CURRENT ISSUES OF CARCINOID HEART DISEASE DIAGNOSIS AND MANAGEMENT (CLINICAL OBSERVATION)

M.S. Khubutiya, G.A. Gazaryan, H.G. Alidzhanova, L.G. Gazaryan, R.S. Muslimov

N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Healthcare Department, Moscow, Russian Federation

ABSTRACT

We report a case of progressive carcinoid heart disease having caused readmission of a patient after excision of endocardium with arterial intima and multiple valve replacement. The data prove that in cases of combined valve heart disease of the right side it is necessary to assume the high probability of the carcinoid disease. Therefore, in spite of the high value of echocardiography, multispiral computed tomography, confirming the diagnosis, detecting metastases in different organs and determining the localization of the primary tumor, becomes particularly important. Open heart surgery can be effective only when accompanied by operative therapy for the primary tumor with the use of somatostatin analogues.

Keywords: carcinoid heart disease, excision of endocardium and arterial intima, multiple artificial heart valves, echocardiography, multispiral computed tomography of the heart.

AV — aortic valve
BA — brachiocephalic artery
BP — blood pressure
CHD — carcinoid heart disease
CHF — chronic heart failure
CS — carcinoid syndrome
DU — doppler ultrasound
EDV — end-diastolic volume
EF — ejection fraction
EDV— end-systolic volume
HR — heart rate
IVS— interventricular septum
LA — left atrium
LV — left ventricle
MSCT — multispiral computed tomography
MV — mitral valve
OT — outflow tract
PA — pulmonary artery
PASP — systolic pressure in the pulmonary artery
RA — right atrium
RF — respiratory failure
RR — respiratory rate
RV — right ventricle
TV— tricuspid valve

Metastatic tumors of the heart, including tumors of neuroendocrine origin, occur 100 times more often than primary neoplasms [1—4]. They are rarely diagnosed lifelong [5—7]. Depending on the location and size of the primary tumor, its growth and invasion degree, the course of the disease is asymptomatic or alternatively with severe clinical manifestations [2, 8—9]. A wide range of symptoms can represent a variety of cardiovascular diseases, such as valvular heart disease, pericarditis, cardiomyopathy, myocardial infarction [5—6, 10], often combined with symptoms of other organs lesion [11]. In a third of cases the causes of death in patients are congestive heart failure, invasion into the coronary arteries and the sinus node, and cardiac tamponade [3, 6]. Metastatic tumors of neuroendocrine origin predominantly affect endocardium which often has intracavitary thickening [8, 12—13]. The latter changes the structure and hemodynamics of the heart, and is often covered with thrombotic masses that are the source of embolization of various organs [3]. Such thickening may cause the myocardial infarction and contribute to the myocardial rupture [13]. The cause of most intracavitary tumors of the heart is the carcinoid — a neoplasm, structurally resembling cancer [14]. It evolves from neuroendocrine cells, widely distributed in the body. Most frequently, the carcinoid tumor develops in the gastrointestinal tract (65%), especially in the small intestine, and much more rarely in the airways (25%) and other organs [15].

According to the literature, the number of carcinoids has increased over the last decade several times.They occur in 1—2 cases per 100000 population [16—17]. The carcinoid syndrome (CS) is its characteristic clinical manifestation [18—19], in some cases acquiring the character of a crisis [14, 20—21]. A typical symptom complex, including series of hypotension, flushing of the face and neck, diarrhea, and telangiectasia often occurs due to the release of a large number of biologically active substances into the blood produced by carcinoid, often as serotonin and kinins [21—24]. In half of the cases they lead to fibrosis of the predominantly right endocardium, involving the valve apparatus, caval veins and coronary sinus [18—22]. Typically, this mechanism is triggered after carcinoid metastatis in the liver, which hinders the biodegradation of vasoactive substances [18, 24—25]. The combination of failure of the tricuspid valve (TV) leaflets with stenosis of the pulmonary artery (PA) occurs only in carcinoid heart disease (CHD) [13, 18, 24]. In 1—2% of patients, heart failure may develop in the absence of liver metastases [20—22]. In these cases, the primary tumor can proceed not from the gastrointestinal tract. The correlation between the duration of CHD and the cardiac lesion has not been detected [16, 19, 22]. The carcinoid plaque consists of smooth muscle and endocardial cells, myofibroblasts, extracellular matrix and elastic tissue, forming a white fibrous layer lining the endocardial surface of the right heart, the leaflets of the TV and subvalvular apparatus, chords and papillary muscles, caval veins, the PA, coronary sinus and coronary arteries [14, 18—21]. According to *Fox D.* [18] and *Bhattacharyya S.* [20], the time from the onset of symptoms to diagnosis of CHD varies from 2 to 5 years. Predictors of risk of death include: older age, liver metastases, and the presence of CS [19, 22]. The average survival of patients from the beginning to the development of systemic symptoms of CHD is 3 years [20]. For the diagnosis of cardiac lesions we use different imaging techniques: echocardiography, magnetic resonance imaging and multispiral computed tomography (MSCT) [12—13, 26—28]. According to *Bernheim A.* [21], the prevalence of CHD has decreased by 20% over the past decade which occurs due to the active detection and surgical treatment of the primary lesion, the use of somatostatin analogues. The method of treatment of carcinoid heart lesions is surgery [29—32], which allows to extend the life for 7 years [33—34]. Three year survival in patients with and without CHD is 31% and 68%, respectively [35]. Half of the patients with liver metastases die within 5 years [36].

We report a clinical observation.

A 75-year-old female patient D. was admitted to the Department of Cardiac Surgery of the N.V. Sklifosovsky Research Institute for Emergency Medicine on 11.04.2012 with the diagnosis "Stenosis of the PA and failure of the TV". Upon arrival, the patient had a complaint of

shortness of breath at rest, a tendency to hypotension, intermittent "hot flashes" in the face and neck, leg swelling, weakness. She had considered herself as sick since 2009. The sharp deterioration — in April 2012. Single telangiectasia on the face. Severe pulsation of neck vessels. RR — 20 breaths per minute. Vesicular breathing, no wheezing. Heart sounds — rhythmical, systolic murmur along the right edge of the sternum. HR — 80 heart beats per min. BP — 100/80 mmHg. Abdomen was soft and painless. Liver at the costal margin, painless. Normal stool. Urination — painless.

Echocardiography on 13.04.12: the aortic root — 2.9 cm, the left atrium (LA) — 3.7 cm, the right atrium (RA) — 4.2 cm; the left ventricle (LV): end-systolic volume (ESV) — 19 ml; end-diastolic volume (EDV) — 53 ml; ejection fraction (EF) — 64%. The thickness of the interventricular septum (IVS) — 1 cm posterior wall thickness — 1 cm. The size of the right ventricle (RV) — 4.2 cm Aortic (AV) and mitral (MV) valves without pathology.TV leaflets were thin with violation of their coaptation, regurgitation grade 3. No sighs of the PA trunk narrowing. Diameter of the PA at the level of the valve — 2.8 cm, above the valve — 2.6 cm, the outflow tract (OT) of the RV — 2.5 cm. OT: indistinct intimal thickening with a floating structure of up to 6 mm, 8 mm beneath leaflets of the PA valve. The maximum gradient on the PA valve: 36—41 mmHg.

Coronary angiography on 13.04.12: no significant stenoses of the coronary arteries.

Doppler ultrasound (DU) of brachiocephalic arteries (BCA) on 12.04.12: atherosclerosis of BCA without hemodynamically significant stenosis.

MSCT with pulmonary angiography on 17.04.12: the heart has increased in size due to the right side; the RA— 6.5x5.5 cm; end-diastolic RV size of up to 4.5 cm; hypertrophy of the RV free wall spreading to the PA valve zone with the presence of funnel-chaped narrowing of up to 12 mm; the outflow tract of the RV and the initial parts of the PA had the form of a long channel with unevenly thickened walls (Fig. 1); the diameter of the right branch of PA — 20 mm, left — 17.5 mm. Conclusion: the symptoms of stenosis of the RV outflow tract, extended infundibular stenosis of the PA ostium, dilatation of the right heart chambers with severe hypertrophy of the RV.

Surgical intervention with cardiopulmonary bypass (23.04.12). The even endocardial thickening of up to 5—7 mm was observed in the RA cavity, the RV endocardium had the same structure as the one of the RA, the PA intima was thickened up to 3—4 mm, in the ostium of the PA — to 1 cm, with narrowing of up to 1 cm in diameter, simulating infundibular stenosis. The changed part of endocardium, including interatrial septum, was dissected from the inner surface of the RA in a blunt way.The changed endocardium of the RV outflow tract was excised off the parietal ridge and the area of the PA valve, and in the same way we removed the changed intima from the trunk of the PA and its major branches up to the level of the lobar arteries. TV leaflets were thickened up to 5 mm, their mobility was limited, the annulus fibrosus diameter — 5 cm, papillary muscles were dramatically thickened. The TV leaflets were excised together with the altered papillary muscles tissue, the xenopericardial bioprosthesis was implanted. The PA valve was degeneratively changed, the leaflets were deformed. The PA valve leaflets were excised and the xenopericardial bioprosthesis was implanted. In IVS, closer to the top, a defect of 5—6 mm diameter with callous edges was revealed. The defect was sutured.

Histological test of the valve leaflets and endocardium revealed unevenly thickened intima of the PA due to severe fibrosis and active fibroblastic reaction (Fig. 2); partial destruction of the endocardial elastic frame with preserved elastic structures of the small vessels of the myocardium; complete destruction of the elastic structure of the PA wall.

The postoperative period was complicated by hypotension that required prolonged use of sympathomimetics, persistent diarrhea, Frederick syndrome. The "ECS-electrode" pacemaker was implanted on 18.05.12.

The check echocardiographic study of the LV on 12.05.12: EDV — 70 ml; ESV — 33 ml; EF — 52%. The RA — 4 cm; The RV — 3.4 cm. The peak gradient of the PA valve prosthesis — 3.5 mmHg, regurgitation — grade 0—1. Average diastolic gradient of the TV prosthesis — 2.4 mmHg, regurgitation into the cavity of the RA — grade 0—1, pulmonary artery systolic pressure (PASP) — 25 mm Hg. The fluid in the pericardial and pleural cavities was not revealed.

The patient was discharged on the 55th day after surgery with the diagnosis: “Endocardial thickening of RA and RV, thickening of the PA trunk and intima of its branches. Valvular and subvalvular stenosis of the PA. IVS defect. The excision of endocardium and intima from RA, RV, PA and its branches, suture of the IVS defect, plastics of the RV outlet, replacement of the TV and the PA valve. Complete atrioventricular block grade III. The implantation of permanent electro-cardiostimulator with epicardial electrodes NK_2A in May 2012”.

Re-admission to the Emergency Cardiology Department occurred on 03.06.13 with the diagnosis of "Prosthetic PA valve thrombosis." Upon arrival: the growing dyspnea at rest, leg swelling, weight loss of 10 kg, transient series of pain in the right iliac region, spontaneous flushing of the face and neck, cough with scanty mucous expectoration, pain in the spine with limitation of motion. Puffy face, teleangiectasy. Severe pulsation of neck vessels. Peripheral lymph nodes were not palpable. BR — 20 breaths per minute. Heart breathing in the lungs, dry rales. Heart sounds — rhythmical, systolic murmur at Botkin’s area. Heart rate — 82 beats per min. BP — 115/80 mmHg. Liver was protruded from under the costal arch; the edge was thick and painless. Tendency to constipation. Urination — painless.

Echocardiography (03.06.13): compared with echocardiography sizes of 12.03.12 heart chambers were without changes. EF — 60%. The function of prostheses was not impaired. The mass in the RV apex with the spread to the RV outflow tract of 35x23 mm without significant obstruction was detected (Fig. 3). The average gradient of the PA valve prosthesis — 16 mmHg. Dilatation of the inferior vena cava, its insufficient contraction at inhale. Pulmonary hypertension grade 2. (PASP — 53 mmHg). IVS flattening due to right ventricular overload.

Electrocardiography on 03.06.13: Rhythm of the ECS with heart rate — 77 beats per min.

Chest X-ray on 03.06.13: venous plethora. The structure of the right pulmonary root was insufficiently observed, the right root was expanded, the left root was shadowed by the heart. The heart was enlarged in diameter. Flat waist.

Ultrasound of the abdomen and kidneys on 05.06.13: diffuse changes of the liver, pancreas and kidneys.

Esophagogastroduodenoscopy on 12.06.13: superficial gastritis.

MSCT of the chest, abdomen, and head on 05.06.13: the soft tissue mass of45x63x43 mm was detected in the outflow tract of the RV (Fig. 4), which accumulated contrast agent heterogeneously. The LA was enlarged; parietal overlay with decreased density of thickness up to 10 mm was revealed. Endocardial thickening of the RV, RA and LA of up to 4 mm. Thrombosis of small branches of the PA, areas of pulmonary fibrosis and infiltrative changes of different prescription. Pathological fractures of the vertebral bodies *Th* 12 and *L*2. Multiple focal masses in the liver. Multiple enlarged mediastinal lymph nodes (Fig. 5). Signs of abnormalities of the brain or the bones of the skull were not found.

Hemoglobin — 106.0 g/L erythrocytes — $3.8x10^{12}$/L, hematocrit — 31.8%, thrombocytes — $140.0x10^{9}$/L, leukocytes — $6.43x10^{9}$/L, ESR —37 mm/hour. INR — 2.27. Prothrombin — 27%. C-reactive protein — 44.8 mg/L, Anti-streptolysin O <13 IU/mL. Other parameters of blood biochemistry were normal. Blood somatostatin and 5-HIAA urine tests were not made due to lack of laboratory facilities.

Consultation of gynecologist on 05.06.13. Ovaries were not palpable. Asymptomatic uterine fibroid.

Consultation of oncologist on 10.06.13. Additional examination in city Oncology Center was recommended.

The final diagnosis was: "Carcinoid heart disease." Metastases in the liver, *Th* 12 and *L* 2. Mediastinal lymphadenopathy. Condition after excision of endocardium and intima of the right heart, PA and its branches, suturing defect of IVS, plastics of the RV outlet, replacement of the TV and the PA valve, implantation of permanent ECS in 2012. Chronic heart failure, II «B» class. Respiratory failure, grade II. Parietal masses in the left atrium. Recurrent thromboembolism of the PA branches.

According to the results of further examination in Oncology Center multiple metastases in the liver, mediastinum, spine and ischium were confirmed. The primary focus was not revealed. The patient died on 22.10.13. The autopsy had not been performed.

From the data performed we may conclude that the pathological condition, which served as an indication for heart surgery using a heart-lung machine, was the CHD. This was indicated by the typical endocardial lesion of the right heart with forming TV leaflets failure and PA stenosis, not occurring in other deseases. In addition, there were other manifestations of CHD, transforming into crisis with hemodynamic instability that caused the prolonged use of sympathomimetics during the postoperative period, various arrhythmias and conduction abnormalities of the heart with the development of the Frederick syndrome which required implantation of an artificial pacemaker.

The diagnosis of CHD was established upon re-hospitalization after echocardiography and confirmed by MSCT data. The latter revealed previously missing multiple enlarged mediastinal lymph nodes, focal changes in the liver and spine. We failed to find localization of the primary site. If we take into account that the patient had no liver metastases before the heart surgery, then at first glance, the localization of the primary site in the gastrointestinal tract becomes problematic. Multiple enlarged lymph nodes in the mediastinum, liver metastases and spine findings upon readmission, might be associated with the primary tumor localized in the airways. However, neuroendocrine neoplasms originating from the ileum are considered to be the most malignant ones [14—15]. It is considered that in their small size, slow growth without infiltration and compression of surrounding tissues, local symptoms of carcinoid tumor can be masked for a long period and the first manifestation of the disease may be diffuse thickening of the endocardium of the right heart without signs of malignancy [3, 6, 8, 18—22]. This unusual way of metastasis makes difficult to find the primary lesion, which does not allow predicting its location and the further development of the CHD. The latter is considered the main cause of death in patients with malignant neuroendocrine tumors. Therefore, in the majority of patients, as illustrated in our observation, the treatment is initiated with the heart surgery instead of verification of the tumor [21—22, 36]. Preference is given to the use of bioprostheses which do not require lifelong anticoagulation therapy increasing the risk of bleeding in patients with liver metastases [37—39]. Surgical correction of the defect has a positive effect on the remodeling process [30—32, 34—39]. In the perioperative period patients often die due to the development of complications caused by the carcinoid crisis [21, 37]. The latter ones are often provoked by anesthesia [40], the use of sympathomimetic drugs lyzing the tumor, as well as by the intervention itself. There has been a tendency of decrease in the early postoperative mortality over the last decade [28, 34]. This is considered to be related to advances in cardiac surgery combined with surgical treatment of the primary tumor and the use of somatostatin analogues [38—39, 41—42]. In the present case, a large amount of surgery, including excision of endocardium and arterial intima of the right heart, multiple valve replacement and suturing the IVS defect, despite the development of carcinoid crisis, helped compensate for the circulatory failure and extend the life of the patient for 1.5 year. Effectiveness of cardiac surgery was limited due to unrecognizable primary carcinoid lesion.

The presented data confirm that in cases of lesions of the endocardium of the right heart with developing TV failure and osteal stenosis of the PA we should mind high probability of CHD. In this regard, along with other manifestations of CHD, echocardiography and MSCT allowing to confirm the diagnosis, identify metastases in other organs, as well as to determine the localization of the primary lesion become especially useful. Method of choice for the treatment of CHD is the heart surgery, which increases the effectiveness of the surgical treatment of the primary lesion and the use of somatostatin analogues.

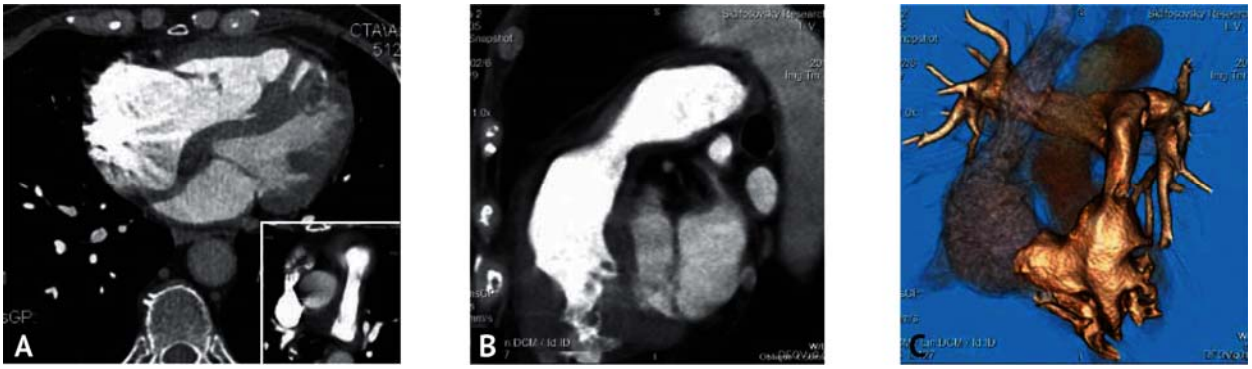

Fig. 1. Multispiral computed angiopulmonogram. Massive wall thickening, papillary muscles, and the outflow tract of the right ventricle with the presence of stenosis at the level of pulmonary valve are being revealed.

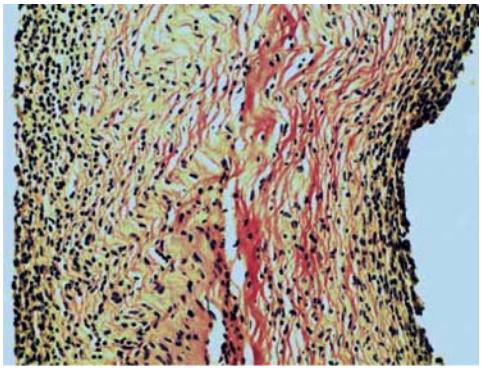

Fig. 2. Histology of an uneven endocardial thickening due to fibrosis with active fibroblastic reaction without evidence of tumor growth (Van Gieson's stain, magnification × 200)

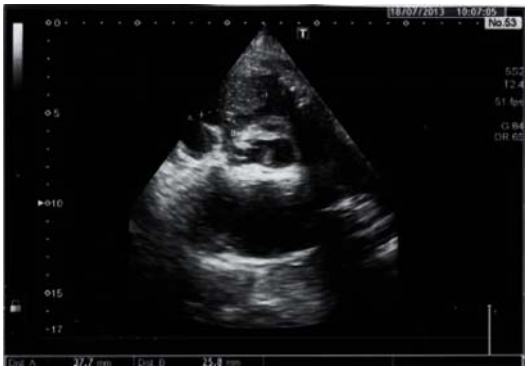

Fig. 3. Echocardiographic mass in the apex of the right ventricle with the spread to the outflow tract of the right ventricle of 35x23 mm without significant obstruction

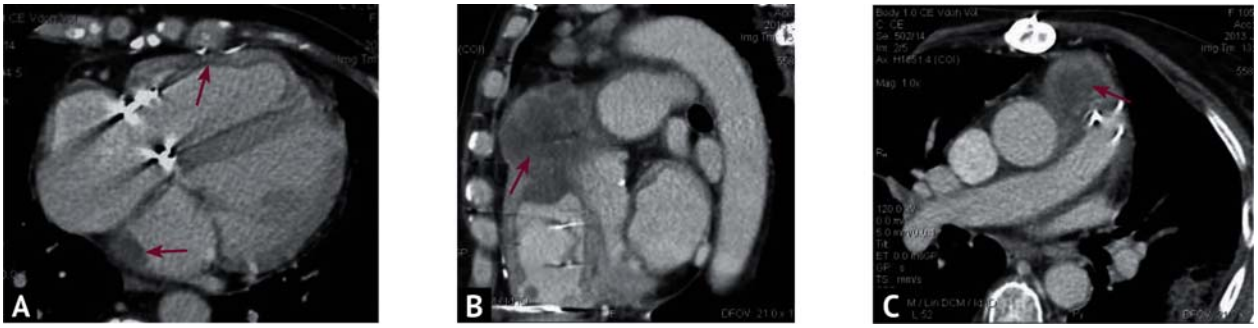

Fig. 4. Multispiral CT scan 14 months after surgery: *A* - myocardial hypertrophy of the right ventricle; *B, C* - tumor formation detected in the outflow tract of the right ventricle, extending into its cavity and in a para-aortic way, accumulative contrast agent. The linear zone of reduced density along the contour of the endocardium of the right ventricle, and the parietal masses in the left atrium should be noted. Enlarged lymph nodes of the mediastinum.

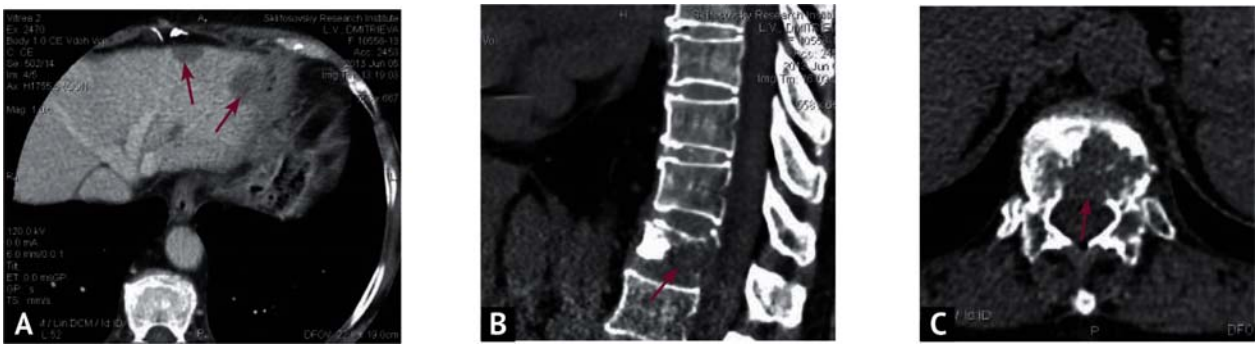

Fig. 5. Multispiral CT scan: *A* – multiple hypovascular focal masses in the liver, *B, C* - destruction of XII thoracic vertebra (metastases)

.

REFERENCES

1. MacGee W. Metastatic and invasive tumours involving the heart in a geriatric population: a necropsy study. *Virchows Arch A Pathol Anat Histopathol*. 1991; 419 (3): 183–189.
2. Bokeriya L.A., Malashenkov A.I., Kavsadze V.E., Serov R.A. *Kardioonkologiya* [Cardio-oncology]. Moscow: NTsSSKh im. A.N. Bakuleva RAMN Publ., 2003. 254 p. (In Russian)
3. Reynen K., Köckeritz U., Strasser R.H. Metastases to the heart. *Ann Oncol.* 2004; .15 (3): 375–381.
4. Grebenc M.L., Rosado de Christenson M.L., Burke A.P., et al. Primary cardiac and pericardial neoplasms: radiologic-pathologic correlation. *Radiographics*. 2000; 20 (4): 1073–1103.
5. Sarjeant J.M., Butany J., Cusimano R.J. Cancer of the heart: epidemiology and management of primary tumors and metastases. *Am J Cardiovasc Drugs*. 2003; 3 (6): 407–421.
6. Butany J., Leong S.W., Carmichael K., Komeda M. A 30-year analysis of cardiac neoplasms at autopsy. *Can J Cardiol*. 2005; 21 (8): 675–680.
7. Lam K.Y., Dickens P., Chan A.C. Tumors of the heart. A 20-year experience with a review of 12,485 consecutive autopsies. *Arch Pathol Lab Med*. 1993; 117 (10): 1027–1031.
8. Yusuf S.W., Bathina J.D., Qureshi S., et al. Cardiac tumors in a tertiary care cancer hospital: clinical features, echocardiographic findings, treatment and outcomes. *Heart Int*. 2012; 7 (1): e4.
9. Shkhvatsabaya L.V. Diagnostika vtorichnogo opukholevogo porazheniya serdtsa [Diagnosis of secondary tumor lesions of the heart. *Klinicheskaya meditsina*. 1983; 11: 61–65. (In Russian)
10. Amano J., Nakayama J., Yoshimura Y., Ikeda U. Clinical classification of cardiovascular tumors and tumor-like lisions, and its incidences. *Gen Thorac Cardiovasc Surg*. 2013; 61 (8): 435–447.
11. Knyshov G.V., Vitovsky R.M., Zakharova V.P. *Opukholi serdtsa. Problemy diagnostiki i khirurgicheskogo lecheniya* [Problems of diagnosis and surgical treatment]. Kiev: Kniga plyus publ., 2005; 254 p. (In Russian)
12. Pandya U.H., Pellikka P.A., Enriquez-Sarano M., et al. Metastatic carcinoid tumor to the heart: echocardiographic-pathologic study of 11 patients. *J Am Coll Cardiol*. 2002; 40 (7): 1328–1332.
13. Pellikka P.A., Tajik A.J., Khandheria B.K., et al. Carcinoid heart disease. Clinical and echocardiographic spectrum in 74 patients. *Circulation*. 1993; 87 (4): 1188–1196.
14. Golovin D.I. *Atlas opukholey cheloveka (gistologicheskoye stroeniye)* [Atlas of human tumors (histology)]. Leningrad: Meditsina publ.,1975. 320 p. (In Russian)
15. Öberg K.E. Gastrointestinal neuroendocrine tumors. *Ann Oncol*. 2010; 21 Suppl. 7: 72–80.
16. Janson E.T., Holmberg L., Stridsberg M., et al. Carcinoid tumors: Analysis of prognostic factors and survival in 301 patients from a referral center. *Ann Oncol*. 1997; 8 (7): 685–690.

17. Maksimova T.M., Belov V.B. Zabolevaemost' zlokachestvennymi novoobrazovaniyami i smertnost' ot nikh v Rossii i nekotorykh zarubezhnykh stranakh [The incidence of malignant neoplasms and mortality in Russia and some foreign countries]. *Problemy sotsial'noy gigieny, zdravookhraneniya i istorii meditsiny*. 2012; 1: 9–12. (In Russian)
18. Fox D., Khattar R. Carcinoid heart disease: presentation, diagnosis, and management. *Heart*. 2004; 90 (10): 1224–1228.
19. Ross E.M., Roberts W.C. The carcinoid syndrome: comparison of 21 necropsy subjects with carcinoid heart disease to 15 necropsy subjects without carcinoid heart disease. *Am J Med*. 1985; 79 (3): 339.
20. Bhattacharyya S., Davar J., Dreyfus G., Caplin M. Carcinoid heart disease. *Circulation*. 2007; 116 (24): 2860–2865.
21. Bernheim A., Connolly H., Hobday T., et al. Carcinoid heart disease. *Prog Cardiovas Dis.* 2007; 49 (6): 439–451.
22. Moller J.E., Connolly H.M., Rubin J., et al. Factors associated with progression of carcinoid heart disease. *N Engl J Med*. 2003; 348 (11): 1005–1015.
23. Zuetenhost J., Bonfrer J., Korse C., et al. Carcinoid heart disease. The role of urinary 5-hydroxyindoleacetic acid excretion and plasma levels of atrial natriuretic peptide, transforming growth factor-betta and fibroblast growth factor. *Cancer*. 2003; 97 (7): 1609–1615.
24. Lundin L., Norheim I., Landelius J., et al. Carcinoid heart disease: relationship of circulating vasoactive substances to ultrasound-detectable cardiac abnormalities. *Circulation*. 1988; 77 (2): 264–269.
25. Moller J., Pellikka P., Bernheim A. et al. Prognosis of carcinoid heart disease analysis of 200 cases over two decades. *Circulation*. 2005; 112 (2): 3320–3327.
26. Ragland M.M., Tak T. The Role of Echocardiography in Diagnosing Space-Occupying Lesions of the Heart. *Clin Med Res*. 2006; 4 (1): 22–32.
27. Bastarrika G., Cao M.G., Cano D., et al. Magnetic resonance imaging diagnosis of carcinoid heart disease. *J Comput Assist Tomogr*. 2005; 29 (6): 756–759.
28. Prakash P., Kalra M.K., Stone J.R., et al. Imaging findings of pericardial metastasis on chest computed tomography. *J Comput Assist Tomogr*. 2010; 34 (4): 554–558.
29. Connolly H.M., Schaff H.V., Mullany C.J., et al. Surgical management of left-sided carcinoid heart disease. *Circulation*. 2001; 104 (12) Suppl 1: I36–I40.
30. Connolly H.M., Schaff H.V., Mullany C.J., et al. Carcinoid heart disease: impact of pulmonary valve replacement in right ventricular function and remodeling. *Circulation*. 2002; 106 (12) Suppl 1:I51–156.
31. Mokhles P., Herwerden P., Herder W., et al. Carcinoid heart disease: outcomes after surgical valve replacement. *Eur J Cardio-Thoracic Surgery*. 2012; 41 (6): 1278–1283.
32. Narine K., Dohmen P., Daenen W. Tricuspid and pulmonary valve involvement in carcinoid disease. *Tex Heart Inst J*. 2000; 27 (4): 405–407.
33. Bhattacharyya S. Cardiovascular surgery in carcinoid heart disease. *Interact Cardiovasc Thorac Surg*. 2012; 15 (3): 471.
34. Thorburn C.W., Morgan J.J., Shanahan M.X., Chang V.P. Long-term results of tricuspid valve replacement and the problem of prosthetic valve thrombosis. *Am J Cardiol.* 1983; 51 (7): 1128–1132.
35. Komoda S., Komoda T., Pavel M.E., et al. Cardiac surgery for carcinoid heart disease in 12 cases. *Gen Thor Cardiovas Surg.* 2011; 59 (12): 780–785.
36. Castillo J.G., Filsoufi F., Rahmanian P.B., et al. Early and Late Results of Valvular Surgery for Carcinoid Heart Diseas. *J Amer Coll Card.* 2008; 51 (15): 1507–1509.
37. Mabvuure N., Cumberwortha A., Hindochab S. In patients with carcinoid syndrome undergoing valve replacement: will a biological valve have acceptable durability? *Interact Cardiovasc Thorac Surg.* 2012; 15 (3): 467–472.
38. Hajj-Chahine J., Jayle C., Houmaida H., Corbi P. Valve replacement in carcinoid heart disease. *Interact Cardiovasc Thorac Surg.* 2012; 15 (3): 471–472.
39. Mokhles P., van Herwerden L.A., de Jong P.L., et al. Carcinoid heart disease: outcomes after surgical valve replacement. *Eur J Cardiothorac Surg.* 2012; 41 (6): 1278–1283.
40. Vaughan D.J., Brunner M.D. Anesthesia for patients with carcinoid syndrome. *Int Anesthesiol Clin*. 1997; 35 (4): 129–142.
41. Connolly H.M., Pellikka P.A. Carcinoid heart disease. *Curr Cardiol Rep*. – 2006; 8 (2): 96–101.
42. Corleto V.D., Angeletti S., Schillaci O., Marignani M. Long-term octreotide treatment of metastatic carcinoid tumor. *Ann Oncol*. 2000; 11 (4): 491–493.

Article received on 13 March, 2014

For correspondence:
Alidzhanova Hafiza Gafurovna,
Dr. Sc. Med., Senior Researcher of the Department of Emergency Clinical Cardiology with Non-invasive Diagnostic Methods,
N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Healthcare Department, Moscow, Russian Federation
e-mail: **DOCTORHAFIZA@MAIL.RU**

ПЕРЕВОД: А.П. БОГОПОЛЬСКАЯ