Isolated Thoracic Perfusion with Carotid Artery Infusion for Advanced and Chemoresistant Tumors of the Parotid Gland

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8.1 Introduction

Although only two patients with most advanced parotid cancers are described in this chapter the results of the new approach in using regional chemotherapy have been so dramatic and encouraging that this limited experience is included in this book.

Regional chemotherapy has many facets and implies that the adequate mode of application is performed. Good results are jeopardized when intra-arterial infusions are performed after the vascular supply has been interrupted or extremely reduced by scars from prior surgery or connective tissue and vascular fibrosis from irradiation [1], or when the tumor having invaded tissues beyond the territory of selective or superselective catheterization of arteries were able to be infused.

The theoretical advantage of intra-arterial drug delivery is most evident [2, 3] clinically; it was investigated in numerous clinical studies [1, 4–11]. In the last two decades chemoradiation gained a firm position in treatment protocols [12–15] and supradose intra-arterial cisplatin infusion achieves a fundamental improvement with regard to increased drug exposure. Actually, the best results in terms of local tumor control have been achieved when chemotherapy has been applied concomitantly with irradiation although there is increased risk of intensified damage to adjacent tissues. In extremely huge tumors, however, irradiation can hardly be applied and chemotherapy alone is not efficient enough to induce substantial remission. Since in intra-arterial chemotherapy all of the advantages occur within the time of the first pass through the tumor bed, as once the drug is diluted in the venous drainage of the tumor area, subsequent tumor exposure of the recirculating blood will be equivalent to systemic administration. A reduction of the circulating blood

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volume, however, may further increase the overall local drug exposure. The question is whether it is possible to induce optimal immediate and long-term results and good quality of life without mutilating side effects.

8.2 Material and Methods

The method described herein is performed as ultimate ratio in patients with huge and non-resectable tumors of the head and neck area that are no longer responsive and are in progression after or during systemic chemotherapy.

The Isolated Thoracic Perfusion (ITP) technique that is applied can be considered a segmental intra-arterial chemotherapy of the isolated head and neck and chest area with a reduced blood volume of one-third or one-fourth of the total body blood volume. Reduction of the circulating blood volume is achieved by means of balloon blocking of aorta and vena cava at the level of the diaphragm. The three-channel balloon catheters are introduced after exposing the femoral artery and vein in the groin. The patient is fully heparinized. For administration of chemotherapeutics, an angiographic side-winder-catheter is proceeded in Seldinger's technique from the contralateral femoral artery into the tumor feeding common carotid artery. Both upper arms are blocked with pneumatic cuffs. After correct positioning of the angiographic catheter, the vena cava balloon is blocked first in order to further reduce the intrathoracic blood volume. Under continuous monitoring of the aortic blood pressure, the aorta is blocked at a pressure of 75–80 mmHg, which immediately adapts and rises to some 100 mmHg shortly after the aorta has been blocked (Figs. 8.1 and 8.2).

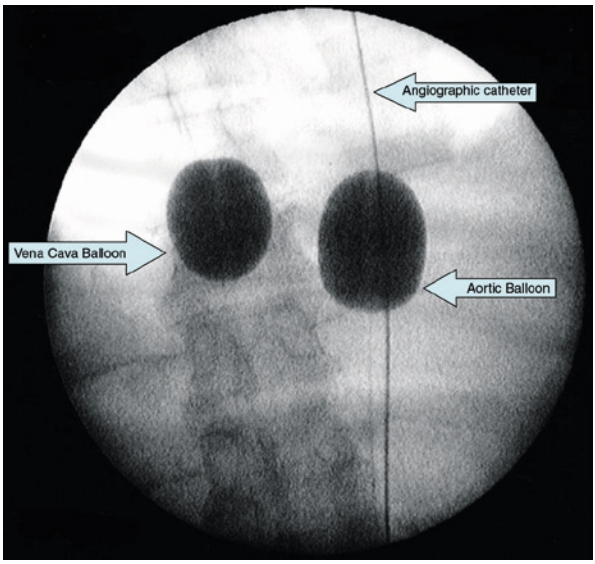

Fig. 8.1 Balloon blocking of aorta and vena cava

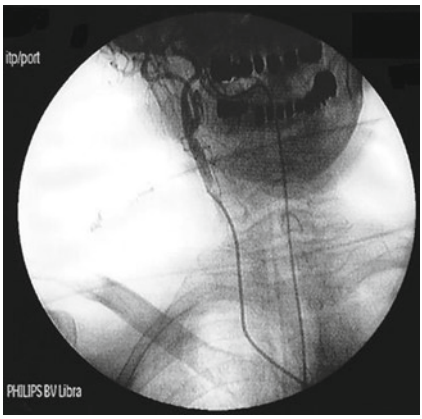

Fig. 8.2 Sidewinder catheter in common carotid artery

Chemotherapeutics are infused over 5–10 min, depending on the total dose into the carotid artery. Vascular isolation of the chest is maintained over 15 min. Subsequently, the vena cava and aortic balloon are deflated first and the upper arm cuffs thereafter. At this point, chemofiltration is started at a flowrate of 500 mL/min with a filtrate flow of 80–50 mL/min (median 100 mL/min). After substitution of 4 L of filtrate the catheters are removed and the vessels repaired with running sutures.

8.3 Patients

Two patients with huge cancers of the parotid gland that were in progression during systemic chemotherapy underwent isolated thoracic perfusion with carotid artery infusion.

The first patient was referred because of repeated bleedings of an advanced chemoresistant tumor of the right parotid gland (Fig. 8.3). He received a total of three courses of Isolated Thoracic Perfusion with subsequent chemofiltration (ITP-F), where the drugs were infused through the angiographic carotid artery catheter. The total dose administered with each cycle was 100 mg of cisplatin and 20 mg of mitomycin at an infusion time of 7 min each. Thoracic isolation perfusion time was 15 min. The tumor responded clearly to the first course of isolated chemotherapy, revealing substantial shrinkage (Fig. 8.4). After three therapies in 3 weeks intervals the residual tumor was resected (Fig. 8.5).

The second patient suffered from a left side parotid gland cancer with a bulky metastasis on the left side of face. He was in progression after systemic chemotherapy with 5-FU and docetaxel (Fig. 8.6). In addition, there were disseminated lung metastases. After three cycles of isolated thoracic perfusion (ITP-F) with carotid artery infusion of 100 mg of cisplatin and 30 mg of mitomycin the residual tumor was resected. Over a period of 4 months after regional chemotherapy there was no progression of lung metastases and no evidence of local recurrence at the primary site (Fig. 8.7).

Fig. 8.3 Advanced chemoresistant tumor of the right parotid gland

Fig. 8.4 Same tumor 3 weeks after first isolated thoracic perfusion with common carotid artery infusion of CDDP and mitomycin

8.4 Discussion

Because the term "regional chemotherapy" is used to describe a number of different approaches, it is important that details of the particular approach used are made clear. Whether or not the result is positive in terms of response and survival time or whether pitfalls and failures are encountered, strongly depends on how the treatment has been carried out [1]. The type of catheters, technique of catheter placement, selection of the arterial access, drug exposure in terms of dosage, drug concentration, and infusion time may promote or jeopardize the outcome.

Fig. 8.5 Resection of residual tumor after three courses of isolated thoracic perfusion

Fig. 8.6 Bulky tumor of the left parotid gland in progression after systemic chemotherapy with 5-FU and docetaxel

In the two cases reported herein, isolated thoracic perfusion was chosen from the clinical aspect because one patient already had lung metastases. In the other case lung metastases could not be entirely excluded, and from the pharmacodynamic aspect isolated thoracic perfusion was chosen in order to reduce the circulating blood volume and therefore create a better second and third pass effect with prolonged augmented drug exposure. In the treatment of advanced and non-operable lung cancer (NSCLC) isolated thoracic perfusion is a technically safe and well-established method with predictable outcome. In far advanced cancers of the head and neck, however, large studies are still to come. In single cases, there has been a high incidence of good palliation, but as long as there is no controlled study with

Fig. 8.7 Same patient 3 months after tumor resection, 6 months after start therapy

a larger number of patients providing reliable data on response and overall survival, the method will further on be considered experimental. However, taking into account the patients presented here lacked any chance of cure, and there was no alternative therapeutic option that offered them good local palliation without those extreme toxic side effects like nerve damage, dry mouth, long-term dysphagia, and aspiration, when chemotherapeutics are infused via the common carotid artery, drug streaming with skin and soft tissue burns was not observed. Drug concentrations at the target site during a 5–10 min short-term intra-arterial infusion most obviously are sufficient to generate effective drug exposure that may induce substantial visible remission. Superselective techniques, however, due to low blood flow and exceeded drug concentration may lead to identical local toxic side effects as are observed with drug streaming [1]. Another complication that may occur with superselective arterial infusion has been intimal damage with subsequent vascular occlusion. This has not occurred with common carotid artery infusion.

Most importantly, there was no essential systemic toxicity because of the systemic detoxification by chemofiltration. Therefore, in patients who have no chance of cure and who already suffer enough from their tumor and face a dismal outcome, every effort should be made to achieve good palliation without causing unacceptable toxicity. These two patients tolerated the treatments without any remarkable side effects and in case of relapse the treatment can easily be repeated.

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