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Rhabdomyosarcoma of the larynx in adults.Review of the literature.Clinical reports.The case of a combination of rhabdomyosarcoma of the larynx and squamous cell carcinoma of the larynx.

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Summary.Rhabdomyosarcoma of the larynx is an extremely rare disease. To date of the literature has been described only about 70 cases of rhabdomyosarcoma of the larynx, including the adult population — 39 cases. There is very little information about the clinical presentation and course of rhabdomyosarcoma of the larynx. The article presents a review of the literature and our own observations of the disease. In our hospital were treated four patients with rhabdomyosarcoma of the larynx. Three of the four patients was referred to ourhospital for the first time, one has previously received radiation therapy for cancer of the larynx. In the analysis of the literature we found no reports of combined rhabdomyosarcoma of the larynx and squamous cell carcinoma of the larynx. All patients received surgical treatment, one received postoperative radiation therapy. The analysis of the literature data and our observations allowed us to conclude that the relatively favorable prognosis of laryngeal rhabdomyosarcoma in adults, given the possibility of early detection of disease, lack of regional and distant metastases in most cases, the possibility of radical surgical treatment.

Keywords: rhabdomyosarcoma of the larynx, the combination of rhabdomyosarcoma of the larynx and squamous cell carcinoma of the larynx.

Review of the literature

Rhabdomyosarcoma is the most common malignant tumor of soft tissue in children and about 50% of their amount. While this tumor in adults is approximately 15–20% of all soft tissue sarcoma [10, 15].Rhabdomyosarcoma is more common in the head and neck, the genitourinary system, limbs, trunk, retroperitoneum. In children about 40% rhabdomyosarcoma localized in the head and neck [11, 13] in adults — approximately 24% [15].

In the head and neck rhabdomyosarcoma affects the orbit, nasopharynx, nasal cavity, paranasal sinuses, temporal bone, soft tissue pterygopalatine fossa and infratemporal fossa, as well as other areas. [15] Some authors allocate a group of anatomical locations rhabdomyosarcoma of the head and neck: the orbital, parameningealand non-parameningeal [3]. In 60% of all cases of rhabdomyosarcoma in the head and neck in patients of all age groups the tumor is localized in the orbit, nasopharynx and nasal cavity [11].

Soft tissue sarcoma of the larynx are rare and account for less than 1% of all malignant neoplasms of the body [2, 7, 11]. More than 50% of the soft tissue sarcomas larynx represented fibrosarcoma [11].

Rhabdomyosarcoma of the larynx is an extremely rare disease. In adults the amount rhabdomyosarcoma larynx is less than 1% of all malignant tumors of the soft tissues of the head and neck [13] and less than 3% of all rhabdomyosarcoma in the head and neck [15]. Up to the present time in the literature reportedly only about 70 cases of laryngeal rhabdomyosarcoma, are among the adult population — 39 cases [4, 8, 10, 11, 14].

In addition to the rarity of the disease in the available publications reported high aggressiveness of the tumor [8, 12, 15].

The literature describes the case of a combination of rhabdomyosarcoma of the larynx and dermatomyositis [15]. Described the case of the larynx metastasis rhabdomyosarcoma hip [7].

Until now, almost no statistical data, there is no systematic information on the diagnosis, presentation and principles of treatment of connective tissue tumors of the larynx.

In 1933Figi first described 4 cases of sarcoma of the larynx from 717 malignant tumors of the larynx [5, 10]. The first case of laryngeal rhabdomyosarcoma in a child in 1944 found Glick [6, 8, 10]. The case of the disease in the adult was first described in 1964 by Filipo&Crifo [10].

The etiology of laryngeal rhabdomyosarcomatoday unknown.According to most authors, not established a link between smoking and the development of the disease [14]. However, there is a single publication indicate a connection between the disease and smoking [4]. No data on the influence of genetic factors on the development and progression of the tumor [8]. No confirmed cases of malignancy rhabdomyomas of the larynx in the adult [12].

Rhabdomyosarcoma — a malignant tumor derived from cells of striated muscle tissue. There are three histological variants of rhabdomyosarcoma: embryonal, alveolar and pleomorphic. In embryonalform stands botryoid subtype [10, 11]. Other authors describe four histologic variants: embryonal, alveolar, pleomorphic and botryoid. The latter species is highlighted as an independent [8, 12, 14]. In some publications allocate and fifth histologic type - spindle cellrhabdomyosarcoma [13]. Also, there is an opinion that there are only two main morphological variants — pleomorphic andembryonal. In this case, the alveolar and botryoid are subtypes of the embryonalrhabdomyosarcoma[4].

Embryonal and alveolar variants are more common in children and adolescents. Pleomorphic occurs mainly in adults [10, 11, 13, 14]. It is believed

that the prognosis of the embryonal type of rhabdomyosarcoma is better than in other types [3, 13].

Cases of rhabdomyosarcoma of the larynx have been reported in patients aged 1 to 82 years. About 90% of the patients were male [4, 10, 11, 13].

Over the past 10 years in the literature have been described only 8 cases of rhabdomyosarcoma of the larynx in adults, of which 6 cases with pleomorphic tumor type [10, 15] and 2 cases with embryonal morphological variant [3, 8].

There is very little information about the clinical presentation and course of rhabdomyosarcoma of the larynx [13, 14]. All authors are inclined to believe that the symptoms of rhabdomyosarcoma of the larynx are similar to the symptoms of laryngeal cancer. For rhabdomyosarcoma characterized considerably more aggressive course compared with laryngeal cancer, with rapid onset and progression of symptoms [9, 12, 13]. Almost all publications the authors point to the short history of the disease, ranging from two weeks to two months [3, 9, 15].

As with other malignant tumors of the larynx, in the form of growth allocation exophytic(papillary and nodular), endophytic(infiltrative) and mixed forms of laryngeal rhabdomyosarcoma growth [1, 2].

By laryngoscopy picture rhabdomyosarcoma of the larynx quite often similar to a polyp or papilloma vocal cord. Review of existing literature shows that laryngeal rhabdomyosarcoma mainly takes the form polypoid masses, often lobed structure, growing on a stem, a red-brown color. The tumor is often localized in the area of the vocal cords and can be shifted to higher or lower relative to the cords, but it is possible the development of the disease in the vestibular and less in the subglottic part of the larynx [3, 8, 9, 11, 13, 14, 15].

Exophytic tumor often can be covered by thinning the mucous membrane with translucent vessels on the surface it may be pockets of ulceration. Rarer form of infiltrative growth [14].

Rhabdomyosarcoma other organs characterized by extensive lymphatic and hematogenous metastasis [10]. However, according to most authors, distant metastasis laryngeal rhabdomyosarcoma in adults occur infrequently, so they regard this tumor is more locally aggressive [10, 11]. In most reported cases over the past years, rhabdomyosarcoma larynx adult patients had no regional and distant metastases [8, 10, 12, 14, 15]. According to literature data distant metastases of rhabdomyosarcomaoften affect the lungs, bone marrow, bone, liver, brain [10, 14].

Several authors have noted the difficulty of diagnosis rhabdomyosarcoma of the larynx. This is due to the rarity of the disease and the unusual clinical

presentation [8, 12]. Diagnosis of rhabdomyosarcoma of the larynx based on the results of laryngoscopy and histology [13, 14]. Clinical signs with rhabdomyosarcoma and other malignant tumors of the larynx may be similar, so the histological examination is fundamental for the diagnosis [10]. Submucosal tumor growth pattern determines the complexity of morphological verification of the tumor primary examination of the patient, which may cause misdiagnosis. It is important to note that most of the authors indicates a significant role of immunohistochemistry in the diagnosis of rhabdomyosarcoma of the larynx [10, 14].

For determine the extent of the process and clarify the diagnosis using endoscopic examination of the larynx, as well as CT and PET of the neck, the chest and etc. [8, 14].

Rhabdomyosarcoma of the larynx has a better prognosis than similar tumors at other sites (including other organs of the head and neck), probably due to the possibility of early detection and radical surgery [8, 10, 14]. For a long time it was thought that the prognosis of laryngeal rhabdomyosarcoma unfavorable, however, a complex treatment with surgery, radiation therapy and chemotherapy, improved the situation [3, 8, 10, 14].

Several prognostic factors have been identified for rhabdomyosarcoma of the head and neck: the patient's age, location, and spread of the disease, histological type of tumor and its degree of malignancy [10, 13].

Since 1972, a group of researchers IRS (Intergroup Rhabdomyosarcoma Study) conducted a series of randomized trials (involving more than 4 thousand patients) to improve cure rates in all localizationrhabdomyosarcoma in children. The results of four serial protocol (IRS-I, IRS-II; IRS-III and IRS-IV) were published [10, 14]. The researchers concluded that the optimal treatment rhabdomyosarcoma is the complex approach involving surgery followed by chemotherapy and/or radiation therapy [10, 14].

According to the IRS-IV, approaches to the treatment of rhabdomyosarcoma are gradually changing, extensive surgery replaced conserving surgery and comprehensive therapy [3].

Thanks to the research IRS, five-year survival rate of rhabdomyosarcoma in children has increased from 25% in 1970 to 70% in 2010.

The study IRMS-V search continues for new drugs and therapeutic regimens which may be effective in the treatment of rhabdomyosarcoma [10].

However, in our opinion interpolate the results of studies on the treatment of rhabdomyosarcoma in all localizations in children for the treatment of laryngeal rhabdomyosarcoma in adults, it would be incorrect.

Rhabdomyosarcoma of the larynx in adults is a rare disease and any standards of its treatment at present no [8].

According to most authors, surgery with adjuvant chemotherapy and/or radiation therapy is the optimal scheme for the treatment of this disease [8, 10, 11, 14]. There is one report of an endoscopic removal of laryngeal rhabdomyosarcoma followed by recovery without radiation and chemotherapy [9].

In the literature there are conflicting data on the efficacy of neoadjuvant radiotherapy and chemotherapy. Some investigators have reported, no regress rhabdomyosarcoma of the larynx after chemotherapy and radiation therapy [8], or relapsing after a few months after a similar treatment [11]. Other authors provide data on the leading role of radiotherapy and chemotherapy in the treatment of rhabdomyosarcoma of the larynx [7, 12]. The same authors talk about the feasibility of surgical treatment only in some cases [7]. Described the cases of complete tumor regression after chemotherapy and radiation therapy [12, 13]. In addition, chemotherapy or chemoradiation therapy in neoadjuvant can reduce tumor volume and make it possible to preserve bodiessurgery [12].

Considered that embryonal type rhabdomyosarcoma (including laryngeal rhabdomyosarcoma) is significantly more sensitive to radiotherapy and chemotherapy than other morphological types. Therefore, there is a perception of greater efficacy of the drugs and radiological treatment of embryonal tumor type [13].

Some publications have been objections to the use of surgery in younger patients due to adverse functional outcomes [9, 13].

With the advent of new drugs and high-tech radiology equipment, combination chemotherapy with radiation therapy is gaining strength and reduces the need for extensive surgery.

However, is not yet clear whether radiotherapy and chemotherapy treatment a significant impact on the prognosis of laryngeal rhabdomyosarcoma in adults, because of the small number of cases [14].

Summarizing the literature, it is possible to make the following conclusions.

- Please keep in mind the possibility of the presence of laryngeal rhabdomyosarcoma in any patient with a polypoid tumor formation in the larynx and a short history of the disease.
- Rhabdomyosarcoma of the larynx is an extremely rare tumor, the main method of cure which, according to the literature to date, is a combined modality treatment of using surgery, chemotherapy and radiotherapy. However, given the small number of observations and the absence of a

standard of treatment, in each case, the therapeutic approach should be determined individually.

- Further research is needed to find the most effective treatments of this disease.

Cases report

Described in the literature of cases laryngeal rhabdomyosarcomain small quantity, so we want to present observations of this category of patients in our hospital.

In Kirovograd Regional Oncology Center throughout 2011 were treated four patients with rhabdomyosarcoma of the larynx (Table. 1), which accounted for 7,4% of all patients with malignant tumors of the larynx registered in Kirovograd region in 2011. Before and after 2011 we have not seen any case rhabdomyosarcomaof the larynx.

Table.

Rhabdomyosarcoma of the larynx in adults.Own clinical observations

№	Gender	Age	T	Metastases	Morphological type	Localization	Treatment	Follow-up
1	M	67	T_{1B}	No	Pleomorphic	Glottic	Laryngectomy	4 months DND.
2	M	59	T_{1B}	No	Embryonal	Glottic	Laryngectomy	42 months NED
3	M	63	T_{1B}	No	Embryonal	Glottic	Laryngectomy	38 months NED
4	M	61	T_{1B}	No	Embryonal	Glottic	Removal vocal cord+ RT	41 months NED

DND – death not from disease, NED – no evidence of disease, RT – radiotherapy.

All four patients were male, age 59 to 67 years.

Histological structure of rhabdomyosarcoma in three cases was embryonal, in one case pleomorphic. By grade rhabdomyosarcoma in three cases had G 3 in one - G 1. Immunohistochemical examination of tumor tissue in our patients was not carried out due to lack of technical feasibility.

Prevalence of the disease in the larynx in all patients corresponded $T1_B$.

Examination of the neck, the chest and the abdomen before treatment was performed in a standard volume.

Metastases to regional lymph nodes and distant organs was not found in all cases.

Three of the four patients was referred to our hospital for the first time, one patient before admission had been receiving radiation treatment for "Cancer of larynx $T_1N_0M_0$I st". By virtue of this characteristic, for more convenient presentation of information, we have divided our clinical observations into two groups: patients were referred for the first time (3 cases), and the patient had previously received radiation therapy (1 case).

Patients were referred for the first time

At admission to our clinic, two primary patients complained of dysphonia, one patient complained of dysphonia and dyspnea (there was a stenosis of the larynx I degree).

All patients had a short history of the disease (1 to 3 months). Clinically determined by the rapid development of the disease: the laryngoscopy showed an increase in tumor size by about 30–40% in two weeks (the period from the primary examination prior to surgery).

When laryngoscopy in all patients in the larynx was determined exophytic tumor reddish-brown color, with a bumpy surface, mobile, with areas of superficial ulceration, coming out of the true vocal fold, the narrowed base. In two cases, the tumor was localized in the anterior third of the vocal cord with the involvement of the anterior commissure, in one case — in the middle third of the vocal cord.

All patients underwent endoscopic examination of the larynx (a clinical picture corresponded with the data of indirect laryngoscopy), biopsy of the tumor.

Morphological examination of the biopsy material in two cases showed stratified squamous epithelium with papillomatosis, hyperkeratosis, acanthosis, in one case showed a malignant tumor tissue, without specifying the morphological type.

All patients underwent surgical treatment. In all cases performed incision of the thyroid cartilage of the larynx (Fig. 1), carriedfrozen section examinationof tumor tissue during surgery (Fig. 2), confirmed rhabdomyosarcoma. Two patients due to the high degree of malignancy rhabdomyosarcoma, prevalence of the process and the involvement of the anterior commissure, performed a laryngectomy. One patient made removal

vocal cord. Removal of vocal cord is made in case ofembryonalrhabdomyosarcoma originating from the middle third of vocal cord, exophytic growth forms on a narrow base (base size of about 0,5 to 0,3sm), without infiltration of the underlying tissues.

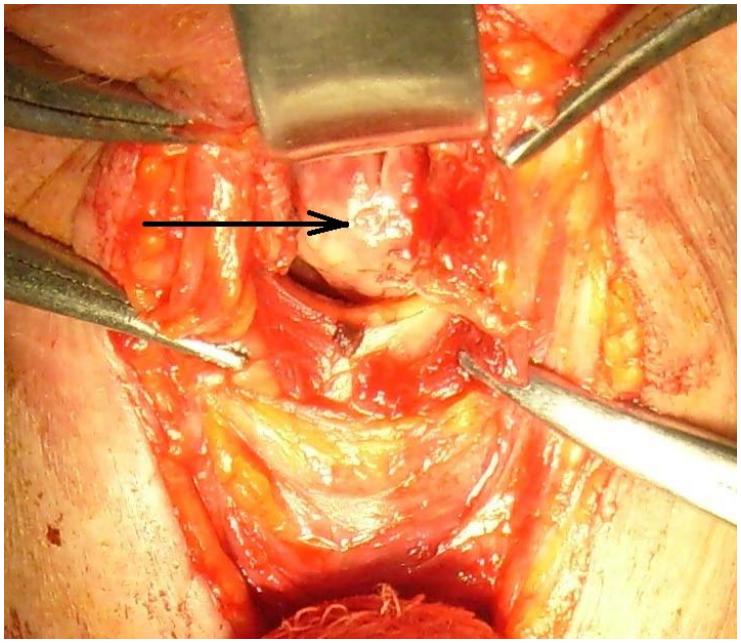

Fig. 1. Rhabdomyosarcoma of the larynx.Achieved incision of the thyroid cartilage of the larynx. In the lumen of the larynx is defined exophytic tumor (indicated by arrow)

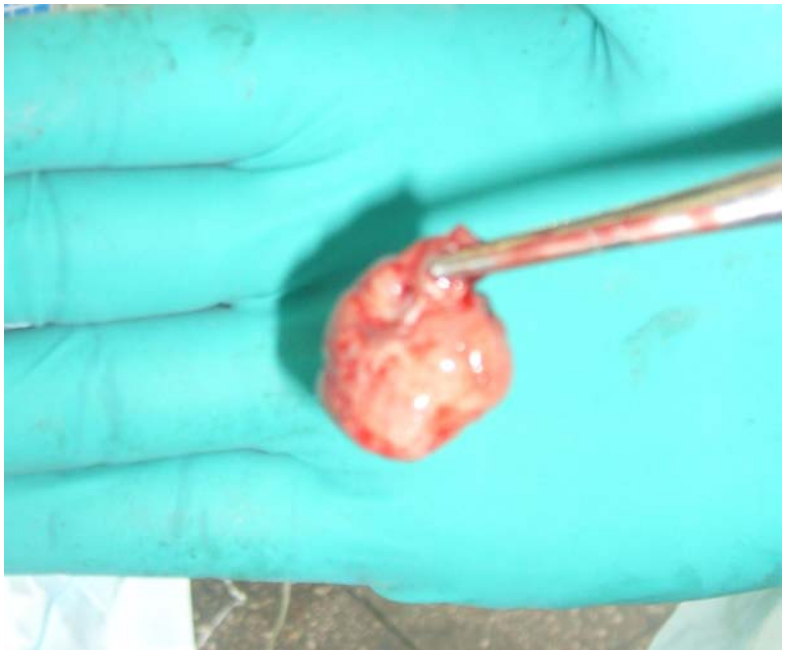

Fig. 2. Rhabdomyosarcoma of the larynx. The tumor was removed for frozen section examination during surgery

By histological examination after surgery in two cases confirmedthe presence of embryonalrhabdomyosarcoma(Fig. 3) and in one case of a pleomorphic variant of it(Fig. 4).

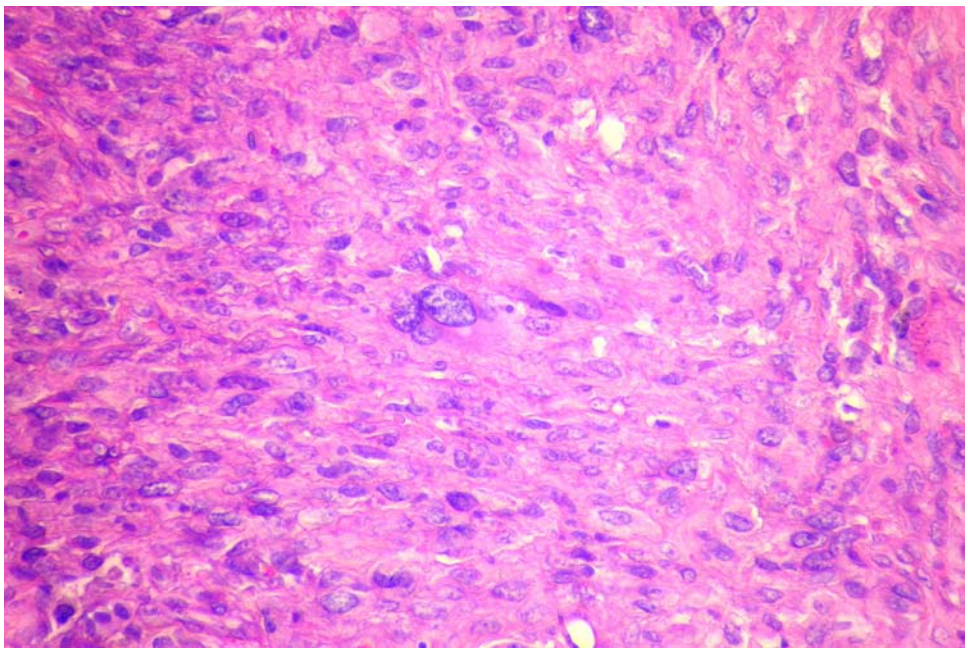

Fig. 3. Rhabdomyosarcoma of the larynx embryonal variant

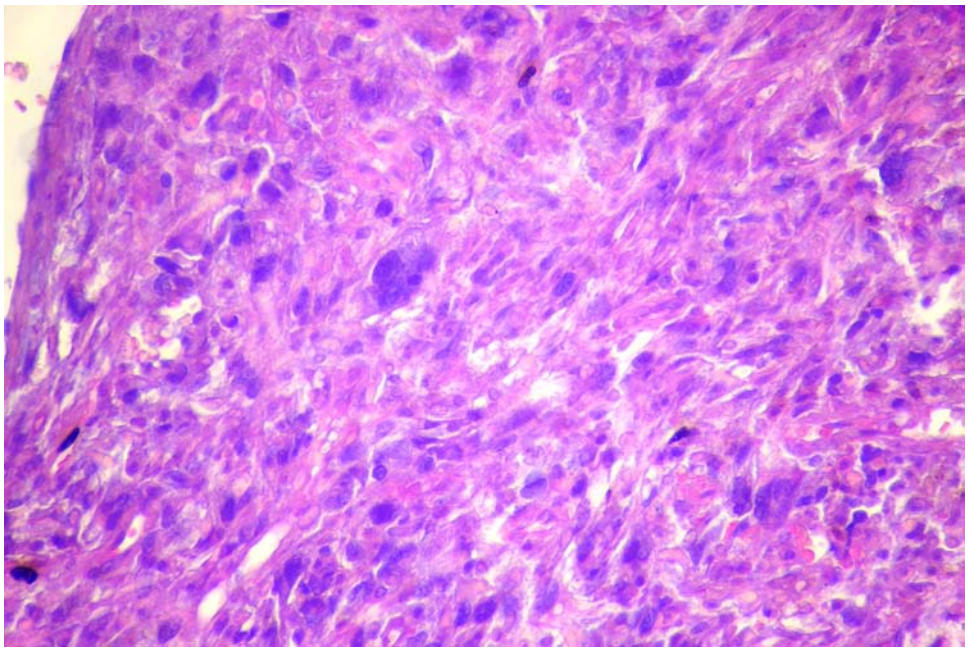

Fig. 4. Rhabdomyosarcoma of the larynx pleomorphic variant

After surgery one patient (after removal of vocal cord) received radiation therapy 40Gy. The other two patients did not receive adjuvant treatment (one patient due to the presence of pharyngeal fistula, the second patient refused to continue treatment). None of our patients did not receive chemotherapy.

One patient died four months after laryngectomy at the age of 68 years from concomitant cardiac disease. Two other patients alive at 38 months and 41 months after surgery, with no evidence of tumor recurrence.

The patient had previously received treatment for laryngeal cancer

One of our patients 59-year-old previously received radiation therapy with the diagnosis "Cancer of the larynx $T_1N_0M_0$ I st". The diagnosis was confirmed by histological examination — squamous cell carcinoma. The patient received a course of TGT 70 Gy.

One month after completion of radiation therapy patient underwent an examination. When laryngoscopy in the larynx was found exophytic tumor formation originating from the region of vocal cord and ventricle of the larynx, lobular structure, grayish color. Performed endoscopic examination of the larynx, the data obtained was similar laryngoscopy. A biopsy of the tumor was performed. Histological examination showed stratified squamous epithelium with severe dysplasia and leukoplakia, polymorphic cells.

Considering history, clinical and endoscopic picture, the tumor in the larynx is regarded as a continuation of the growth of squamous cell carcinoma. Produced resection of the larynx.After the operation prepared histological conclusion — embryonalrhabdomyosarcoma(Fig. 5).

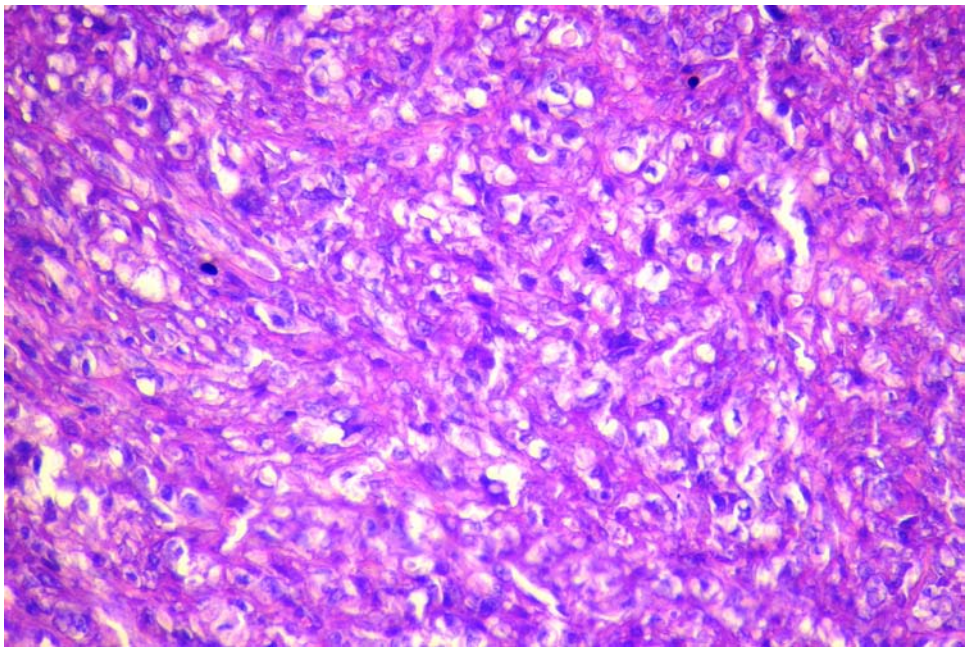

Fig. 5. Rhabdomyosarcoma of the larynx embryonal variant

Two months after the operation revealed a tumor recurrence. When laryngoscopy and endoscopy, in the larynx in all parts are determined by multiple foci of exophytic growth, grayish, with a diameter of 0,4 to 1,3sm.

Performed laryngectomy. Histological examination of all foci confirmed the growth of embryonalrhabdomyosarcoma. Adjuvant radiation therapy patient did not receive, in connection with the previously held TGT. Patient did not receive chemotherapy.

42 months after surgery, the patient is alive without evidence of disease.

In the analysis of the literature we have not met reported aboutcombined rhabdomyosarcoma of the larynx and squamous cell carcinoma of the larynx.

Conclusions

- The data laryngoscopy and a short history of the disease in all our patients are completely consistent with the literature data on the course of rhabdomyosarcoma of the larynx.
- Availability four cases of this extremely rare disease for one year in our hospital, confirms the thesis about the possibility of the presence of rhabdomyosarcoma in any patient with exophyticpolypoid masses in the larynx.
- The diagnosis rhabdomyosarcoma larynx difficult due to the rarity of the disease and submucosal tumor growth.
- The occurrence of laryngeal rhabdomyosarcoma in a patient who received a TGT for laryngeal cancer, suggests a possible etiologic role radiation impact.
- Surgical treatment as a standalone or in combination with adjuvant radiation therapy for rhabdomyosarcoma of the larynx, can give good results in survival and relapse-free flow.
- Despite the high aggressiveness of the tumor, whenrhabdomyosarcoma of the larynx is possible to perform a radical organ-preserving operations with good long-term results, which confirms the example of one of our patients.
- Given the possibility of early detection of the disease, locally aggressive itscourse, lack of regional and distant metastases in most cases, the presence of the possibility of radical surgical treatment, it is possible to talk about a relatively favorable prognosis of laryngeal rhabdomyosarcoma.

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