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Regional Cancer Treatment

Editorial

Regional chemotherapy – where are we now?

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The roots of regional chemotherapie can be followed back to the 1950s in the United States where Biermann and Klopp pioneered intra-arterial infusion therapy. Isolated perfusion therapy using heart-lung machines was first used by Creech and Krementz at the Tulane Medical School in New Orleans for high-dose chemotherapy of locally metastasizing melanoma of the limbs. Since then, it can be said that regional chemotherapy has developed in fits and starts. Each decade it has experienced a boom, a wave of enthusiasm, usually followed by sober disillusion. This can easily be explained by the fact that spectacular one-off results animated some groups to use these methods with little more than rudimentary knowledge. The results were positive or less positive, respectively. Three factors delayed the final breakthrough:

1. The know-how for the technical and pharmacological prerequisites
2. The correct definition of the indications
3. Reliable studies on a homogeneous patient group

A few groups of investigators felt that the criticism was mainly based on lack of knowledge of the basic principles, techniques and indications. Again, they started from the very beginning, working out guidelines for favorable indications in tumors with different chemosensitivity and vascularity, trying to optimize techniques and drugs schedules that are still in evolution and far from being perfect. In other words, there are still many unknown factors and possible deadend streets that must be recognized and, as a consequence, should be avoided, but there are also new and promising indications that should be followed up and investigated.

In the meantime, reliable studies, such as those conducted by Kemeny on liver metastases, have established one advantage that regional chemotherapy possesses over systemic therapy with regard to the survival time. By virtue of many years' endeavor and, above all, through the exchange of ideas at congresses such as the ICRCT series, the know–how in individual research groups inevitably reached a far higher standard. However, the answer to the question of whether regional chemotherapy is now superior to systemic treatment has so far always been examined on the basis of hepatic metastasis from colorectal carcinomas.

At first, such logic appears plausible since one regards the liver as the first filter in the metastatic spread of the tumor and, therefore, assumes that regional therapy would cure the patient, or at least his life would be significantly prolonged. However, this argument fails to consider that colorectal liver metastases are certainly not an ideal and in fact, not even a representative model on which to assess the value of regional tumor therapy. Colorectal liver metastases have a poor blood supply in approximately one-third of all patients, which means that intra-arterially administered chemotherapy has hardly any chance at all of reaching its target. Patients with colorectal liver metastases are frequently caught up by extrahepatic, peritoneal, hepatic portal or lung metastases which manifest in parallel. The percentage of the incidence of intrahepatic relapses and progression during and after regional chemotherapy must not be underestimated. In turn, this indicates that the ideal therapy concept or cytostatic agent has not yet been determined. Certainly, the value of this method cannot be assessed on the basis of one single defined tumor, of one single form of application such as a port or pump system, and one single cytostatic agent. The prognoses for liver metastases must be classified in different groups, depending on whether they are central of peripheral. A partial response by a metastasis near the hilus may prolong life, while such a response by a peripheral metastasis may have no effect whatsoever on the survival time.

As a matter of fact, the real potential of regional cancer therapy can only be estimated when the wide range of solid tumors in various locations of the body are investigated. For example, liver metastases from other primary tumors, such as the breast or gastric and pancreatic carcinomas, respond far better to regional chemotherapy than do colorectal metastases. However, since these tumors tend to manifest at many sites, one can only treat them palliatively. In hepato-cellular carcinomas, chemoembolization offers the best chance for succes and, by reducing the size of the tumor, may make curative resection possible.

In addition to liver metastases, which only illustrate one aspect of regional chemotherapy, e.g., carcinomas of the stomach and breast and tumors of the thoracic wall and extremities, regional chemotherapy may prevent invasion of local tissues within the framework of a multimodal concept.

It should always be remembered that regional chemotherapy is still in its early days and that, when defining the indications, strict distinctions must be drawn between the palliative and curative possibilities. In this regard there is still a lot of work to be done and we are just at the beginning. One thing is for sure, however. Regional chemotherapy at its present standard offers the patient a higher quality of life.