Radioembolization with yttrium as neoadjuvant therapy in initially unresectable intrahepatic cholangiocarcinoma

Radioembolización con ytrio como terapia neoadyuvante en el colangiocarcinoma intrahepático inicialmente irresecable

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary liver tumour. Surgical resection is the only potentially curative treatment. However, 60%–70% of cases are not candidates for surgery at diagnosis, either because of disease dissemination or because the hepatic location does not leave sufficient remnant[1,2]. Although most of these cases are treated with chemotherapy (CT), radioembolization with yttrium microspheres, also known as selective internal radiation therapy (SIRT), has been proposed as a treatment that can salvage patients for surgery with curative intent; however, there is little published evidence on this indication[2–4].

SIRT is an intra-arterial brachytherapy primarily used to treat hepatocarcinoma and hepatic metastases, however its use in ICC is not as widespread[3,4]. In addition to direct locoregional therapy to the tumour, SIRT can induce contralateral liver hypertrophy, allowing liver resection with curative intent in patients with previous insufficient liver remnant[2].

We present the case of a 55-year-old woman with no history of interest, histologically diagnosed with a 60 × 48 × 56 mm ICC located on the bifurcation of the hepatic pedicle, affecting segments IV, V, VIII and in direct contact with the middle hepatic vein without extrahepatic dissemination (Fig. 1a). Initially a right trisectionectomy was required, but the remaining liver (IBS-III) did not have sufficient residual volume (200 cm^3 [18%]). Therefore, combined chemotherapy with gemcitabine-oxaliplatin and SIRT was given at two doses of .9 (80%) and .2 (20%) GBq via the right hepatic artery and an S4 branch, respectively. Six months after radioembolization and after 12 cycles of chemotherapy, there was slight decrease of the lesion and hypertrophy of the liver remnant of up to 527 cm^3 (40%), representing a growth of 160% (Fig. 1b). The functionality of the future remnant liver was calculated by Tc^{99}-mebrofenin SPECT scintigraphy, resulting in a De Graaf index of 2.1%/min/m^2 and HIBA index of 20%. The patient had adequate liver function at all times, with normal bilirubin and liver enzyme values. In view of these findings, surgical resection was proposed.

The operation was performed 339 days after diagnosis, revealing significant atrophy of the right liver and hypertrophy of the left lateral sector (Fig. 1.2). A right trisectionectomy with caudectomy and resection of the extrahepatic bile duct with lymphadenectomy was performed. Biliodigestive reconstruction was performed with a double Roux-en-Y hepaticojejunostomy. Portal pressures were taken at the beginning and end of the surgery, showing a gradient of 10 mmHg between the portal vein and the suprahepatic inferior vena cava, and therefore we decided not to act on portal flow. The definitive pathology report confirmed a poorly differentiated ICC (G3) with free margins without perineural or vascular infiltration (pT1bN0).

On the 8th postoperative day, with no test data of liver failure (Br 0.8, FA 120, GGT 990 GOT/GPT 75/38, TP 1.02), the patient developed ascites, and therefore a new pressure measurement was taken, showing a gradient of 13 mmHg between free and wedged hepatic vein. In view of these findings, a selective partial embolization of 60% of the splenic parenchyma was performed. After one year of follow-up, the patient is free of disease, and her tumour marker levels Ca 19.9, CEA and AFP remain within normal limits.

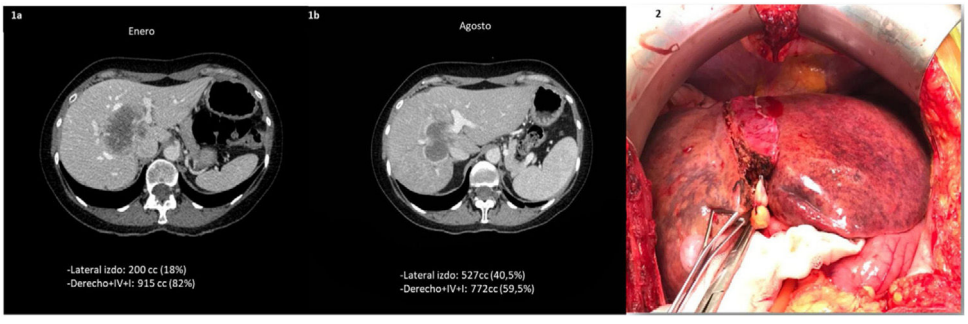

Fig. 1 – (1) Progress after neoadjuvant treatment. (1a) Venous phase of initial CT scan, prior to treatment: large hypodense mass in central position in direct contact with the middle hepatic vein. (1b) Post-embolization CT scan: significant contralateral hypertrophy (S II–III). (2) Surgical intervention: right hepatic atrophy and contralateral hypertrophy, of segments II–III.

Table 1 – Summary of published results of patients with ICC treated with neoadjuvant chemotherapy with yttrium and subsequent surgical resection.

Publication	Type of tumour	Type of neoadjuvant chemotherapy	Patients with salvage surgery	Type of resection	Hypertrophy of liver remnant (%)	Months of follow-up	Recurrence
Vouche et al.[7]	ICC	Gemcitabine ± Cisplatin	1	Right hepatectomy	38	ND	1/1
Rayar et al.[8]	ICC	Gemcitabine + Platinum	8	Right hepatectomy 2 Right Tri. 5 Left Tri. 1	9	7.2	2/8
Servajean et al.[9]	ICC	GEMOX + FOLFIRINOX	1	Left hepatectomy	ND	12	0/1
Lewandowski et al.[10]	ICC	No	2	Right hepatectomy	30	20	1/2
Gaba et al.[a]	ICC	No	3	Right hepatectomy	36,3	ND	1/3

ICC: Intrahepatic cholangiocarcinoma; Left Tri.: Left trisectionectomy; ND: no data; Right Tri.: Right trisectionectomy.
[a] Gaba et al. Ann Surg Oncol 2009; 16:1587–1596.

SIRT involves the controlled infusion of yttrium-loaded microspheres through the arteries supplying the tumours causing controlled tissue damage[5]. It can be used as a stand-alone therapy in CT-refractory patients or in combination with CT[4]. There is currently insufficient evidence to recommend initial SIRT versus CT + SIRT, they can be used concomitantly or even months after CT. In ICC, SIRT has been proposed as salvage treatment in patients initially not candidates for surgery, and achieves similar survival to patients treated with initial surgery[2,5,6]. This treatment, on the one hand, produces tumour necrosis, thus achieving local control of the disease in half of cases and even a reduction in tumour size in up to 36.4% of cases[2]. On the other hand, contralateral hypertrophy occurs, resulting in an increased liver remnant. In our case, because the remnant was insufficient, we decided to add SIRT to standard chemotherapy (CT) to achieve both benefits.

Several studies have identified low FDG avidity in tumours on PET/CT scan, adequate hepatic reserve, radiological response, and low tumour burden as potential prognostic factors for response to SIRT[3–5]. Although there is little published evidence in this field, several studies listed in Table 1 show the benefit of SIRT in the management of ICC.

In conclusion, SIRT could be considered in conjunction with CT in the treatment of an initially unresectable ICC, to achieve local control of the disease and offer the possibility of surgical salvage. However, prospective studies with long-term follow-up are needed.

Conflict of interests

The authors have no conflict of interests to declare.

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Ex-situ splitting of a severe injured liver for transplantation. Case report and review of the literature

Reducción *ex situ* de un injerto hepático procedente de un donante con un traumatismo hepático severo. Presentación de un caso y revisión de la literatura

The liver is one of the most frequently affected organs in abdominal trauma. Classically, severe liver trauma (AAST grade ≥ IV) has been a contraindication for liver donation.[1] Increased experience and more refined surgical technique allow these organs to be used safely without adding morbidity and mortality to the procedure, thus allowing the donor pool to be expanded.

We present the case of a 27-year-old woman with no previous history of interest who was admitted for polytrauma secondary to a traffic accident. During transfer, the patient suffered a cardiorespiratory arrest which lasted 10 min after recovery. The cranial CT scan showed massive subarachnoid haemorrhage and the abdominal CT scan, in addition to other injuries, showed severe liver trauma with a haematoma of about 10 cm with parenchymal disruption affecting segments 6, 7 and part of segment 8 (AAST grade IV) with no associated major vascular and/or biliary injuries. Given the poor prognosis of the brain lesions, optimisation measures for possible organ donation were initiated, but encephalic death occurred a few hours after admission. The maximum dose of noradrenaline was 1.8 μg/kg/min. Peak AST and ALT values were 248 U/L and 231 U/L, respectively, slowly decreasing to 183 U/L and 196 U/L at the time of donation. During extraction, a macroscopically normal liver was observed with a large haematoma on the posterior aspect of the LHD affecting segments 6, 7 and part of segment 8 with no associated major vascular or biliary lesions. Extraction was performed according to the usual technique and subsequently, given the extent of the trauma and the good appearance of the rest of the parenchyma, it was decided to perform an *ex situ* reduction, eliminating the entire area affected by the trauma (250 g), leaving a sufficient liver remnant with a weight of 1,168 kg (Fig. 1). Parenchymal transection was performed with a cold scalpel, progressively suturing all vascular and biliary nozzles and finally a fibrin sealant was sprayed over the entire surface. The recipient was a 63-year-old male with compensated enolic cirrhosis and secondary hepatopulmonary syndrome requiring oxygen therapy 16 h per day. Liver transplantation (LT) was performed with preservation of retrohepatic vena cava and conventional vascular anastomoses, followed by end-to-end choledocholedocholedochostomy without Kehr. Cold ischaemia time was 445 min and warm ischaemia time 55 min. During reperfusion there was no haemorrhage on the liver section surface and transfusion of blood products was not necessary, and a collagen fibre dressing was applied over the section edge to reinforce haemostasis. The postoperative period was uneventful and the patient was discharged after optimisation of his respiratory status 7 days after transplantation. After 2 years of follow-up, the patient evolved favourably, with complete resolution of the hepatopulmonary syndrome and normal liver function.

For years, the use of severely traumatised livers has been an absolute contraindication for donation, having been associated with higher rates of primary failure and retransplantation.[1] However, different studies have shown that with proper donor selection, optimal livers can be salvaged for transplantation.[2–4] However, few studies have been published describing the performance of LT with a severely traumatised graft that requires reduction. In 2009, Geenen et al.[4] published the results of 15 LTs performed with trauma grafts, the largest series to date. Five cases had trauma ≥AAST grade II, with 100% survival at 3 months and 80% survival at 1 year. In 3 of these cases, liver graft reduction was necessary at bench surgery. In addition, we can find some published cases of living donor LT and heart-stopping donor LT with liver trauma. In 2005, Tucker et al.[5] stated that AAST grade I-II liver trauma