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Treatment of focal liver lesions

Thanks to advances in diagnostic procedures, particularly radiological ones, hepatic focal lesions are easier to differentiate. The diagnostic process requires close cooperation among physicians-clinicians, radiologists, histopathologists and surgeons. Such cooperation allows us to collect all possible data from case histories, laboratory tests, radiological and histopathological findings which enable proper classification of the observed focus. From the clinical point of view, it is most important to divide focal lesions into those requiring only further observation (US follow-up) and those in which surgical intervention is indispensible.

Focal lesions of benign nature in the majority of cases require only US follow-up. It is believed that small lesions are likely to become smaller once oral contraception is discontinued (7). However, the lesions big in size or localized in the regions causing compression symptoms and other complaints are treated as the cases in which their removal is indicated. Such lesions include big adenomas and focal nodular hyperplasia, which in most cases occur as single and big tumours. The lesions larger than 5 cm should be removed with an oncological margin due to the risk (low) of malignant lesions (11). Big hemangiomas are treated similarly, especially those causing thrombocytopenia (12). The following hemangiomas should be removed: • rapidly growing (>5 mm a year), particularly those localized centrally • giant • symptomatic • arousing suspicion of the presence of malignant lesions.

In the majority of cases, cysts also occur as small lesions, not requiring treatment but observation. Big cysts causing pain and compression symptoms should be enucleated or anastomosed with the intestinal loop (11).

Special focal lesions in the liver are abscesses as they are infective. Mortality is high in patients undergoing treatment ranging from 5 to 30% (8,11). If left untreated, they result in serious complications e.g. sepsis, peritonitis, inflammation of the retroperitoneal space. Treatment with antibiotics alone is not recommended due to its low effectiveness. It may be used only in patients whose general condition excludes invasive procedures. In such cases the patients are given antibiotics for many months and are closely followed up. The action spectrum of antibiotics administered should be as wide as possible until the abscess culture is available. The best choice is the combination of carbapenems with the second generation of cephalosporins. Simultaneously, metronidazole or clindamycin should be administered to fight anaerobic bacteria. If fungal infection is suspected, amphotericin B should be used. Generally, however, attempts should be made to collect the abscess contents by percutaneous aspiration, which can be cultured and antibiotic susceptibility determined (8). The optimal time of antibiotic administration is still being disputed. Short courses of therapy (two weeks) following percutaneous drainage give positive results only in small groups of patients. At present, 4–6-week antibiotic therapy following successful drainage is recommended. The treatment of multifocal abscesses is more problematic and requires over 12 weeks (11). Recently the reports have been published describing successive treatment of abscesses by infusing antibiotics to hepatic arteries. The procedure was used in patients who could not be subjected to percutaneous drainage and intravenous antibiotics did not result in any improvement. The patients received wide-spectrum antibiotics 2–4 times a day (9).

One of the methods combined with antibiotic treatment is percutaneous aspiration of the abscess contents. It enables the collection of the material for microbiological examinations and cleaning of the abscess cavity. The procedure is performed under US or CT guidance. Another method is percutaneous catheter drainage, which was first used in the 70's as an alternative to surgical management. The catheter is inserted under US or CT guidance . The catherter is washed every day until the outflow lower than 10 cm^3/day is achieved. An indication for surgical intervention is lack of effective drainage. Rare complications include haemorrhage and peritonitis. Contraindications for surgical treatment are coagulopathy, difficult access to the abscess cavity or complex, multifocal abscesses with thick walls and dense contents. The patients should be closely monitored. Treatment effects should be evaluated once a week by CT. If after two weeks of treatment the temperature is still high, more intensive action should be undertaken, including surgical management (11).

The therapeutic effectivenes of percutaneous aspiration as well as drainage of the abscess is similar (13). However, due to its lower invasiveness, patients' comfort and costs, aspiration should be used as the first procedure.

Amoebic abscesses are treated differently. Abscesses up to 10 cm in diameter, uncomplicated may be treated exclusively with metronidazole. Percutaneous drainage of the abscess combined with antibiotic treatment did not result in higher effectiveness (2).

Surgical drainage of abscesses was commonly used since the introduction of less invasive procedures. At present, the indications for this procedure include: the symptoms of peritonitis; the presence of the inflammatory focus in the abdominal cavity, e.g. diverticular abscesses; the percutaneous drainage failure; the presence of multifocal, thick-walled abscesses with dense contents. The most important contraindications include: shock, renal or pulmonary failure, weight loss bigger than 10 kg, albumin levels lower than 3 g/dl.

The procedures may be performed in the following way: 1) transperitoneal approach, which enables abscess drainage and abdominal cavity exploration in order to detect abscesses earlier undetected and to localize the infection sources; 2) posterior transpleural approach, particularly to the foci located high at the back. Although this access is easier, the identification of possible, concomitant intra-abdominal pathology is impossible. Postoperative complications occur in about 20–40% of cases and include recurrent abscesses, the development of abdominal abscesses, renal and hepatic failure and wound infections (11).

The treatment of primary and secondary hepatic neoplasm is equally difficult as the former coexists with serious pathology – cirrhosis of the liver, the latter indicates generalization of the neoplastic process.

Treatment of hepatocellular carcinoma (HCC). The treatment of primary neoplasms of the liver is undertaken to cure or to provide palliative therapy (allevation of complaints and prolongation of life). The functional reserves of the liver should be considered while making a decision about treatment, as the majority of HCC develops from cirrhosis (1). If the tumour is small or confined to one lobe, surgical treatment gives the chance of recovery. The patients with advanced disease unsuitable for surgical treatment survive only several months. The patients with resected tumours have slightly better prognosis with the mean survival of 2–4 years (11). In the cases of big tumours or those developing in both hepatic lobes the chance of recovery is liver transplantation. However, according to Milano criteria, the best candidates for transplantation are patients with a single tumour not exceeding 5 cm in diameter or with maximum 3 tumours up to 3 cm in diameter. The average time of waiting for transplantation in most European and American centres is 10–12 months (4). The preliminary results of studies in which transplantation was used in patients with inoperable HCC were disappointing. During corticosteroid and cyclosporin treatment after transplantation, the development of tumour promoted by immunosuppressive factors is observed. The observed recurrency index is high, therefore attempts should be made to use neoadjuvant therapy. Most commonly, pretransplantation chemotherapy, chemoembolization and radiotherapy are used, separately or in combination with other methods (1, 6).

In patients with more advanced neoplasms the palliative methods may be used. At present, there are several methods of palliative treatment including:

1. US-guided percutaneous ethanol injection to the tumour (PEI). It results in non-selective denaturation of proteins and formation of coagulative necrosis of tumour cells, necrosis of endothelial cells and aggregation of platelets leading to thrombi of small vessels nourishing the tumour. The treatment effects are evaluated by imaging examinations which visualize the necrotic part of the tumour. The survival after PEI depends on the cirrhosis stage and tumour mass. However, all the treated patients develop new tumours. After 5 years recurrences occur in 64–100% of patients (1).

2. Embolization or chemoembolization of hepatic arteries (TAE). This procedure is based on the fact that hepatic tumours receive 80% of blood from the hepatic arteries. Due to embolization the vessels nourishing the tumour are closed. For this purpose the gelatinous-spongostan emboluses are commonly used, which are resorbed within 2 weeks. Nowadays the embolizing material is used as a carrier for the chemotherapeutic agent. The tumour necrosis in its centre is achieved in about 50% of cases, however, the living cells nourished by the portal vein remain at the periphery. The most common chemotherapeutic drug used for embolization is doxorubicin. Implicit contraindications for TAE are: complete thrombosis of the portal vein, class C cirrhosis of the liver (Child's classification) and severe coagulation disorders (1).

Systemic chemotherapy is of no significant role in the HCC treatment, particularly in patients with cirrhosis as it leads to side-effects. It is believed that differences in general condition of the patient have bigger effects on survival than the differences in chemotherapies. At present, the results of treatment with 5-fluorouracil, mitoxantrone, cisplatin, etoposide, neocarcinostatin and epirubicin are being analysed. However, the medicine of choice in standard HCC therapy is thought to be doxorubicin. The average percentage of responses to doxorubicin is about 20%, and the average survival – about 4 months (10). Recently, subcutaneous IFN-alfa injections combined with arterial administration of 5-fluorouracil (5-FU) have been used. The preliminary results are quite promising (10). The experiments in which immunotherapy is used are in phase I and II of clinical studies (5).

The results of HCC radiotherapy are definitely disappointing. The development of post-radiation hepatitis is observed at the doses below 20–35 Gy, which are smaller than those required for tumour treatment. The survival in patients subjected to radiotherapy followed by fourfold chemotherapy was shorter than in patients undergoing only chemotherapy (1).

Treatment of cholangiocellular carcinoma (CCC). Similarly to HCC, only surgical treatment gives chances to cure CCC. However, diagnoses are made too late and treatment is rarely performed. The average survival without surgical treatment is 6 months. Chemotherapy and radiotherapy give disappointing effects. Prognosis is also related to the tumour location, slightly better when tumours are located in the liver hilus. It is thought that patients with CCC located outside the hilus should not be qualified for transplantation procedures (1, 6, 11).

Treatment of liver metastases. The treatment of patients with metastatic lesions depends mainly on the kind of primary neoplasm and general status of the patient. There are several possibilities corcerning the presence of metastases: 1) patients subjected to removal of the primary focus in whom the hepatic lesions were found after some period of time; 2) patients with the primary focus and metastases detected simultaneously; 3) patients with detected hepatic metastases and the unknown primary focus.

Group 1 patients are most often administered systemic chemotherapy, particularly in cases of metastases originating from the large intestine. It is believed that once infiltration of hepatic lymph nodes has been excluded, surgical removal of foci 1–4 is possible. Without resection, most patients with hepatic metastases of the large intestine carcinoma die within 3 years, the 5-year survival is observed in 1–3% of cases. Among metastases from other locations, the best results are achieved in patients with endocrine neoplasms. In recent years, increasingly higher number of reports has been published about good late results of resection of hepatic metastases from the clear cell carcinoma of the kidney (11).

When the primary lesion is detected simultaneously with metastases, it is recommended to remove the primary focus and then apply systemic chemotherapy, PEI or TAE. When the primary focus is not located, the diagnostic procedures should be focused on finding it, usually in the di-

gestive tract. If the procedures fail, US-guided biopsy of metastases should be performed in order to evaluate them histopathologically (1).

In recent years the survival of patients with hepatic metastases has prolonged, mainly due to more effective chemotherapy. Despite this evident progress, many patients may receive only symptomatic treatment. Hopes for improved prognosis are connected with researchers working on new drugs selectively destroying the neoplastic tissue.

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SUMMARY

Thanks to advances in diagnostic procedures, particularly radiological ones, hepatic focal lesions are easier to differentiate. From the clinical point of view, it is most important to divide focal lesions into those requiring only further observation (US follow-up) and those in which surgical intervention is indispensible. Focal lesions of benign nature in the majority of cases require only US follow-up. Liver abscesses are usually bacterial, amebic and fungal. The methods combined with antibiotic treatment are percutaneous aspiration of the abscess contents and percutaneous catheter drainage. The indication for surgical drainage is their failure. The treatment of primary neoplasms of the liver is undertaken to cure or to provide palliative therapy. The functional reserves of the liver should be considered while making a decision about treatment, as the majority of HCC develops from cirrhosis. The treatment of patients with metastatic lesions depends mainly on the kind of primary neoplasm and general status of the patient.

Leczenie zmian ogniskowych wątroby

Dzięki postępom w diagnostyce, zwłaszcza radiologicznej, łatwiej zróżnicować zmiany ogniskowe w wątrobie. Z punktu widzenia klinicznego najważniejszy jest podział zmian ogniskowych na te wymagające wyłącznie dalszej obserwacji (kontrola ultrasonograficzna) i te, które podlegają interwencji chirurgicznej. Zmiany ogniskowe o charakterze łagodnym w większości przypadków wymagają tylko kontroli usg. Leczenie ropni obejmuje antybiotykoterapię razem z przezskórną aspiracją lub przezskórnym drenażem treści ropnia. Ich niepowodzenie jest wskazaniem do zastosowania procedury chirurgicznej. Leczenie pierwotnych nowotworów wątroby jest podejmowane bądź to z intencją wyleczenia lub jako leczenie paliatywne. Podejmując decyzje o leczeniu, należy brać również pod uwagę rezerwy czynnościowe wątroby, gdyż większość HCC rozwija się na podłożu marskości. Leczenie pacjentów ze zmianami przerzutowymi zależy przede wszystkim od rodzaju nowotworu pierwotnego oraz od stanu ogólnego pacjenta.