MÁ REGIONÁLNÍ CHEMOTERAPIE MÍSTO JAKO METODA DRUHÉ ŘADY LÉČBY POKROČILÉHO NEMALOBUNĚČNÉHO KARCINOMU PLIC?

IS THERE A ROLE FOR REGIONAL CHEMOTHERAPY AS SECOND – LINE TREATMENT IN ADVANCED NON SMALL CELL LUNG CANCER ?

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Souhrn: *Účel:* Studie byla vytvořena k posouzení účinnosti a toxicity regionální chemoterapie za použití isolované perfuze hrudníku (ITP) jako metody druhé řady léčby pokročilého nemalobuněčného karcinomu plic (NSCLC). ***Pacienti a metody:*** Do studie s podáním regionální chemoterapie použitím ITP bylo zařazeno 30 pacientů s relabujícím NSCLC. Všech 30 pacientů bylo předléčeno chemoterapií, chirurgickým výkonem a/nebo radioterapií. Byly použity dva různém režimy: skupina A: regionální chemoterapie formou ITP samotná Mitomicyn 10 mg/m^2, Aclarubicin 22 mg/m^2 a Melphalan 10 mg/m^2. Skupina B: regionální chemoterapie formou ITP den 1 Mitomycin 10 mg/m^2, Navelbin 25 mg/m^2, a Cis-platina 30 mg/m^2, kombinovaná s nízkodávkovanou systémovou chemoterapií (5-Fluorouracil 250 mg/m^2, Cis-platina 20 mg/m^2 kontinuálně v infusi 24 hodin den 1-4). V obou skupinách bylo po 15 pacientech, základní data byla srovnatelná. Sledovány byla odpověď, toxicita a přežití. ***Výsledky:*** U všech 30 pacientů byly hodnoceny toxicita, odpověď a přežití. Ve skupině A bylo 6/15 odpovědí (CR:1, PR: 5, RR:40%) a 8/15 ve skupině B (CR:0, PR: 8, RR: 53,3%). Nežádoucí účinky byly v obou skupinách přechodné a přijatelné, nepozorovali jsme úmrtí spojené s léčbou. Medián přežití byl ve skupině A 16 měsíců a 22 měsíců ve skupině B, jednoroční přežití bylo ve skupině A 53,3 % a 82,5 % ve skupině B. Rozdíly nebyly statisticky významné. ***Závěr:*** Ve srovnání se standardní systémovou chemoterapií je regionální chemoterapie formou ITP vysoce účinná u relabujícího pokročilého NSCLC s povzbudivými výsledky přežití. V této malé skupině pacientů lze využitím kombinované systémové a regionální chemoterapie zvýšit počet odpovědí a dobu přežití až dvojnásobně.

Klíčová slova: karcinom plic - izolovaná perfuze - chemoterapie druhé řady.

Abstract: ***Purpose:*** This study was undertaken to determine the activity and toxicity of regional chemotherapy using an isolated thoracic perfusion (ITP) technique as second line treatment in advanced Non Small Cell Lung Cancer (NSCLC) patients. ***Patients and methods:*** 30 patients with relapsed NSCLC defined to thoracic region entered onto the study were to receive regional chemotherapy using ITP as application form. All 30 patients had been pretreated with some form of chemotherapy, surgery and/ or radiotherapy. Two different cytostatic regimens has been used: group A: regional chemotherapy alone using Mitomycin 10 mg/m^2, Aclarubicin 22 mg/m^2 and Melphalan 10mg/m^2 during ITP, group B: regional chemotherapy using Mitomycin 10 mg/m^2, Navelbine 25 mg/m^2 and Cis-Platin 30 mg/m^2 during ITP on day 1 plus low dose systemic chemotherapy (5-Floururacil 250 mg/m^2, Cis-Platin 20 mg/m^2 given as continuous infusion over 24 hours, day 1–4. There were 15 patients in each group of chemotherapy; baseline data were comparable between both groups. Response, toxicity and survival data were noted. ***Results:*** All 30 patients were assessable for toxicity, response and survival. There were 6/15 responses in group A (CR.: 1; PR 5; RR 40 %) and 8/15 in group B (CR.: 0; PR 8 ; RR 53.3 %). Sideeffects were transient and acceptable in both groups. No treatment related death was observed. Median survival was 16 months in group A and 22 months in group B.1-year survival rate was 53.3 % in group A and 82.5 % in group B. Differences were not statistical significant. ***Conclusion:*** Compared to standard systemic chemotherapeutic regimens regional chemotherapy using an ITP application form is highly active in relapsing advanced NSCLC with an encouraging survival outcome. In this small group of patients response rates as well as survival rates could be doubled with an advantage to a combined regional plus systemic application form.

Key words: lung cancer – isolated perfusion – second line chemotherapy

Introduction

In recent years, the role of chemotherapy in the treatment of Non Small Cell Lung Cancer (NSCLC) has been more evident. Some controversies still exist over the ultimate benefit of systemic chemotherapy in advanced disease, though the use of platinum based combination chemotherapy has become more established. A meta-analysis using updated data on individual patients from 52 randomized clinical trials of Cis-Platin based chemotherapy compared with best supportive care only showed a benefit of chemotherapy with a reduction in risk of death of 27 % and an absolute increase in one-year survival rate of 10 %(20). Another more recent meta-analysis compared the effect of single-agent versus combination chemotherapy on response rate, toxicity and survival in 25 trials including 5156 patients with advanced NSCLC. Overall, combination chemotherapy produced a nearly two-fold increase in response rate compared with single – agent chemotherapy, while survival at 6 and 12 months were increased by 10 % and 22 % with combination chemotherapy, respectively. (16) The achievement of response to chemotherapy induce improvement of tumor associated symptoms, indicating that the use of chemotherapy, which are able to induce high response rates may have a good Palliative effect, even though the benefit in terms of survival may be modest (5,12)

Second line chemotherapy in advanced or recurrent NSCLC is not usually indicated, as all attempts have been, until recently, almost unsuccessful. (6) On the other hand, several meta-analyses have shown that the survival benefit obtained with first-line platinum based chemotherapy for advanced NSCLC is limited to a few weeks, and in pretreated patients with recurrent or progressive NSCLC, the rapid worsening of general conditions often contraindicates further treatment (23).
In order to improve affectivity of second-line chemotherapy in advanced NSCLC we tried to increase regional cytostatic drug concentration in thoracic region by using a regional application form – isolated thoracic perfusion (ITP). Thoracic perfusion means the limitation of the greater circulation to the thoracic region by placing two balloon catheters in the aorta and vena cava as well as two Esmarch bandages at the roots of both arms. Pharmacokinetic studies about this application form using different cytostatic drug like Doxorubicin, Melphalan, FUDR, Cis-Platin or Mitomycin have shown a 6 to10 –times increase in locoregional drug concentrations compared to systemic application (1,17,18,19,21).
Aim of this study was to evaluate the efficacy and toxicity profile of two different cytostatic regimen applicated as ITP in advanced NSCLC patients who have recurrent or refractory disease after one or more inductive treatments. The first regimen consists of a triple combination of cytostatics with Mitomycin , Aclarubicin and Melphalan given during ITP. The second regimen was used as a combination of regional plus low-dose systemic chemotherapy using Mitomycin, Navelbine and Cis-Platin as regional chemotherapeutic and 5-Fluorouracil and Cis-Platin as systemic cytostatics.

Patients and Methods

Patients with histologically or cytological confirmed unresectable or metastatic NSCLC entered this trial, provided that they had an acceptable performance status Karnofsky – index of 60 and more, a life expectancy of > 3 months, and adequate bone marrow, hepatic and renal function. Patients with severe atherosclerosis, concurrent severe cardiac, metabolic or infectious disease were excluded from this trial. Patients were eligible, if they had received one or more prior treatment such as systemic chemotherapy, radiotherapy of the chest and / or mediastinum or operative interventions. Patients in stage IV disease were enrolled only when distant metastases were located in thoracic region.
Definitions of response (i.e. partial or complete response), stable disease and progressive disease were based on the standardized response criteria established by the World Health Organization (WHO). All patients with advanced and recurrent NSCLC were enrolled after giving informed consent. Prior start of treatment patients were staged with chest x-ray, abdominal ultrasound and computed tomography (CT-scan) of the chest. During treatment patients were monitored with a weekly blood count . Toxicity were graded according to WHO criteria before each therapy course.
Responses were assessed after second therapy cycle with CT-scan and determination of tumormarker levels, if positive. Survival and response were both determined in all enrolled patients and calculated starting from the beginning of second-line chemotherapy treatment.

Treatment plan

This is prospective, not randomized trial with two different therapeutic regimen:
Group A: regional chemotherapy alone ;
All cytostatics (mitomycin 10 mg/m^2, aclarubicin 22 mg/m^2 and melphalan 10mg/m^2) were applicated during first two minutes of ITP via central venous line.
Group B: regional plus systemic chemotherapy.
The following cytostatics were administered during ITP via central venous line (mitomycin 10 mg/m^2, navelbine 25 mg/m^2 and cisplatin 30 mg/m^2) whereas 5-Floururacil 250 mg/m^2 and cisplatin 20 mg/m2 was given as continuous infusion over 24 hours on day 1 – 4.
Second-line chemotherapy was administered after a minimum 4-week interval after previous chemotherapy in patients showing progressive disease. Treatment free interval was 4 weeks, also. In case of leucocytopenia or thrombocytopenia WHO grad 3 or 4 next therapy cycle was postponed until WBC count was > 3000 /dl and platelet count > 100.000 /dl. The use of granulocyt stimulating factor G-CSF was possible. Treatment was discontinued, if disease progression or major toxicity occurred or according to patient's and / or physician's decision.

Operative technique

Under general anesthesia both femoral vessels were exposed via an inguinal approach. After systemic heparinisation with 150 I.E. Heparin / kg . BW both vessels were crossclamped and two 10 french balloon catheters were inserted. Under x-ray control both balloons were insufflated in the aorta just above the celiac axis and in the inferior caval vein below the right atrium. In order to reduce the perfusion volume Esmarch-bandages were insufflated around both roots of the arms (occlusion pressure: 250 mg / Mercury). For continuous arterial pressure measurement a arterial line was placed into descending aorta. Cytostatics were given via central venous line in first two minutes after start of perfusion; perfusion time was 20 minutes.

Results

From January 1995 to April 1997 15 patients entered this study as group A with regional chemotherapy alone and between May 1997 and December 1999 another 15 patients could be accrued in this study as group B with regional plus systemic chemotherapy. Patient characteristics are listed in Table 1. Both group of patients were comparable in terms of stage, Karnofsky-Index and histology. There was a difference for age (group A: mean 64.9 y, group B: mean 53.1y) and number of pretreatments (group A: 30, group B: 20) only.

Table 1: Patient Characteristics

Characteristics	Group A	Group B
Total Number	15	15
Male	7	6
Female	8	9
Age mean:	64.9 years	53.1 years
Range:	52 - 81	36 – 68
Performance Status		
Karnofsky – Index mean	82.0	84.7
median	80	80
Stage		
III	8	6
IV	7	9
Histology		
Adenocarcinoma	5	7
Squamous	7	3
Large cell	2	4
Bronchoalveolar	1	1
Pretreatments		
Radiation	11	8
Chemotherapy	7	6
Operation	12	6

Responses were evaluated in all 30 patients. Fourteen patients (46.7 %) achieved a complete 1/ 30 or partial response 13/30 with two patients who could be re-operated for cure. As shown in table 2 response rate was 40 % in group A and 53.3 % in group B (Fischer test, p = 0,357, not significant).There were 9 patients achieving a stable disease and in 7 cases the tumor was progressive. Responses occurred with equal frequency in all

Table 2: Response to Treatment

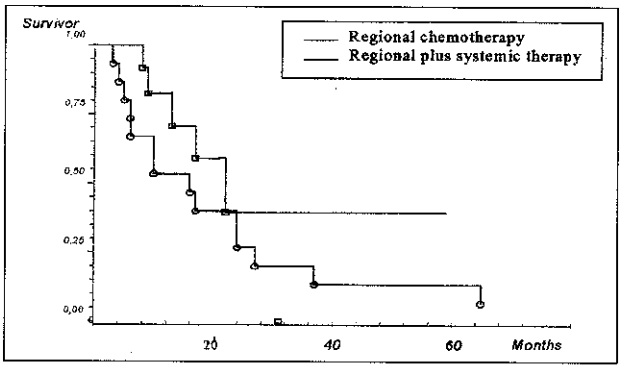
Response	Group A	%	Group B	%
Complete Response	1	6.7	0	–
Partial Response	5	33.3	6	40
Partial Response + OP	0	–	2	13.3
Stable Disease	5	33.3	4	26.7
Progression	4	26.7	3	20

histologic subtypes, in patients with stage III disease as well as in patients with stage IV disease.
The median survival time for all patients from start of regional chemotherapy was 17 months, 1-year and 2 year survival rate was 67.3 % and 31.3 %. Looking for the same data dependent to both subgroups there was a clear difference in favor of group B with combined regional plus systemic chemotherapy. Due to the small number in each group of patients this difference was not statistically significant (Wilcoxen-test, p = 0.116) . There was also an advantage for recurrent stage III patients with a median survival of 24 months compared to 16 months in stage IV. This difference was also not significant (p = 0.127).

Table 3: Survival data

	Group A	Group B	P – value
Median survival	16 months	22 months	0,116
1-year survivalrate	53.3 %	82.5 %	–
2-year survivalrate	26.7 %	39.3 %	–
	Stage III	Stage IV	P - value
Median survival	24 months	16 months	0,127
1-year survival	75.5 %	60 %	–
2-year survival	38.8 %	25 %	–

Diagram 1: Overall survival time from start of regional chemotherapy



Toxicity

Toxicity was evaluated for all 30 patients (Table 4,5) giving 58 cycles for 30 patients. Hematologic toxicity was the main, but not severe side effect in this trial. 4 patients in group A and 6 patients in group B developed WHO grad 3 / 4 Hematologic toxicity, but growth factors have to be administered in only 2 cases. Duration of leucocytopenia was usually brief, no infectious episodes occurred. Nonhematologic toxicity consisted of mild and transient fever and Cis-Platin dependent neurotoxicity. A deep vein thrombosis occurred in two cases and a lymphatic fistula after operative placement of catheters in another 3 cases, treated conservatively.
In none of all cases ITP has to terminated early due to disturbance in blood pressure parameters.

Table 4: WHO – Toxicity Group A (30 cycles)

	Grad 1	Grad 2	Grad 3	Grad 4
Vomitus	6	10	–	–
Fever	–	–	2	–
Alopecia	–	2	3	1
Hemoglobin	–	2	–	–
Platelets	–	1	–	–
Leucocytes	2	3	3	1
Alk. phophatase	2	–	–	–
Liver enzymes	1	–	–	–

Table 5: WHO – Toxicity Group B (28 cycles)

	Grad 1	Grad 2	Grad 3	Grad 4
Vomitus	2	16	–	–
Fever	8	2	–	–
Hemoglobin	8	5	1	–
Platelets	1	–	2	–
Leucocytes	3	3	3	–
Peripheral neurotoxicity	1	–	1	–
Thrombosis	–	2	–	–
Pain	2	7	–	–

Discussion

In recent years, the role of chemotherapy has seemed to extend to the treatment of advanced NSCLC, mainly thanks to new drugs with innovative mechanisms of action and mild toxicity profiles, which have widened the indications for chemotherapy in advanced and disseminated disease. Although there is no evidence that second –line chemotherapy can influence survival in nonresponding advanced NSCLC patients or in those who experience disease progression, there is some suggestion that second-line treatment may be appropriate for patients with good performance status who experience disease progression after front-line chemotherapy or for patients who responded to initial chemotherapy and then experienced a progression free interval off treatment.
The options available to patients with advanced non-small cell lung cancer (NSCLC) resistant or refractory to first-line chemotherapy are very limited. The older-generation drugs (etoposid, vindesine, epirubicin, and cisplatin) that are active against previously untreated NSCLC do not achieve a response rate greater than 10% when used in the second-line setting (2). The newer-generation agents with activity in previously untreated NSCLC include Carboplatin, Paclitaxel, Docetaxel, Vinorelbine, and Gemcitabine. Although NSCLC remains relatively resistant to chemotherapy, the fact that second-line chemotherapy is being considered is tribute to the progress being made with first-line therapy.
One of the first data about second-line chemotherapy were given in 1992 by Gridelli et al.; in a phase II trial of 40 patients with advanced and recurrent NSCLC they have shown that Mitomycin /Vindesine regimen is not active, but a combination chemotherapy using Epirubicin and Cis-platin lead to

Table 6: Prospective trials about second-line treatment in recurrent NSCLC

Author	Year	No.pts	Cytostatic drug	Response %	Survival (weeks)
Gridelli	1992	28	Cis–Platin, Epirubicin	25	–
Gridelli	1992	12	Mitomycin, Vindesine	0	–
Georgoulias	1997	26	Gemcitabine,Paclitaxel	29	32
Fossella	1997	88	Docetaxel	17	39
Stathopoulos	1999	80	Paclitaxel, Cis–Platin	16	42
Crino	1999	81	Gemcitabine	19	34
Gridelli	1999	30	Gemcitabin	20	22
Herrero	2000	16	Gemcitabine, Vinorelbine	6,25	25

an objective response rate of 25 % and an amelioration of tumor-related symptoms in 35.7 % as well as an improvement in performance status in 25% (10,11).
Recently Georgoulias et al. showed in a phase II trial of 26 patients in 1997 the significant activity of Gemcitabine combined with Paclitaxel as second-line treatment in platinum refractory NSCLC (9). In this study, a response rate of 29 % and a median survival rate of 8 months were achieved. Severe neurotoxicity (31 %) and fatigue (15 %) was the most interesting nonhematologic toxicity .
A similar phase II - studie given by Fossella et al. in 1997 has shown the significant clinical activity of docetaxel (100 mg/m^2 every 21 days) as second line treatment in platin resistant NSCLC. Response rates were 21 % leading to a 1-year survival rate of 41 %.
During last two years results of three different clinical trials about effectivity of Gemcitabine were given by Crino et al, Gridelli et al. and Herrero et al.(4,11,14). A pilot study done by Herrero was stopped due to a high rate of side-effects combined with a minimal responserate of 6.25 %. In contrast to this pilot study the results of the other two phase II – trials were combined with a much higher response rate of 19 and 20 %, leading to a median survival of 22 and 34 weeks.
Recently Stathopoulos et al. have published data about a combination of Cis-Platin and Paclitaxel in 80 recurrent NSCLC patients leading to an overall response rate of 16 % and a median survival time of 42 weeks showing that combination therapy should not be better than monotherapy (24).
In this study we have tried to overcome tumorcell resistance in recurrent NSCLC by using a high local cytostatic drug concentration. To reach this goal we used a simplified technique for isolation of the chest and lung compared with older application forms. In none of all cases ITP has to terminated early due to disturbance in blood pressure parameters. This is in accordance to published data from Berkenstadt et al., who has shown that ITP does not lead to increased cardial stress (3).
In 1995 Johnston et al. presented a special technique for isolated lung perfusion leading to an excellent separation of the lungs (15). Shunting rate was between 0 and 15 %, but we have to keep in mind that NSCLC is infiltrating the thoracic wall as well as the organs of the mediastinum in a high percentage of cases that an isolation of the lung does not necessarily correspond with the way of expansion in NSCLC.
In an animal model of bronchial adenocarcinoma Hendriks et al. have shown in 1999 that an isolated lung perfusion with Melphalan can prolong survival compared with no treatment or with systemic chemotherapy of the same drug in the same dosage (13). Pharmaco-kinetic evaluations in different mouse models have shown that using thoracic as well as lung perfusion techniques cytostatic drug concentrations of Melphalan, Doxorubicin, Cis-Platin, 5-FU and Mitomycin are 6 to 10 times higher compared with systemic administration (8,21,22).
Our own data in this study have shown a acceptable toxicity profile for these pretreated NSCLC patients who are in a reduced general condition and performance status. There were only two cases with special application form related side-effects such as lymphatic fistulas in the groin. In two other cases a deep vein thrombosis did occur. Systemic side-effects related to administration of cytostatic drugs were acceptable and not more frequent or more severe compared with other studies about second-line therapy in NSCLC.
Keeping in mind that this NSCLC patient population is selected to those having tumorformations defined to thoracic region only, response rates and survival rates are very encouraging. Compared with other second-line treatment studies response rate could be nearly doubled combined with a high percentage of patients in whom an amelioration of tumor related symptoms could be achieved (data not given).
Survival rate in our study was 24 months for stage III and 16 months for stage IV patients, which is also nearly doubled compared with other studies and protocols. This means that it will be possible to reach higher response rates leading to a longer median survival in NSCLC, if we can increase the locoregional drug concentration. Data in this study seem to support the hypothesis that isolated thoracic perfusion is an application form which increase local drug concentrations high enough to break through tumorcell resistance in NSCLC.

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knihy

ANGIOGENESIS IN HEALTH AND DISEASE - BASIC MECHANISMS AND CLINICAL APPLICATIONS

RUBANYI G. M. (Ed.)
Marcel Dekker, Inc., New York - Basel 2000
552 str., 103 obr., 33 tab., ISBN 0-8247-8102-3, cena 195,-USD

Cílem editora bylo uspořádání monografie shrnující poznatky z posledních let, které objasňují buněčné a molekulární mechanizmy vaskulogeneze a angiogeneze.
Úvodních 5 částí této obsažné knihy je věnováno kapitolám pojednávajícím o tématice bazálního výzkumu, následné 4 části pojednávají o nových terapeutických strategiích a klinických aplikacích. Učebnice tak poskytuje zevrubný rozbor těchto problematik: cévy a jejich vývoj, růstové faktory ovlivňující tvorbu cév a jejich receptory, geny řídící angiogenezu, modulátory angiogenezy, modelování angiogenezy in vivo a in vitro, inhibice angiogenezy v experimetálních modelech, klinické aplikace antiangiogenní terapie u karcinomů, angiogeneze a její ovlivnění při zánětech, hojení ran a revmatoidní artritidě, podpora angiogeneze v ischemizované tkáni. Autory 33 jednotlivých kapitol rozdělených do uvedených celků je 80 špičkových odborníků z USA a Evropy zabývajících se výzkumem uvedených problematik, a proto jimi sepsaný text není pouze širokým souhrnem poznatků, ale přináší i nejnovější informace o současných objevech (regulace angiogenezy angiopoetiny a TIE-receptory, angiogenní geny ß-4, EDG-1, ARNT proteiny, analýza významu vaskulárního endoteliálního růstového faktoru atd.) V textu jsou popsány také nové postupy potenciálně použitelné v klinické praxi, například genová terapie.
Příkladem zajímavé onkologické problematiky je terapie thalidomidem u nádorových onemocnění. Vzhledem k jeho antiangiogennímu efektu zjišťovanému při preklinických studiích na rohovkových modelech byly zahájeny klinické zkoušky tohoto preparátu u řady malignit. Jde především o Kaposiho sarkom, glioblastom, karcinom prsu, karcinom prostaty a nejnověji i o mnohočetný myelom. Na základě studií lze předpokládat, že aktivita thalidomidu je zprostředkována regulací integrinových podjednotek buněčných povrchů a tedy že jeho antiangiogenní účinek je spojen s ovlivněním exprese vaskulárního integrinu nebo s antagonistickým efektem na této úrovni.
Opačným směrem je zaměřen výzkum usilující o podporu neovaskularizace v ischemické tkáni růstovými faktory (FGF, VEGF). Jsou popsány tři možné postupy aplikace těchto látek do cílové oblasti: přímá injekce, inkorporace růstových faktorů do alginátových zrn implantovaných do ischemické tkáně a intraarteriální aplikace s použitím proteinových nebo genových vektorů.
Celkově je nutno ocenit kromě již výše uvedené aktuálnosti textu i přehlednou strukturu, s jakou byla upořádána celá kniha i její jednotlivé kapitoly. Na potřebných místech ilustrují text grafy, obrazy a fotografie. Unikátní je rejstřík citované literatury obsahující přes 3000 položek.
Kniha je určena nejen výzkumníkům zabývajícím se pouze obecnou problematikou vaskulogeneze a angiogeneze, ale i odborníkům řešícím praktické klinické aplikace na poli onkologie, revmatologie, hematologie, kardiologie, biochemie, farmakologie a dalších oborů. Naznačuje totiž cesty, jak lze tlumit angiogenezu v tumorech, v chronických zánětech typu revmatoidní artritidy a psoriázy, v oční sítnici při diabetické retinopathii a nebo naopak podporovat novotvorbu cév v ischemické tkáni.
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MALIGNANT LIVER TUMORS, CURRENT AND EMERGING THERAPIES

CLAVIEN P. A. (Ed.)
Blackwell Science, Malden 1999
363 str., 139 obr., 95 tab., ISBN 0-632-04406-3, cena 112,- GBP.

Editor, který je profesorem hepatobiliární chirurgie a transplantace jater na Duke University v Durhamu, předkládá monografii pojednávající o maligních nádorech jater a jejich léčbě. K spoluúčasti na knize přizval dalších 48 přispěvovatelů ze sedmi zemí, převážně z USA.
Kniha je rozdělena do pěti částí s 31 kapitolami. První série kapitol pokrývá patologii s podrobnějším zaměřením na hepatocelulární karcinom, hepatoblastom, cholangiokarcinom, karcinom žlučníku a metastázy, hlavně kolorektálního karcinomu. Dále je rozebrána epidemiologie a přirozený vývoj jaterních malignit. Dosti podrobně je pojednáno o jednotlivých diagnostických možnostech, UZ, CT v různých modifikacích a MRI včetně paramagnetických látek, jsou zmíněny i invazivní přístupy. V další části je podán přehled terapeutických postupů, systémová a selektivní chemoterapie, radioterapie, embolizace a chemoembolizace hepatické tepny. Dále jsou analyzovány postupy u resekcí hepatických tumorů spojené s adjuvantní a neadjuvatní léčbou, opakované resekce pro recidivu a ablační techniky (kryoablace, termická ablace radiovými vlnami, mikrovlnami, laserem), které vedou k nekróze nádorového ložiska a jeho blízkého okolí. Je popsána technika podání etanolu a dále transplantace jater, její indikace a přehled možných komplikací. Čtvrtá část se zabývá experimentálními pracemi, které se týkají genové terapie, imunoterapie a antineovaskulární léčby. Humorální a buněčné strategie se budou zřejmě dále rozvíjet a přecházet z experimentální fáze do praxe. Do této skupiny spadají i studované přípravky indukující apoptózu v nádorových buňkách potlačující tumor a jeho progresi. Pátá část obsahuje několik speciálních temat, jež se zabývají maligními nádory jater u cirhotiků, neuroendokrinními nádory a jejich jaterními metastázami, některými vzácnými nádory, malignitami u starších pacientů, nádory jater dětí a anesteziologickými otázkami při chirurgických výkonech na játrech.
Kniha demonstruje, že jen málo oblastí medicíny je doprovázeno tolika kontroverními názory jako ošetřování maligních nádorů jater. Současná dostupnost různých metod diagnostiky a léčby primárních a sekundárních nádorů jater a vzrůstající zájem o různé biologické a imunologické manipulace s maligními buňkami vzbuzují naději na vyléčení dříve letálního onemocnění nebo alespoň na prodloužení života o dobré kvalitě. Adekvátní přístup k terapii předpokládá součinnost multidisciplinárního týmu, v němž je zastoupen onkolog, hepatolog, hepatální chirurg, radioterapeut a intervenční radiolog. Kniha poskytuje jasný a kritický přístup k zavedeným léčebným metodám a možnostem využití nových cest.
Detailní text s četnými tabulkami a zajímavými příklady ze zobrazovacích metod zaujme všechny pracovníky, kteří jsou angažováni v ošetřování pacientů s tímto onemocněním od studentů lékařství až ke specialistů různých oborů. Řada kapitol přináší přehled o technikách, jež se propracovávají a představují výhledové nadějné metody blízké budoucnosti.
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