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9 years long-Term Survival of metastatic Intrahepatic Cholangiocarcinoma: A case report

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Abstract:
Cholangiocarcinoma is the second most common hepatic cancer, with a poor prognosis and a high mortality rate.
We report the case of a 73-year-old woman, followed for intrahepatic cholangiocarcinoma in 2010, she had a left hepatectomy with lymph node dissection followed by surveillance for one year. The evolution has been marked by a metastatic relapse, and was put under chemotherapy-based gemcitabine with a good response. Currently the patient is under good control.

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I. Introduction:

Cholangiocarcinoma is the second most common primary malignant liver tumor, accounting for 10-20% of primary liver cancers.

The average age of onset is 50 years and the majority of cases in the western world are diagnosed at age 65 or later.

The prognosis of cholangiocarcinoma is very poor with the mortality rate is higher for men than for women. The one-year relative survival rate increased from 16.4% in the 1970s to 27.6% in the 1990s, but the 5-year survival rate has not changed since then (<5%).

II. Case Presentation:

We report the case of a 73-year-old patient, followed in the department of medical oncology at Hassan II University hospital for intrahepatic cholangiocarcinoma.

The patient presented to the ER with pain in the right hypochondrium, with an abdominal CT scan of tumor proliferation in the gall bladder, she underwent left hepatectomy with lymph node dissection. The pathological examination showed a moderately differentiated and infiltrating cholangiocarcinoma measuring 7*6.5*6cm, classified pT2N0Mx.

She had not receive chemotherapy in adjuvant because the patient refused other treatment.

After a delay of 12 months, the patient had an abdominal pain, the clinical exam found the patient with Karnofsky index < 60 and abdominal distension. The thoraco-abdominal CT shows a recurrent liver with peritoneal carcinomatosis with increased ACE marker at 122. We had put our patient under monochemotherapy with gemcitabine, having received 14 cures for 2 years, with a good tolerance and good clinical, biological and radiological response, the decision was to make a therapeutic break. After two years of follow-up, the patient presented a radiological progression, the decision was to restart gemcitabine. The patient has received 16 cures during 2 years with good response, then an another therapeutic break was conducted. Three months later, the patient presented a new radiological progression from which the resumption of gemcitabine 7 cures, with a good biological and radiological response, hence a therapeutic break, once again.

Seven months later, she presented a new radiological progression, hence the initiation of gemcitabine, this time the patient received 14 cycles.

Currently the patient is in clinical, biological and radiological stability under chemotherapy.

III. Discussion:

Cholangiocarcinoma (CCA) is the most common malignant tumor of the bile ducts (1). Histologically, 90% of SCCs are adenocarcinomas associated with other variants, including ring-type rings, clear cells, papillary adenocarcinomas, intestinal adenocarcinomas, oat cell carcinomas, adenosquamous carcinomas and squamous cell carcinomas (2).

The exact cause of cholangiocarcinoma is unknown and most cases occur sporadically, but there are several well-defined risk factors. The most common of these is primary sclerosing cholangitis (PSC).

Generally, cholangiocarcinoma develops in the context of chronic inflammation and cholestasis (3). Pre-inflammatory cytokines such as interleukin-6 (IL-6) have been associated with cholangiocarcinogenesis (4,5).

Surgical treatments are the only potentially curative therapeutic options for intrahepatic CCAs. Unfortunately, only a minority of patients are eligible for surgical resection. The surgical results depend largely on the success of the R0 resection (negative surgical margins). The rates of resecability vary between 19 and 74%. Recidivism rates are generally high around 60-65% (6). The survival rates depend on the R0 resection and the state of the lymph nodes. After R0 resection, the 5-year survival rates are 23-42% versus 0% after R + resection (7.8,9).

The five-year survival rate in patients with N1 status after surgical resection is 0-9% and up to 43% in the case of N0 disease (8, 10).

For patients unable to undergo curative surgical treatment; the current standard treatment is bi-chemotherapy with gemcitabine and cisplatin, which has shown a significant increase in progression-free survival compared to the regimen containing gemcitabine alone, based on the ABC-02 trial (11).

For intrahepatic cholangiocarcinomas with residual local disease after resection, the National Comprehensive Cancer Network (NCCN) category 1 recommendation is combination therapy with gemcitabine-cisplatin. Locoregional care is a category 2B recommendation, with fluoropyrimidine or other chemotherapy based on gemcitabine or the best supportive care as an alternative.

For unresecable extrahepatic cholangiocarcinoma, NCCN recommends combination therapy with gemcitabine and cisplatin (category 1). Alternatives are a chemotherapy regimen based on fluoropyrimidine or other gemcitabine or fluoropyrimidine chemoradiotherapy. NCCN also recommends gemcitabine cisplatin combination therapy as a Tier 1 option for metastatic extrahepatic cholangiocarcinoma, with fluoropyrimidine or other gemcitabine-based chemotherapy regimens.

In a Korean study, adjuvant therapy improved the prognosis in patients with positive metastatic lymph nodes (median OS 21.9 vs. 11.5 months, p = 0.003). The overall recurrence rate was 55.0% and distant metastases (39.7%) were more frequent than locoregional recurrences (20.8%). The true rate of 5-year OS after R0 resection of hilar cholangiocarcinoma is 30.1%. Adjuvant therapy may be beneficial in patients with lymph node metastases (12).

The cohort study based on the Netherland population showed that in patients with hilar cholangiocarcinoma, 26% were found to be resecable. The long-term survival rate of 7% of unresectable patients is remarkable. Patients with metastases had a much worse prognosis with a median of 4 months (13).

The median survival for unresectable tumor is 9 to 15 months (14).

The results of the available randomized trials demonstrate the superiority of a bi-chemotherapy comprising a platinum, mainly with gemcitabine, over a monotherapy with fluoropyrimidine or gemcitabine or over the best exclusive supportive care.

the most widely used protocol in cholangiocarcinoma is the cisplatin gemcitabine combination, with a response rate around 8 months (15).

In a Scandinavian phase III trial in 90 patients with advanced biliary or pancreatic cancer, chemotherapy with 5FU and folinic acid (plus etoposide in patients in good general condition) was not significantly superior to exclusive supportive care in the sub. -group of patients with biliary cancer, and the toxicity was significant (grade 3-4: 41%) (16).

An Indian single-center phase III trial in 81 patients with advanced gallbladder carcinoma showed an overall survival benefit of a gemcitabine-oxaliplatin combination compared to exclusive supportive care, but also compared to a 5FU-folinic acid combination. (9.5, 4.5 and 4.6 months respectively, p = 0.039) (17).

IV. Conclusion:

Cholangiocarcinoma is an uncommon malignancy tumor. Its prognosis is dark with a survival of less than 5% at five years. Radical surgery is the only modality of potentially curative treatment, while the impact of chemotherapy on survival remains controversial.

References:

[1]. Shaib Y, El-Serag HB. The epidemiology of cholangiocarcinoma. Semin Liver Dis 2004;24:115-25.
[2]. Olnes MJ, Erlich R. A review and update on cholangiocarcinoma. Oncology 2004;66:167-79.
[3]. Liu R, Cox K, Guthery SL, Book L, Witt B, Chadwick B, *et al.* Cholangiocarcinoma and high-grade dysplasia in young patients with primary sclerosing cholangitis. Dig Dis Sci 2014;59:2320-4.
[4]. Sugawara H, Yasoshima M, Katayanagi K, Kono N, Watanabe Y, Harada K, *et al.* Relationship between interleukin-6 and proliferation and differentiation in cholangiocarcinoma. Histopathology 1998;33:145-53.
[5]. Park J, Tadlock L, Gores GJ, Patel T. Inhibition of interleukin 6-mediated mitogen-activated protein kinase activation attenuates growth of a cholangiocarcinoma cell line. Hepatology 1999;30:1128-33.

[6]. Endo I, Gonen M, Yopp AC, Dalal KM, Zhou Q, Klimstra D, *et al.* Intrahepatic cholangiocarcinoma: Rising frequency, improved survival, and determinants of outcome after resection. Ann Surg 2008;248:84-96.
[7]. DeOliveira ML, Cunningham SC, Cameron JL, Kamangar F, Winter JM, Lillemoe KD, *et al.* Cholangiocarcinoma: Thirty-one-year experience with 564 patients at a single institution. Ann Surg 2007;245:755-62.
[8]. Guglielmi A, Ruzzenente A, Campagnaro T, Pachera S, Valdegamberi A, Nicoli P, *et al.* Intrahepatic cholangiocarcinoma: Prognostic factors after surgical resection. World J Surg 2009;33:1247-54.
[9]. Lang H, Sotiropoulos GC, Sgourakis G, Schmitz KJ, Paul A, Hilgard P, *et al.* Operations for intrahepatic cholangiocarcinoma: Single-institution experience of 158 patients. J Am Coll Surg 2009;208:218-28.
[10]. Morimoto Y, Tanaka Y, Ito T, Nakahara M, Nakaba H, Nishida T, *et al.* Long-term survival and prognostic factors in the surgical treatment for intrahepatic cholangiocarcinoma. J Hepatobiliary Pancreat Surg 2003;10:432-40.
[11]. Okusaka T, Nakachi K, Fukutomi A, Mizuno N, Ohkawa S, Funakoshi A, *et al.* Gemcitabine alone or in combination with cisplatin in patients with biliary tract cancer: A comparative multicentre study in Japan. Br J Cancer 2010;103:469-74.
[12]. Kang, M. J., Jang, J.-Y., Chang, J., Shin, Y. C., Lee, D., Kim, H. B., & Kim, S.-W. (2016). Actual Long-Term Survival Outcome of 403 Consecutive Patients with Hilar Cholangiocarcinoma. World Journal of Surgery, 40(10), 2451–2459
[13]. Ruys, A. T., van Haelst, S., Busch, O. R., Rauws, E. A., Gouma, D. J., & van Gulik, T. M. (2012). Long-term Survival in Hilar Cholangiocarcinoma also Possible in Unresectable Patients. World Journal of Surgery, 36(9), 2179–2186.
[14]. Endo 2008, Eckel 2007, Valle 2010, Sharma 2010
[15]. Eckmann K.R., Patel D.K., Landgraf A., Slade J.H., Lin E., Kaur H., Loyer E., Weatherly J.M., Javle M. Chemotherapy outcomes for the treatment of unresectable intrahepatic and hilar cholangiocarcinoma: A retrospective analysis. Gastrointest Cancer Res. 2011;4:155–160.
[16]. Glimelius B, Hoffman K, Sjödén PO, Jacobsson G, Sellström H, Enander LK, Linné T, Svensson C. Chemotherapy improves survival and quality of life in advanced pancreatic and biliary cancer. Ann Oncol. 1996 Aug;7(6):593-600.
[17]. Sharma A, Dwary AD, Mohanti BK, Deo SV, Pal S, Sreenivas V, Raina V, Shukla NK, Thulkar S, Garg P, Chaudhary SP. Best supportive care compared with chemotherapy for unresectable gall bladder cancer: a randomized controlled study. J Clin Oncol. 2010 Oct 20;28(30):4581-6.)

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