 tumor is discovered by chance, a GBC has the best chance of being healed. A simple cholecystectomy is all that is required to treat these cancers. More advanced GBC has a poor prognosis, although evidence that extensive radical surgical therapy, most often radical cholecystectomy and regional lymphadenectomy, may improve results. With increased suspicion and rigorous surgical resection, survival rates for those with minimal GBC should improve. Because the preponderance of GBC patients have visible or concealed metastases, they will not be treated until and until new systemic medications improve the results seen with current therapies.

3. CONCLUSION

A GBC has the greatest chance of being cured if a Tis or T1 tumor is found by accident. For these malignancies, a simple cholecystectomy is sufficient treatment. The prognosis for more advanced GBC is generally bleak, although intensive radical surgical treatment, most frequently radical cholecystectomy as well as regional lymphadenectomy, has been shown to improve outcomes. Survival results for individuals with limited GBC should improve with greater suspicion and aggressive surgical resection. Because the majority of GBC patients have visible or hidden metastases, they will not be treated until novel systemic medicines improve the outcomes observed with existing treatments.

Certain surgeons have advocated for more extreme hepatic resections, such as an extended right hepatectomy or a central segmentectomy with caudate lobectomy. Japanese surgeons looked at patients who had a pancreaticoduodenectomy to improve distal ductal margins after lymphadenectomy for T3 or T4 cancers. These individuals had a lower risk of local recurrence but no improvement in survival. Treatment options for adjuvant therapy are currently limited.

Radiation therapy using fluorouracil radio sensitization is the most common postoperative treatment. In clinical trials, capecitabine, oxaliplatin, and bevacizumab are being investigated for the treatment of gallbladder cancer.

REFERNCES:

1. Y. A. Wang *et al.*, "Germline breast cancer susceptibility gene mutations and breast cancer outcomes," *BMC Cancer*, 2018, doi: 10.1186/s12885-018-4229-5.

2. K. M. Reid, A. R. De La Medina, and J. H. Donohue, "Diagnosis and surgical management of gallbladder cancer: A review," *J. Gastrointest. Surg.*, 2007, doi: 10.1007/s11605-006-0075-x.

3. H. Watson *et al.*, "Does a second resection provide a survival benefit in patients diagnosed with incidental T1b/T2 gallbladder cancer following cholecystectomy?," *HPB*, 2017, doi: 10.1016/j.hpb.2016.11.006.

4. R. Hundal and E. A. Shaffer, "Gallbladder cancer: Epidemiology and outcome," *Clinical Epidemiology*. 2014, doi: 10.2147/CLEP.S37357.

5. R. Kanthan, J. L. Senger, S. Ahmed, and S. C. Kanthan, "Gallbladder cancer in the 21st century," *Journal of Oncology*. 2015, doi: 10.1155/2015/967472.

6. G. Younan, M. Schumm, F. Ali, and K. K. Christians, "Gallbladder Volvulus in a Patient with Type I Choledochal Cyst: A Case Report and Review of the Literature," *Case Rep. Surg.*, 2016, doi: 10.1155/2016/5626531.

7. D. Tartaglia *et al.*, "Less is more: an outcome assessment of patients operated for gallstone ileus without fistula treatment," *Int. J. Surg. Case Rep.*, 2017, doi: 10.1016/j.ijscr.2017.07.007.

8. E. S. McDonald, A. S. Clark, J. Tchou, P. Zhang, and G. M. Freedman, "Clinical diagnosis and management of breast cancer," *J. Nucl. Med.*, 2016, doi: 10.2967/jnumed.115.157834.

9. X. Dai, H. Cheng, Z. Bai, and J. Li, "Breast cancer cell line classification and Its relevance with breast tumor subtyping," *Journal of Cancer*. 2017, doi: 10.7150/jca.18457.

10. J. M. Lebert, R. Lester, E. Powell, M. Seal, and J. McCarthy, "Advances in the systemic treatment of triple-negative breast cancer," *Current Oncology*. 2018, doi: 10.3747/co.25.3954.