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Selective Portal Vein Embolization as Introduction in Major Surgery

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A B S T R A C T

In the period between the December 2000 and September 2004, altogether 13 patients underwent preoperative portal vein embolization (PPVE); 9 patients with colorectal metastases and 4 patients with hepatocellular carcinoma. The indirect splenic portography was performed after catheter was introduced into superior mesenteric artery via femoral artery approach. The portal vein was punctured percutaneously transhepatic under fluoroscopy. Following portography, selected portal vein segments were embolized by injecting polyvinil alcohol (PVA) particles until stasis of blood flow was achieved. Proximal parts of branches and the channel in the liver parenchyma were occluded with Gelfoam particles. The increase of the remnant liver parenchyma was measured by magnetic resonance imaging. Two patients experienced post-embolization syndrome and another one had subcapsular hematoma. The volume of the liver parenchyma increased minimally for 8% and maximally for 109%. Altogether, 10 patients underwent surgical resection. In two patients, the disease progressed and carcinoma spread to the previously healthy liver lobe and in one there was no hypertrophy and we decided for artery chemoembolization (AC). The results show that PPVE triggers a strong regenerative response resulting in hypertrophy of normal liver parenchyma and expand possibilities of curative surgery for patients who would not otherwise have been candidates for extended resection.

Key words: *liver tumors, liver hypertrophy, portal embolization, hepatectomy*

Introduction

Hepatic malignant tumors are characterized by aggressive growth and can cause local complications. Therefore, curative surgical resection is considered the method of choice in the treatment of primary hepatic tumors and metastases.

The incidence of hepatocellular carcinoma (HCC) shows marked geographical variation, with the majority of cases arising in high-risk areas such as Africa and Asia. In Europe, HCC is relatively rare. Between 60 to 80% of patients with HCC have underlying cirrhosis[1]. The majority of patients treated with preoperative portal vein embolization (PPVE) had liver metastases from colorectal carcinoma. Long-term results after liver resection show 5-year survival rates up to 70%. Five-year disease-free rate is up to 40%[2]. The resection of colorectal and other metastases can also produce favorable survival results[3]. With surgical resection up to 60% of liver parenchyma can be removed[4].

One of the most critical elements in the evaluation of potential surgical candidates is prediction of postoperative liver function. There is no test to determine the maximum parenchymal volume to be resected and predict the function of the remnant liver after surgery[2].

When the surgical resection involves the removal of a large part of the affected liver parenchyma, there is a risk that it may not leave enough liver tissue to sustain life. Such problems can be mostly anticipated in case of large tumors, especially if they are located in the central portion of the liver (segments 4, 5 and 8), or in case of the small left lateral section and a extended right hepa-

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tectomy is required removing most of the liver parenchyma. Similar difficulties can also be expected when extensive resection is required in patients whose liver function is compromised by underlying cirrhosis, severe cholestasis, extensive fibrosis and steatosis[5].

The problem of postoperative liver failure following hepatic resection can be solved by liver transplantation[6], which, when used in patients with small tumors and metastases, can yield similar or even better 5-year survival rate than resection[7]. In patients with the underlying functional liver parenchyma defect such as cirrhosis, the best outcome is offered by transplantation. However, the limited organ supply makes this option unattainable for some. Therefore another approach is used to improve the outcome of surgical resection, i.e. the preoperative increase of liver volume so as to stimulate compensatory hypertrophy of non-cancerous liver parenchyma areas[8–11]. Liver parenchyma is namely known to possess remarkable regenerative capacity and the liver cell proliferation is possible under humoral control. Regulators are various metabolites, polypeptides and hormones. It is known that such agents can be found in portal blood circulation[12].

The goal PPVE is to induce atrophy of liver parenchyma affected by tumor and compensatory hypertrophy of non-diseased liver parenchyma, increasing the possibility of resection of primary tumor as well as metastases[5,13–15]. Apart from restricting the centripetal progression of tumor thrombus, PPVE prevents tumor cell dissemination through the portal circulation, and in combination with the transcatheter arterial chemoembolization (TACE) causes ischemic necrosis of the tumour[16,17]. This method has proved very effective with primary liver tumors and metastases regardless whether the unresected liver area was normal or affected by cirrhosis[18].

Careful injection of embolic material is therefore mandatory. Balloon occlusion catheters can also be used to unwanted reflux of the embolic material to non-target organs[8]. PVA particles of various sizes and Gelfoam particles used in our procedures proved as an appropriate solution, since they did not migrate to surrounding unaffected liver parenchyma. From the tumour's perspective various approaches can be used, i.e. contralateral as well as ipsilateral. Also, the puncture can be US- or fluoroscopy-guided. In exceptional cases, the procedure can also be performed by surgical preparation of mesenteric vein and positioning of an appropriate chateter[5].

Subjects and Methods

In the period between the years 2000 and 2003, 13 patients with unresectable liver tumors (9 men and 3 women, median age 62.8 years, 8 colorectal hepatic metastases and 4 hepatocellular carcinoma) were selected for PPVE. Patient selection was based on the consensus of the abdominal surgeon and the radiologist, and the size of the lesion to be removed. They were all potentially at risk of postoperative liver failure. In most cases, patients left anatomical liver lobe (lateral section) was too small and predicted future liver remnant (FLR) volume was less than 25% of the total liver volume. In 2 patients liver function was further compromised by underlying cirrhosis[19]. Patients were informed about the surgical procedure and the risks and complications associated with the procedure, and their consent to surgery was obtained.

PPVE was performed on digital substraction angiography (DSA), Philips – INTEGRIS C – 2000, under general anesthesia. The anesthesiology technique was chosen on the basis of the patient's age, constitution, clinical status and concomitant illnesses as well as following the radiologist's requests for the performance of the procedure. The anesthetic technique that allows for unconsciousness, lack of movement and rapid recovery is always preferred.

Just prior to the procedure an intravenous premedication (Midazolam 1–3mg) was administered to the patients. The introduction into the anaesthesia[25] was performed either with Propofol (1.5–2.5 mg/kg) or Etomidate (0.2–0.4 mg/kg) and Fentanyl in the dose 1–3 μg/kg. For the muscular relaxation and intubation Atracurium 0.3 mg/kg or Mivacurium 0.2 mg/kg was applied. The procedure was performed under balanced, general anaesthesia with mixture of O_2 and N_2O and Sevofluran (MAC=1.7%) together with periodically administered boluses of Fentanyl paying regard to the patient's response to stimulation during the procedure. During the procedure the patients were monitored by means of a standard noninvasive monitoring. Patients were extubated when their protective laryngeal reflexes had been present. The anesthesia itself did not trigger any complications during the procedures.

For all patients we initially used a retrograde common femoral artery (CFA) approach. After the CFA was punctured a 5F sheat was placed and 5F diagnostic catheter Simon-Sidewinder 2 (Angiopass Plus, Angiomed – Bard Inc.) was positioned into origin of superior mesenteric artery (SMA) and indirect splenoportography was obtained.

Under fluoroscopy guidance portal vein (PV) was punctured with 22G needle (IPS, Angiomed – Bard Inc.) and a 0.35 guide wire was introduced and a 5F sheat with coiled shaft design (Super-Arrow Flex, Arrow Inc.) was positioned. The sheat construction offers extraordinary flexibillity and allows at the end of the procedure occlusion of the liver parenchyma channel with greater Gelfoam particles.

A 4F Cobra diagnostic catheter was inserted and a preprocedural portography was obtained to display the portal vein branches. We usually chose between a softer catheter with soft tip (Balton Medical Equipment, Poland) and a little stronger one with exellent placement accuracy and good pushability (Angiopass Plus – Bard Inc.). The catheter tip was selectively placed into segmental branches and the embolization material was applied under fluoroscopy control until complete stasis was achieved.

We started with spheric particles size 100μ and concluded with particles up to 1000μm (Embosphere – Biosphere Medical Inc.). Proximal vein segments were occluded with Gelfoam particles and in two patient with large size coils. (COOK Inc.)

All patients underwent embolization of the right portal vein and its segmental branches.

The procedure lasted on average 23 minutes. After the procedure, the patients remained in hospital for 48 hours on average. In 10 patients a surgical resection was performed on average one month after the embolization.

Liver volumetry

The liver parenchymal volume and the volume of unaffected parenchyma were measured using magnetic-resonance tomography (MRT) – TOSHIBA Visart 1.5 Tesla in transverse plane in T1 sequence[20]. The entire liver parenchyma was covered with thick 8-mm sections with 2-mm gap. The intervals were taken into account in the calculation. The boundaries of the liver and of the residual non-diseased parenchyma were outlined by a trackball-driven cursor and the volume was calculated using the corresponding software. The volume was measured before PPVE and 30 days after it.

Results

The procedure was successful in all patients and primary technical success was achieved. All but one patient tolerated the procedure well. Volume changes were measured using MRT volumetric measurements of transversal slices of liver parenchyma before PPVE and just before the planned operation. The volume of the entire liver and the volume of unaffected remnant liver parenchyma were measured. FLR exhibited 8–109% increase in volume. On average, the liver parenchymal volume increased by 158 cm^3 or 41%.

Liver resection was successfully performed in 10 out of 13 patients approximately 40 days following PPVE. In one patient the disease progressed and in two patients the expected hypertrophy did not occur and for that reason only AK was performed.

Complications

In one patient bleeding was reason for developing a subcapsular liver heamatoma. Also post-embolization syndrome was present, accompanied by severe pain and symptoms of diaphragm irritation. These changes were treated conservatively. The controlling MRT examination showed that the disease progressed and that metastases spread to previously healthy liver parts, thus preventing surgical resection.

In 2 patients mild symptoms of post-embolization syndrome (increase of temperature to 37.6 °C and slight right upper quadrant pain) were noted one day after the procedure.

Discussion

Papers reporting the use of PPVE before hepatic resection first appeared in the literature in the 1980's. Since then many authors have reported favorable outcomes for patients with primary hepatic carcinoma that underwent PPVE[8]. Beneficial effects of PPVE in patients with colorectal carcinoma metastases[6,10,18] and those with bile duct carcinoma[8,16] have been less frequently reported.

The commonly used embolic materials include ethanol, fibrin glue, lipiodol, Gelfoam, gelatine sponge particles, Polyvinil alcohol particles (PVA), Embosphere particles and various coils[9,14,24]. We mostly used the PVA and Embosphere particles of various sizes and Gelfoam. No evidence was found in the literature of the superiority of one material over another.

The embolization of the segmental branches of the portal vein induces ischemia of embolized area, causing an increased flow of portal blood to non-embolized areas. This triggers paracrine and endocrine response, which results in hypertrophy of the remnant part of liver parenchyma. During liver regeneration, increased levels of various mediators such as growth factor, transforming growth factor α and hepatocyte growth factor can be detected, which is why it is believed that liver regeneration is controlled and managed by all these mediators together[16,17].

All the above-mentioned factors also have a promoting effect on the development of tumors. It is well known that tumor development and accelerated tumor growth directly coincide with liver regeneration[22,23]. Elias observed and described the accelerated metastasis growth in patient who underwent PPVE[6].

This is the reason why PPVE remains limited to patients with no alternative way of treatment available. One should bear in mind that the above effects can be produced after every liver resection during parenchyma regeneration. The accelerated growth can uncover micrometastases and/or occult tumors in segments that seemed unaffected, thus preventing the planned resection. Altogether 9 patients underwent surgical resection about one month after the embolization. In two patients the disease progressed and the surgical resection was not possible. In one patient the expected hypertrophy was not achieved, which indicated a need for further treatment with TACE.

In two patients TACE had been performed before PPVE. It is known from the literature that the combination of PPVE and TACE provokes substantially greater necrosis of tumor and metastases than TACE alone. Moreover, PPVE reduces the possibility of intrahepatic migration of tumor cells and prevents the spread of metastases[8].

Mean FLR increased by almost 40%, allowing surgery in patients initially deemed unresectable and improving their chance of survival in the event of any possible postoperative complications.

Conclusion

A rapidly increasing number of patients surgically treated due to HCC or colorectal metastases in Maribor General Hospital have brought about the question of patient's ability to tolerate a liver resection. To address this problem, PPVE was introduced in an attempt to turn patient´s unresectable disease to resectable one, making them candidates for curative liver resection. The results of our three-year work are comparable to the data published by other authors and confirm that PPVE induces a strong regenerative response, which is reflected in the hypertrophy of the FLR, increasing the resectability rate. The method was equally successful in patients with HCC and those with colorectal metastases. Still, embolization procedures are not without risk. They require the skill and experience of the interventional radiologist.

An evaluation of all treatment options available to a patient is of vital importance. In carefully selected patients with no alternative treatment option available PPVE may prove beneficial. By inducing the hypertrophy of the FLR, PPVE can improve patients' survival chances.

Even though the time interval between the embolization and the surgical resection is not yet determined, many authors believe that it plays a very important role[2,4,5,8]. It is widely considered that the interval should be longer in patients with additionally compromised liver parenchyma. As the time interval between the embolization and operation appears to be more important than the maximum hypertrophy achieved, it is of paramount importance that it is optimized. The mean time was 33 days. As the procedure is limited to a subset of patients, where no alternative treatments seem possible and where the resection may prove fatal, a careful patient selection is an important issue. In such cases PPVE may enable patients to benefit from potentially curative resection by increasing the remnant liver volume prior to an operation.

Even though the method has been known for more than 20 years, there is a need for more randomized studies that would provide the evidence of effectiveness of PPVE in increasing the safety of surgical resections and reducing the postoperative liver dysfunction[5].

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SELEKTIVNA EMBOLIJA PORTALNE VENE KAO UVOD U OPSEŽAN KIRURŠKI ZAHVAT

SAŽETAK

Između prosinca 2000. godine i rujna 2004. godine, 13 bolesnika podvrgnuto je preoperativnoj embolizaciji vene vratarice od kojih je 9 imalo metastaze kolorektalnog karcinoma, a 4 pacijenta imalo je hepatocelularni karcinom. Indirektna flebografija vene lijenalis izvedena je nakon što je kateter uveden u gornju mezenteričnu arteriju femo-

ralnim putem. Vena vratarica punktirana je perkutano pod kontrolom dijaskopije. Nakon flebografije vene vratarice, pojedini njeni djelovi embolizirani su ubrizgavanjem čestica polivinil alkohola. Proksimalni dio ogranka vene vratarice i kanal unutar jetrenog parenhima embolizirani su Gelfoam česticama. Porast jetrenog parenhima mjeren je magnetskom rezonancom. Dva bolesnika imala su postembolizacijski sindrom, dok je kod jednog nastao subkapsularni hematom. Volumen jetrenog parenhima porastao je za minimalno 8%, a maksimalno 109%. Deset bolesnika podvrgnuto je kirurškoj resekciji. U dva bolesnika bolest je napredovala i karcinom se proširio na prije zdravi jetreni režanj, a kod jednog bolesnika nije došlo do hipertrofije te smo se odlučili za kemoembolizaciju. Rezultati pokazuju da preoperativna embolizacija vene vratarice potiče jaki regenerativni odgovor koji se očituje hipertrofijom urednog jetrenog parenhima, te proširuje mogućnosti kirurškog liječenja bolesnika koji inače nisu kandidati za proširenu resekciju.