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TIPS AND TRICKS

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Transarterial chemoembolization in the treatment of hepatoblastoma in children

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Abstract Hepatoblastoma is one of the clinical challenges in children, as it is common and frequently unresectable. Chemotherapy can be administered regionally instead of systemically by transarterial chemoembolization (TACE) and thus improve prognosis. The advantages of this technique over systemic chemotherapy led to developing its role from being a palliative or an adjuvant preoperative treatment to being a potentially independent palliative or curative therapeutic option. The technical aspects and complications of a combined transarterial administration of chemotherapeutic and vascular occlusive agents in cases of hepatoblastoma in children are discussed, to give a comprehensive idea about the value of TACE in this context.

Keywords Hepatoblastoma · Chemoembolization · Transarterial chemoembolization (TACE) · Pediatric liver tumors

Hepatoblastoma: a pediatric clinical problem

Hepatoblastoma in children is the most common malignant hepatic tumor and the third most common abdominal malignant tumor following neuroblastoma and nephroblastoma [1–3]. About 50% of cases occur before the age of 18 months and almost all before the age of 2 years. In about 33% of patients the tumor is bilobar or multicenteric. For a long time, surgical treatment in the form of resection with or without liver transplantation was considered to be the only option for complete cure and long-term survival. However, 50% of cases are unresectable at the initial presentation either due to metastatic spread or to local bilobar or porta hepatis invasion. In this situation patients rarely survive more than 12 months [2].

Preoperative systemic chemotherapy plays a vital role in reducing tumor size and controlling tumor spread to convert an unresectable tumor to a resectable one, thus improving prognosis [3, 4]. However, the associated systemic adverse effects, such as myelosuppression and cardiotoxicity, sometimes lead to delayed surgery and hence tumor regrowth and chemotherapy-related death [1]. Moreover, there are the problems of drug resistance [6] and induction of a second malignancy [7, 8] by anticancer drugs.

Transarterial chemoembolization

Transarterial chemoembolization (TACE) is a highly practical and effective alternative, in which the chemotherapeutic drugs are selectively injected into the tumor-feeding arteries. This approach has the advantages of maximum drug uptake by the tumor and minimal systemic exposure to the drug. Furthermore, it can be combined with arterial embolization to occlude feeding arteries and thus to induce ischemic tumor necrosis and prolong the dwell time of anticancer drug in the tumor vasculature which enhances its effect [1]. Embolization also makes resection easier by

reducing volume and hemorrhage [10]. Thus, transarterial chemoembolization (TACE) has a dual benefit.

Temporary versus permanent embolizing material

Temporary embolizing material is more widely used because it minimizes collateralisation and allows retreatment through the recanalized vessel [4]. Permanent occlusion using stainless-steel coils might sometimes be preferable, taking into consideration the surprising capacity for neovascularization of malignant tumors [10]. Lipiodol is effective as an emulsion in chemoembolization when mixed with chemotherapeutic agents, because it is selectively absorbed and retained by emulsification and pinocytosis [12] in hepatic tumor cells. Lipiodol also occludes the tumor microvasculature [1].

Role of TACE in hepatoblastoma

Nowadays, TACE is even performed in resectable lesions to control intrahepatic tumor spread, reduce metastases related to surgical manipulation and as a temporising measure while waiting for a liver donor [4]. Chemotherapy combined with surgical resection has shown to provide better results than either procedure alone [9]. However, the use of TACE in hepatoblastoma patients is limited by the presence of distant metastases, which require systemic chemotherapy until controlled. After that, treatment with TACE can be performed [3].

With TACE alone, tumor control and tumor-free survival in non-metastatic hepatoblastoma patients, reaching up to 33 months in some studies [10], can be achieved. This challenges the established belief that surgery is the only chance for a complete cure.

Advantages and disadvantages

TACE is a minimal invasive technique, and in expert hands it can be very simple and usually requires less than 30 min. Nevertheless this technique is not free of hurdles. A single session of TACE might not be sufficient to reduce the tumor volume adequately, because a new feeding artery might develop. Therefore, repeated TACE might be needed for the desired outcome [10].

In children, general anesthesia is normally required, with all its precautions, requirements and complications. In this particular situation it is a complicating factor when we bear in mind the potential respiratory complications of TACE [5, 11].

Another technical challenge is the very small vessel diameter of the pediatric vessels, demanding more skill and experience to avoid perforation or dissection [1].

Despite all its advantages, there are a few infrequent complications associated with TACE which are not totally inevitable. Pulmonary lipiodol embolism is the most serious complication. However, it is symptomatic in only 2–4% of cases. Its predisposing factors are the amount of lipiodol administered and the extent of intratumoral arteriovenous communications. It can present after 2–4 days as a respiratory distress syndrome, due to fatty acids released from lipiodol breakdown by esterases leading to pulmonary edema in addition to the mechanical occlusion of small pulmonary vessels. An even more delayed factor in the development of the respiratory distress syndrome is chemical pneumonitis induced by anticancer drugs [11].

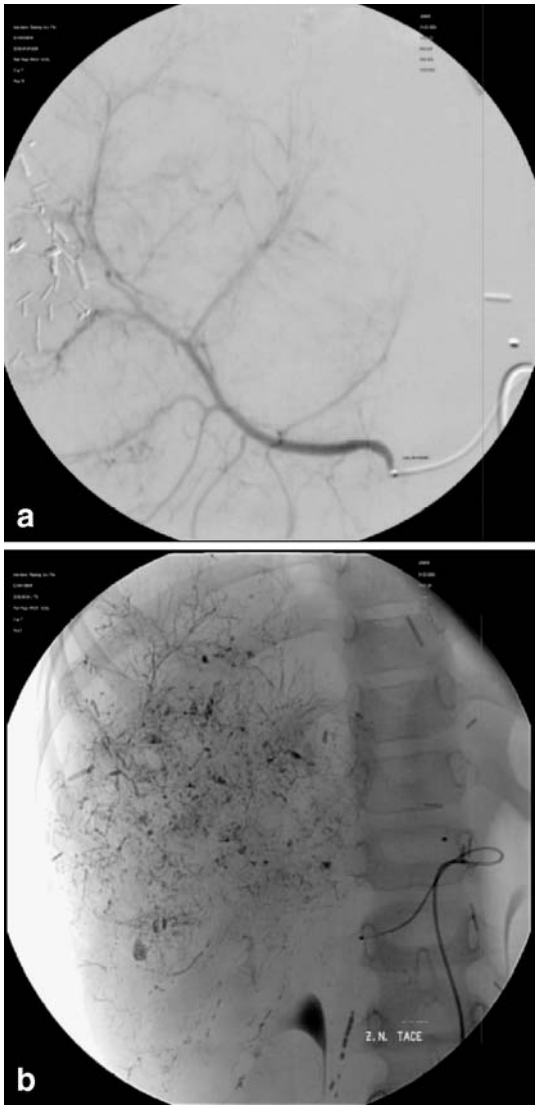

Fig. 1 First TACE session. Note the inhomogeneous hypervascular nature of the tumor in the angiogram. **a** Selective hepatic arteriogram using microcatheter. Surgical clips are noticed. **b** Lipiodol retained by the tumor after injection, outlining its large size. The microcatheter is seen in the lower right corner of the image

Liver infarction may especially occur if portal vein thrombosis is present, which has to be evaluated during preinterventional angiography. The tumor lysis syndrome consisting of mild transient fever, nausea, vomiting, abdominal pain, elevated liver enzymes and bilirubin occurs in some patients. Other infrequent complications are acute liver failure, liver abscess or tumor rupture [1].

Technical application

In our institute we have performed TACE in a 4-year-old female with stage IV hepatoblastoma. Following surgical resection of the tumor, postoperative CT revealed multicenteric tumor spread within the liver. Thus, liver transplantation was intended. In the meantime, the patient underwent four sessions of TACE within 2 months at 2-or 3-week intervals in order to control the tumor progression.

Preembolization magnetic resonance imaging (MRI), postembolization computed tomography (CT) and MRI studies were performed to evaluate tumor response. Before each session the patient was given a prophylactic antiemetic drug. The procedure was performed under local anesthesia and thus all the burdens of general anesthesia were avoided. Chemotherapeutic agents used were Mitomycin (3–5 mg per session) and Gemcitabin (Gemzar, Lilly & Co., 300–350 mg per session). Vascular embolization was performed using Embocept (100 mg) and lipiodol (2 ml). Selective injection into the feeding arteries was done using 4F Cobra catheters and microcatheters (Fig. 1).

Pain was controlled by systemic analgesics. No significant complications occurred during or after the procedure. The response of the tumor was favorable, as shown by the CT and MRI follow-up images (Fig. 2).

Conclusion

In conclusion, TACE can play a major role in the treatment of hepatoblastoma patients, either as a single line of treatment or in combination with other treatment modalities.

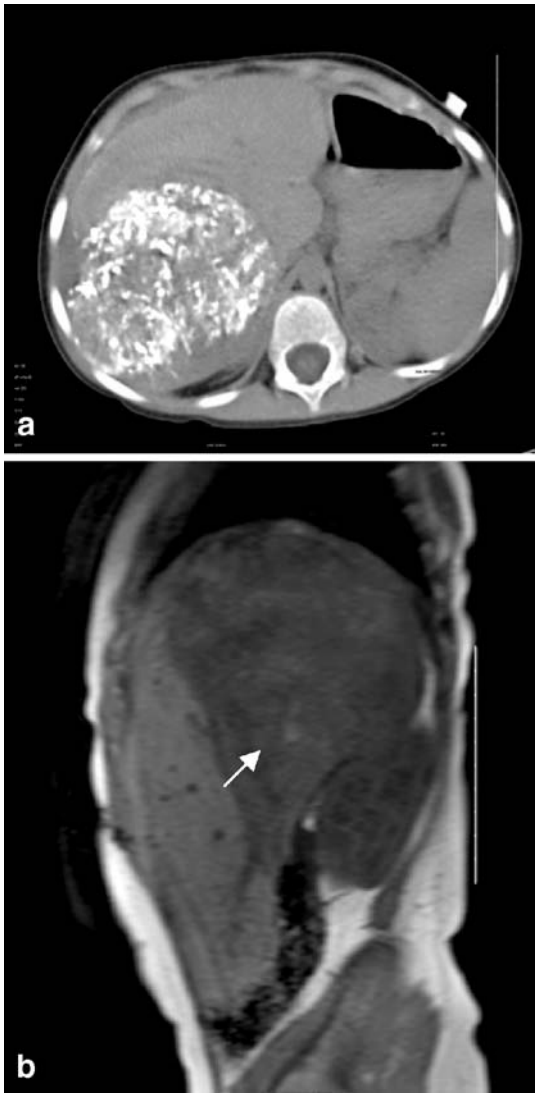

Fig. 2 **a** Control CT without i.v. contrast after the first session. The tumor outlined by retained lipiodol occupies most of the right hepatic lobe. Relatively reduced lipiodol uptake in the tumor center, denoting tumor necrosis. **b** MRI, T1WI, sagittal view (TR/TE 500/17) after the fourth session showing stable size and central scarring (*arrow*)

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