Possibilities of contrast-enhanced ultrasound tomography in the diagnosis of metastatic liver lesions in patients with cervical cancer

Yakubov Doniyor Javlanovich, Turanov Aziz Rustamkulovich, Baymuratova Aziza Chori kizi

Department of Medical Radiology, Samarkand State Medical University, Samarkand, Uzbekistan.

Objective: to study the possibilities of contrast-enhanced ultrasound (CUSI) in the diagnosis of metastatic liver damage in patients with cervical cancer.

Materials and methods. The results of 4 clinical observations were analyzed, of which 3 cases were diagnosed with metastatic liver damage and 1 case with nodular hyperplasia.

Results and conclusions. Despite the small number of observations, it is concluded that the use of CUSI allows expanding the possibilities of ultrasound examination in the differential diagnosis of focal changes in the liver.

Keywords: cervical cancer, ultrasound, contrast-enhanced ultrasound, contrast enhancement, metastases, liver

Introduction

Therapy for the progression of malignant tumors is one of the most urgent problems of modern oncology. Features of relapse and metastasis of malignant neoplasms determine the clinical course of the disease, its prognosis, and treatment tactics for this category of patients. The effectiveness of treatment largely depends on the timeliness and quality of diagnosis.

With the progression of cervical cancer (CC), there are several ways to spread the tumor, depending on the type of its growth. With exophytic forms of cervical cancer, metastases in the vagina are more often diagnosed, with endophytic and mixed forms - in the uterine body or vaginal stump after surgical treatment, which characterizes the local spread of the tumor. Regional spread is characterized by metastasisof m to retroperitoneal (pelvic andlumbar) lymph nodes, which is an unfavorable prognostic factor. Hematogenous metastases in cervical cancer are rarely diagnosed; they are localized in the lungs, liver, and bones [1].

After surgical treatment, approximately 25 % of relapses occur in the dome of the vaginal stump or subcultal region. After radiation therapy, relapses in the body, cervix and upper third of the vagina are detected in 27 % of cases, in the lower third of the vagina-in 6 %, and distant metastases — in 16 % of cases [1].

According to P. Zola etal. (2007), in a multicenter retrospective study, 79 out of 327 patients with recurrent cervical cancer were found to have distant metastases, while 41 (51.9%) patients had liver metastases [2].

In the study of N. Bacalbasa etal. (2016), evaluating the effectiveness of liver resection for metastatic lesions in cervical cancer, included 15 patients, 2 of whom were diagnosed with synchronous metastases, i.e. those that occurred within 6 months of the start of tumor treatment. In 13 cases, metachronous metastases were diagnosed, which occurred after 6 months from the start of treatment and were detected during dynamic follow-up. The median overall survival for the entire cohort was 18 months after liver resection [3].

In a study involving 65 patients who received complex and combined radiation treatment for stages I—III cervical cancer, liver metastases were diagnosed in 2 (3 %) patients. At the same time, the authors note that the occurrence of relapse of the underlying disease does not always have a clinical picture, and point out the importance of a comprehensive dynamic examination of patients after treatment [4].

Currentlyонкогинекологии, various methods of visual diagnostics are used in oncogynecology to dynamically monitor patients after specialized treatment for cervical cancer: ultrasound (ultrasound), computed tomography, magnetic resonance imaging (MRI) and positron emission tomography. Each of these methods of radiation diagnostics has its own advantages and disadvantages [5].

Ultrasound occupies one of the leading positions in modern oncogynecology due to such advantages as non-invasiveness, harmlessness of the method, the possibility of multiple studies, accessibility and relatively low price of the study.

Recently, more and more new, additional techniques aimed at improving the quality and information content of images have appeared in ultrasound diagnostics. One of these techniques is contrast-enhanced ultrasound (CUSI). The essence of this technology is to use a contrast agent, which is a suspension of microbubbles with a diameter of 2.5 microns, filled with анных inert gas with a low level of solubility in water and surrounded by an elastic membrane of phospholipids,which ensures their highstability in the bloodstream.

Initially, data on the use of CUSI were published in theEuropean Journal of Ultrasound Diagnostics Ultrasoundin 2004 and were devoted only to the study of the liver [7]. Subsequently, KUSI was presented in other important recommendations for the diagnosis of liver foci, including the recommendations of the American Association for the Study of Liver Lesions and the Japanese Society of Hepatologists [8].

As mentioned earlier, unfortunately, it is not always possible to visualize signs of metastatic liver damage in seroscal mode, especially in the absence of clinical manifestations and complaints from the patient, and in this case, the use of contrast enhancement (CU) allows timely detection of even small metastases, which further affects the patient's management tactics.

When performing CUSI, liver metastases have a certain picture, which depends on the characteristics of the blood supply to the focus and the duration of the study. There are 3 phases of the study: arterial, portal and late. The arterial phase provides information about the degree and nature of contrast agent accumulation in the studied formation and begins on average from the 20th second after administration of the drug and lasts up to 30-45 seconds. The portal and late phases characterize the features of the contrast agent washout; the portal phase lasts from 30-45 to 120 seconds, the late phase-from 120 seconds to the complete disappearance of bubbles (4-6 minutes) [9].

Liver metastases are characterized by active leaching of the contrast agent in the portal and late phases, so in most cases they look like black (anaechoic) foci against the background of uniformly increased liver echogenicity [9].

Materials and methods

In our study, we analyzed the results of CUSI in 4 patients diagnosed with cervical cancer who were examined and treated at the N. N. Blokhin National Medical Research Center of Oncology of the Ministry of Health of the Russian Federation (N. N. Blokhin National Research Center of Oncology) in the period from 2015 to 2017. At the same time, 1 patient initially applied to the scientific and advisory department after treatment of cervical cancer with metastases in retroperitoneal lymph nodes at the place of residence, 3 patients were found to have progressed the disease 2 years after treatment at the N. N. Blokhin National Research Medical Centerof Oncology. " Complex treatment was performed in 1 patient, 3 patients received combined radiation therapy and chemotherapy. Stage IVb was established in 3 patientsIVb стадия, у 1 — IIa, and stage IIa was established in 1patient. Morphologically, in 1 case — glandular squamous cell carcinoma, in 2 — squamous cell carcinoma, in 1 case-squamous cell and cancer, light-cell variant. Patients underwent ultrasound of the liver in seroscalemode and CU mode on the SONOSCAPE S50device. препарата использован SonoVue (Bracco Suisse, Switzerland) — a second-generation ultrasound preparation, was used as a contrast agent. The microbubble membranes that makerpa- ж upit serve as the interface between phases and have a high level of « противлениярressure resistance, which leads to a strong backscattering of the ultrasound signal, which is expressed опухоли женской репродуктивной системы in tumors of the female

reproductive system Оригинал ъные статьи в высокой эхогенности. The CU mode allows you to maintain vibrations of microbubbles and visualize them in parenchymal tissue in real time. The ultrasound machine is able to detect the echo signal from microbubbles and distinguish it from the linear signal of tissues, which allows you to effectively separate the signal from the contrast agent and the signal from the tissues and form a separate image of the contrast agent in combination with an anatomicalimage of the tissue.

Seroscal ultrasound was used to assess the structure of the liver parenchyma, the presence of additional foci, their location, echogenicity, and size. Then, a contrast agent was introduced through an intravenous catheter and the nature of accumulation and washing out of microbubbles in all 3 phases in the liver parenchyma and foci was evaluated in the CU mode, which was visualized in seroscal mode.

The data obtained with CUSI were compared with the MRI data that was performed in all 4 patients, and in 3 cases they coincided.

Results

In patient 1, focal formations in the liver were detected during MRI at the place of residence and confirmed at the N. N. Blokhin National Research Medical Center of Oncology during disk revision, but they could not be detected during ultrasound in seroscalemode, which prompted us to conduct CUSI for this patient. In the 2nd patient, a 1.5 cm diameter lesion was visualized in the second segment of the liver, and its structure should be differentiated between metastasis, cavernous hemangioma, and nodular hyperplasia. In the 3rd patient, several metastases were detected in the W-1U segments of the liver, merging into a conglomerate of 3.8 x 4.0 cm in size, in the Y segment — a single metastasis with a diameter of 1 cm (ultrasound of December 22, 2016, performed before chemotherapy); with repeated ultrasound after 2 courses of "chemotherapy" (February 7, 2017 positive dynamics was notedwith a decrease inости образоваthe length of the formation in the III—1st segmentof the ax to 3 cm and thickness to 2 cm, the remaining foci were not visualized. In the 4th patient 99У, гипоэхогенныеhypoechoicfoci with a diameter of 0.8 to 1.6 cm were found in the Y, VI, and US segments-= ги, although the US structure did not allow us to unambiguously judge their nature. To clarify the diagnosis, all patients underwent CUI.

In patient , no focal formations were detected in the liver parenchyma during the entire arterial phase; by the end ofthe arterial phase, at 40 seconds еУ сегментах стали определяться , hypoechoic 4 foci with a diameter of 0.6 to 2.5 cm were detected in Y segments (Fig. 1), which became anechoic by the end of the portal phase, 3). Other focal formations of I - in the liver parenchymawere not found that C. F. Dietrich etal. [10] on the example of 125 patients with liver

metastases from various localizations (gastrointestinal tract, pancreas, etc.). et al.) proved that in the portal and late phases, liver metastases are visualized oas hypoechoic and anechoic foci against the background of isoechoic parenchyma, which is a reliable sign of metastatic liver damage. These features of contrast agent elimination in patients with metastatic liver damage were noted and justified by a number of other authors, which allowed us to draw a similar conclusion.

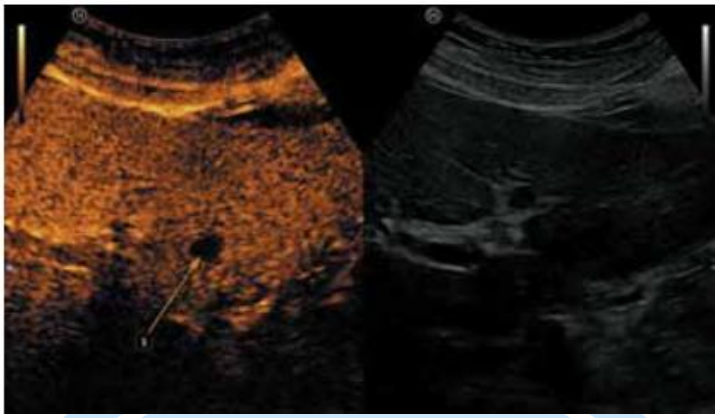

Figure 1. Ultrasound tomogram of the liver with contrast-enhanced ultrasound examination: at the 6th minute (late phase), an anechoic focus is detected in segment II (indicated by an arrow)

In the arterial phase, we studied the image of a cervical tumor and metastases in retroperitoneal lymph nodes. At the same time, an anechoic focus with a smooth contour was detected in the second segment of the liver until the 6th minute (Fig. 4). We emphasize that to date, a number of authors have defined fairly clear criteria for differential diagnosis between metastases, hemangiomas and nodular hyperplasia of the liver during CUSI [10-13]. According to the data of Y Dong etal. [13], obtained on the example of 45 patients, hemangiomas with CUSI in the arterial phase are characterized by peripheral accumulation of microbubbles in the centripetal direction and visualization of a hyperechoic focus in the late phase in 98% of cases. Thus, the above data allowed us to narrow the differential series in favor of metastatic liver damage in this case.

In the 3rd patient, in the arterial phase at the 15th second, the appearance of vesicles in the structure of the liver parenchyma was detected, while the formation determined in the gray-scale mode was visualized as an isoechoic focus. Closer to the portal phase, at the 50th second, this focus became hypoechoic and by the late phase (at the 120th second)-completely anechoic (Fig. 5). As in the 1st patient, it was the nature of contrast drug withdrawal in the venous and late phases that suggested metastatic "liverand liver damage". identify even small foci. In the 4th patientand when using CU, the ultrasoundpicture differed from previous observations: hyperechoic formations were visualized throughout theentire arterialphase гиперэхогенные образов(Fig. 6a), whichbecame isoechoic in the portal phase (from the 40th second) изоэхогенными и and retained this structure

throughout the entire late phase (Fig. 6b). According to F. Piscaglia etal. [11], who studied the possibilities of CUSI on the example of 72 patients with adiagnosis of "focal nodular hyperplasia", the characteristicfeatures of all types offocal hyperplasia are strong hyper-4 perfusion in thearterial phase and visualization of an iso-эechogenic or hyperechoic focus in the portal phase and late phases. They observed the phenomenon of leaching of the contrast agent only when the vesicles were destroyed or due to degenerative changes in large formations, especially in patients older than 35 years [14]. Similar features of accumulation and elimination of the contrast agent allowed us to conclude about focal liver hyperplasia.

Conclusions

The use of new technologies to improve the quality of early diagnosis of disease progression is certainly justified, since clarifying the prevalence of the tumor process allows you to choose an adequate treatment strategy and thereby increase survival rates. The cases analyzed by us convincingly prove that the use of CUSI can expand the capabilities and increase the informative value of the ultrasound method in the diagnosis of cervical cancer metastases in the liver.

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