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CLINICAL AND MORPHOLOGICAL ASPECTS OF MULTIPLE PRIMARY MALIGNANT SKIN TUMORS.

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Abstract:

Malignant diseases, predominantly affecting the aging generation over 60 years of age, are distinguished by their particular insidiousness, manifesting their likelihood of multiple lesions of the same individual by tumors of a different nature. Such cases, called primary multiple malignant tumors (PMMT), have become not rare, and manifest themselves in all the variety of oncological pathology. The authors conducted a unique study of PMMT on a large material - cancer patients - residents of Tashkent, having comprehensively studied the situation with PMMT for a separate period of time (2018-2019), identified and studied all cases of combination with skin cancer. Further, focusing on the most common form of cancer in the elderly population in general - basal cell skin cancer, we drew parallels of the frequency of occurrence of PMMT with a separate histotype. A high percentage of PMMT occurrence in basal cell carcinoma was established - more than 60%, especially in micronodular histotype. These data require careful clinical examination of patients with basal cell carcinoma of the skin for not only relapse of the disease, but also for early detection of a second independent cancer of any localization, both skin and any other organ.
The article will be useful not only for specialists associated with skin pathologies - oncologists and dermatologists, but also for general practitioners who conduct dispensary control of the attached population registered on oncology, especially among the elderly.

Keywords: Basal cell skin cancer, multiple primary malignant tumors.

Primary multiple malignant lesions were known as early as the 10th century, when our great compatriot Abu Ali ibn Sina described 2-sided lesions of the mammary glands. Already in those distant times, it was suggested to them that cancer in these organs was the result of independent causes. [1.6].

T.Billroth is considered the founder of the theory of primary multiplicity of tumors, who in 1889 had 30 observations and was the first to define the primary multiplicity of tumors, it is he who is credited with the formulation of three mandatory conditions for the differential diagnosis of primary multiple malignant tumors, which, in contrast to secondary multiple (metastatic) should have a different histological structure, be located in different organs and each has its own metastases. [2].

Due to advances in early detection, supportive therapy and effective cancer treatment, as well as with longer follow-up, against the background of global aging of the population, according to respected scientists [3,7], the number of multiple primary tumors will continue to grow. Over the past several decades, there has been a significant increase in the 5-year relative survival rate for all types of cancer, and is still offset by the long-term long-term consequences of cancer and its treatment. Patients with a previous cancer diagnosis usually undergo several follow-up tests and examinations, often over several years, to rule out a recurrence of the disease. With the increasing use of more sophisticated and sensitive imaging techniques such as positron emission tomography - computed tomography, more and more cancer survivors are discovering new suspicious lesions of the thyroid, colon, breast, esophagus, bile ducts, and organs of the head and necks that might otherwise have been overlooked. [4,5].

Even in the last century, authoritative oncologists recognized that multiple primary tumors (polyneoplasias) are a biological phenomenon in which a patient develops two or more tumors developing in

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one or more organs, simultaneously or sequentially, independently of each other, which had different histological picture (D.M. Abdurasulov 1968, 1977,1982) [3]. One of the most frequent localization of multiple primary malignant tumors (PMMT) is the skin [6].

According to V.Yu. Skoropad et al. (2012), multiple primary malignant tumors of three or more localizations occur in patients with stomach and colon cancer [8].

Multiple primary tumors are defined as more than one synchronous or metachronous cancer in the same person [11].

The problem of differentiating the synchronicity and metachronism of PMMT has arisen in the interpretation of the time interval between the diagnosis of the first and second cancers, as well as between the IARC world methodological centers and the American Methodological Center for Cancer Registration SEER. SEER biostatisticians recommend adhering to a 2-month interval in the diagnosis of PMMT, however, IARC, taking into account the sensitively large range of the possibility of the quality of examination of primary cancer patients for exclusion of PMMT, suggests keeping the time range of 6 months as the world standard. [8,9,10,11].

In our study, we will adhere to the IARC recommendation - a period of metachronism - a period of more than 6 months between the occurrence of the second cancer and the first.

TARGET:

To conduct a retrospective analysis of the prevalence of multiple primary malignant tumors (PMMT) of the skin in general and in combination with basal cell skin cancer in particular.

MATERIAL AND METHODS:

according to the "Cancer-Register" of the city of Tashkent for 2018-2019, 835 patients with malignant skin pathology were registered, in whom 87 cases (10.4%) of primary multiple malignant tumors (PMMT) were registered, that is, a combination of second independent cases cancer. Of the 87 cases of PMMT, 53 (60.9%) had a malignant lesion of only the skin (PPC), among which 14 (16.1%) had a primary multiple malignant process registered during the last 2018-2019. For an in-depth histological study, the available material was taken from the archive of histological preparations of the Tashkent city branch of the RSPMCO&R. For the purpose of histotyping of basal cell skin cancer (BCSC), 358 histological preparations were revised and a post-factum pathological diagnosis of BCSC with an appropriate histotype was established.

Methodological aspects: in view of the well-known complexity of the topic of multiple primary cancers, in the design of our study, priority was given to skin lesions, in which the general structure of dermato-oncological malignant morbidity was studied, with an emphasis on cases of skin cancer in general, and basal cell cancer in particular. In other words, the difficult question of which of the cancers we put at the forefront when detecting 2 primary synchronous cancers in one individual. In this case, the case of skin lesions was first subjected to statistical processing. The issue of establishing synchronicity was also resolved in favor of the IARC recommendations; the time period for synchronicity is 6 months.

Thus, in 2018-2019, only 835 cases of malignant skin lesions were initially registered, including 22 cases (2.6%), multiple primary lesions of only the skin of which were detected within 2 years.

RESULTS:

within the framework of scientific research, the obtained material was subjected to a comprehensive statistical analysis.

Of 835 patients, 605 (72.5%) had basal cell skin cancer (BCSC), 122 (14.6%) patients had squamous cell skin cancer, 89 patients (10.6%) had melanoma, 15 patients (1.8 %) - Kaposi's sarcoma, in 4 patients (0.5%) - dermatofibrosarcoma.

Figure №1 The structure of initially registered patients with malignant skin tumors (n = 835)

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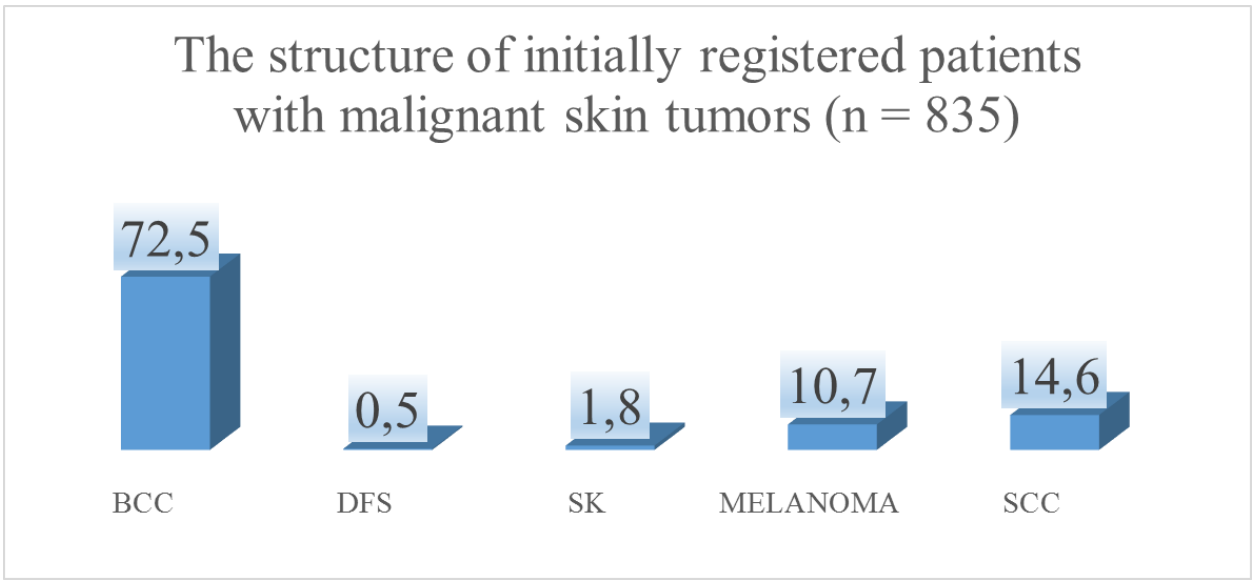

Note: BCSC - basal cell carcinoma; DFS - dermatofibrosarcoma; KS - Kaposi's sarcoma; SCCS is a squamous cell carcinoma of the skin.

Of 835 patients with skin lesions, 690 (82.6%) had lesions of the skin of the limbs, trunk, head and neck, 20 (2.4%) had cancer of the upper and lower lip, 17 (2.0%) - skin cancer of the vulva, 89 (10.7%) - dermatofibrosarcoma.

The second synchronous and metachronous tumors were lesions of other organs and systems: malignant tumors of the head and neck (10.3%), hemoblastosis (5.7%), colon (4.6%), breast cancer (3.4%) , female genital organs (3.4%) and male reproductive (4.6%), urinary system (2.3%), soft tissue sarcomas (1.1%), brain tumor (1.1%).

In the study group, the total PMMT was established in 87 cases, of which 22 cases were associated with synchronous cancer (25.3%). When analyzing the structure of synchronously emerging second cancers, it was found that the predominance of skin cancer is also noted - 36.4%. The time interval between metachronous cancers ranged from 1 to 27 years.

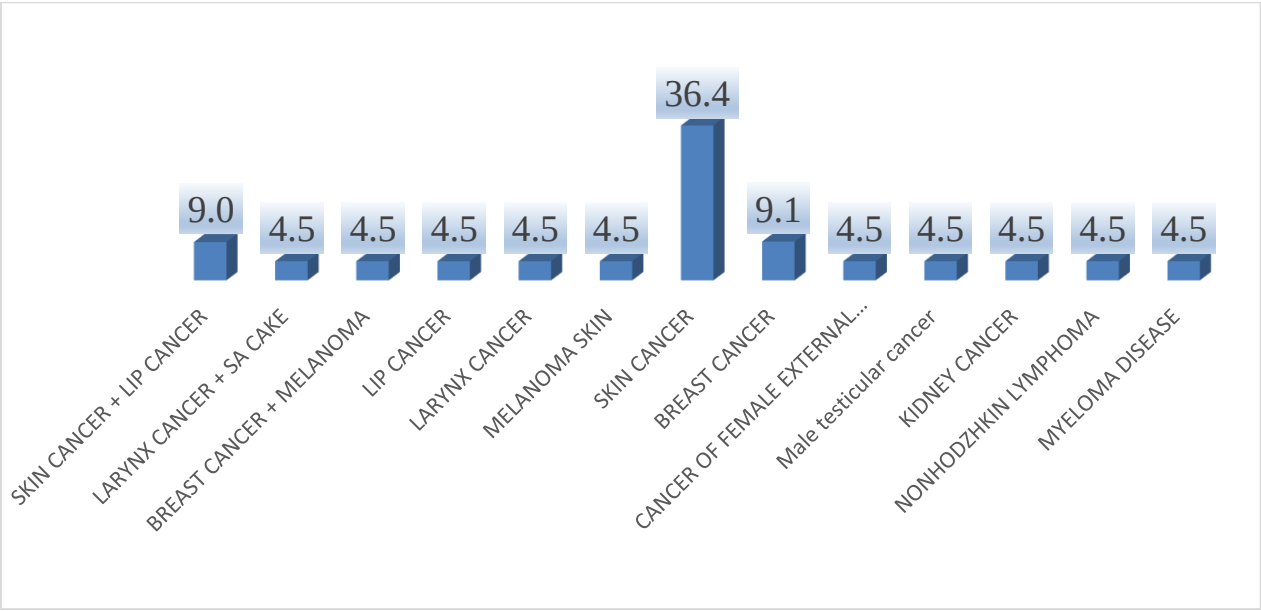

Figure №2. The structure of synchronous "second tumors" (n = 22)

When analyzing the first cancer, skin cancer prevailed in our observations - 86.0%, lip cancer - 3.5%, Kaposi's sarcoma - 2.3%, skin melanoma - 7.0% and vulvar skin cancer - 1.2 %.

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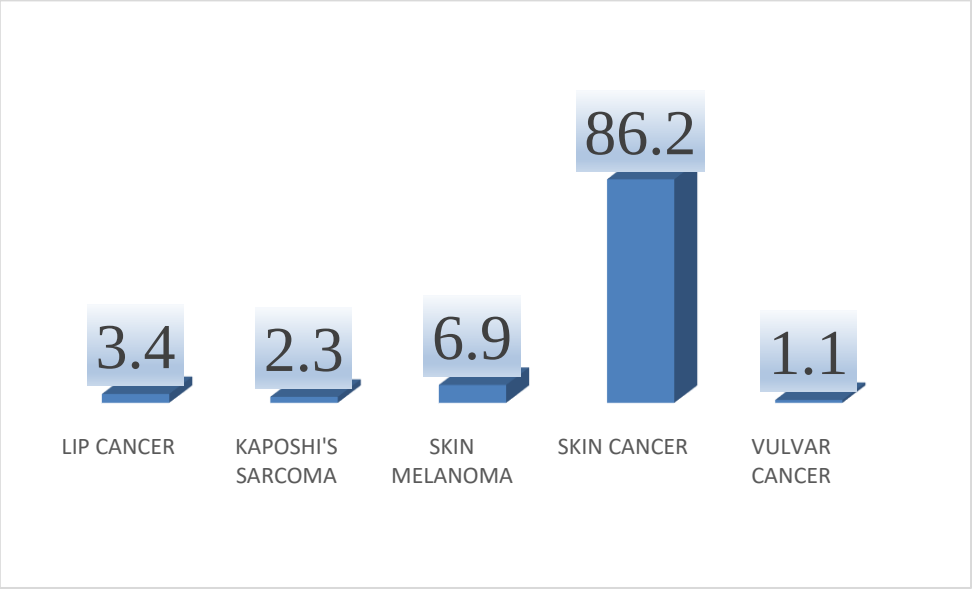

Figure №3. The structure of skin lesions with PMMT (n = 87).

The analysis showed that the combination of different localizations of skin cancer, with skin cancer of other localization was 54.7%. While the rest covered almost the entire spectrum of oncological diseases, the incidence rate of which ranged from 1.3% to 6.7%. After skin cancer, the second most frequent combination was breast cancer - 6.7%, the third place was prostate cancer - 4.0%. Melanoma of the skin, cancer of the sigma and rectum, cancer of the female external genital organs were found in 2.7% of cases. In other cases, a malignant skin tumor was combined once, with an incidence of 1.3%: chronic lymphocytic leukemia, multiple myeloma, non-Hodgkin's lymphoma; malignant neoplasms of the head-neck - cancer of the larynx, paranasal sinuses, hard palate, tongue and thyroid gland. In the study group, one case was noted for a combination with cerebral glioblastoma, lymphosarcoma of the orbit of the eye, kidney, bladder and testicular cancer. There were also isolated cases of PMMT combination with uterine body cancer and soft tissue sarcoma.

As you can see, skin cancer has a high potential for the development of PMMT, far ahead of such a formidable tumor as melanoma. PMMT associated with skin cancer in terms of combination with second tumors, also differs in combination with a wide range of a number of localizations of malignant neoplasms.

In our observations, skin cancer consisted of squamous cell (17.0%) and basal cell (83.0%) nature, the latter, in turn, are divided depending on the further histological examination of histotyping. In order to reveal the relationship between the histotype and the tendency to develop PMMT, we carried out a statistical processing of the BCSC material with histipation and identification of PMMT in them.

Thus, depending on the in-depth study, we divided the BCSC group into 2 groups: prohistotyped - 358 (including 4 lip cancers and 3 vulvar skin cancers) and, for one reason or another, non-progistotyped - 247, which in the total general sample BCSC (n = 605), accounted for 59.2% and 40.8%, respectively.

Within the framework of the study, 358 cases of BCSC were progistotyped from the total sample, that is, the patients initially identified in 2018-2019 in whom PMMT was detected over the years.

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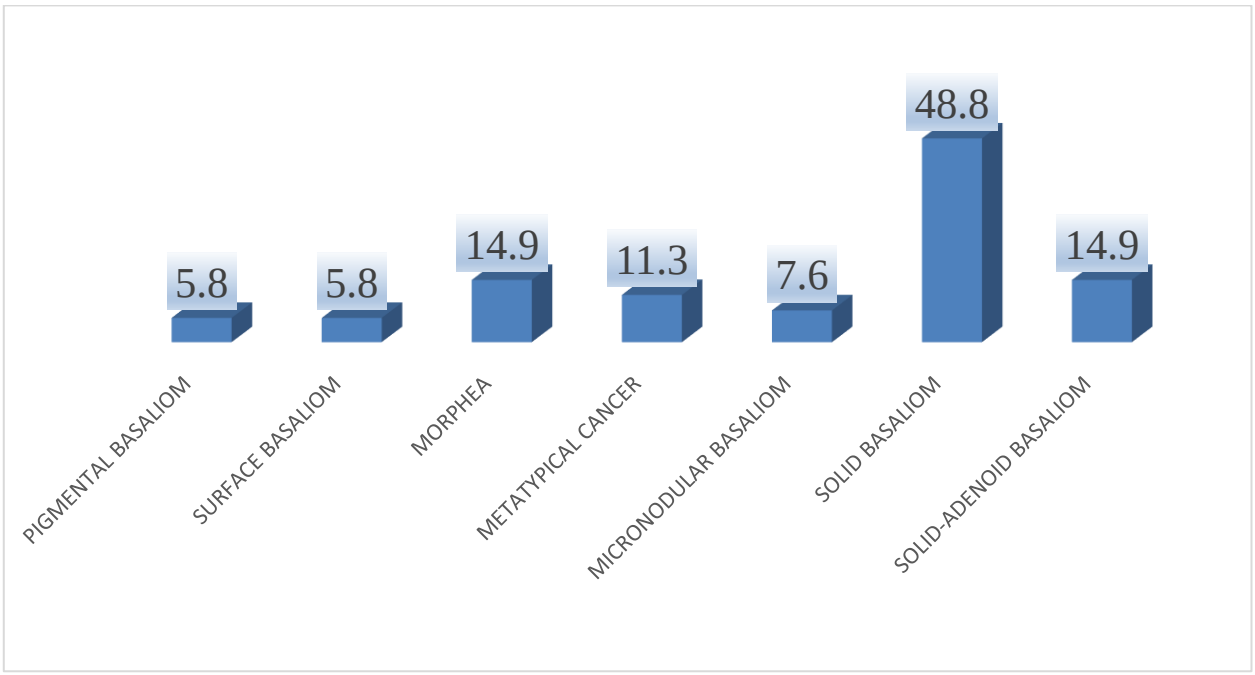

Figure №4 Histotyping of basal cell skin cancer (n = 358)

In the future, we studied a group of histotyped BCSCs - that is, 358 cases of initially registered patients, in whom the presence of a second cancer was established in 30 cases, which amounted to 8.4%.

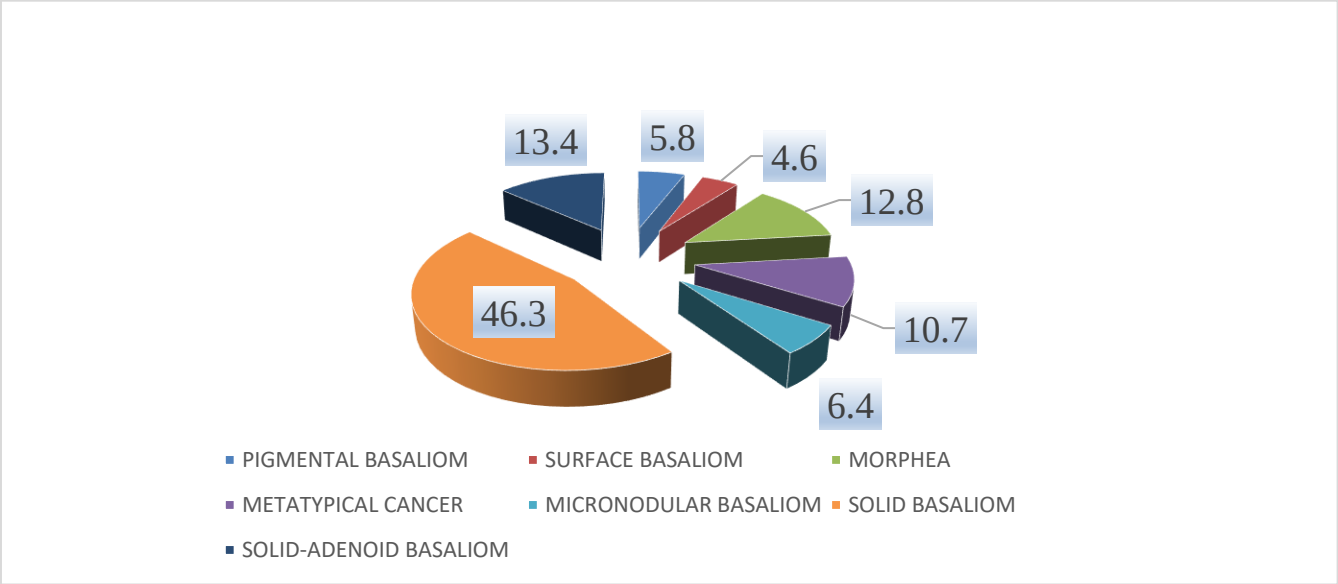

Figure № 5. The structure of PMMT associated with the histotype BCSC.

As can be seen from Figure 5, in our study, multiple primary neoplasias were most associated with a solid type of BCSC - 46.7%, less with a superficial one - 4.6%. Solid adenoid is the second most frequent - 13.4%, followed by: morphea - 12.8% and metatypical cancer - 10.7% and more rarely PMMT occurs in micronodular and pigmented forms of BCSC - 6.4% and 5, 8% respectively.

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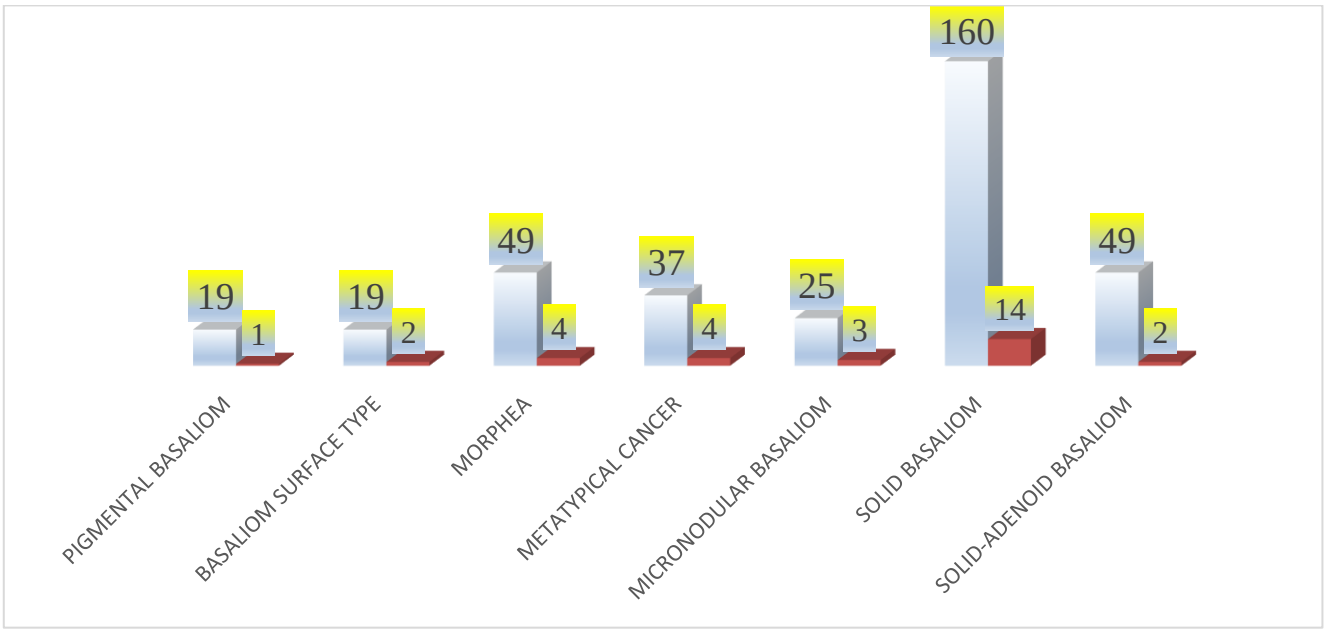

Figure 6. Structure of BCSC histotypes (n = 358) in combination with PMMT (n = 30)

Figure 6 clearly shows how much PMMT occupies for each histotype: as you can see, although the solid type of BCSC prevails in frequency of occurrence in our observations - 160 patients, PMMT was found only in 14 cases - 8.8%. A lower incidence of PMMT was noted only in patients with solid-adenoid type - 4.1% (out of 49 patients in 2 PMMTs) and pigmented histotype –5.3% (19 and 1, respectively). With the type of morphea, it left 8.3% (out of 49 in 4). At the same time, the micronodular type is 1.5 times ahead of the solid type in the frequency of occurrence of PMMT - 12.0% (25 and 3, respectively). The frequency of occurrence in the superficial and metatypical type of BCSC varies within 10%, that is, every 10 case with a given histotype is included in the PMMT group.

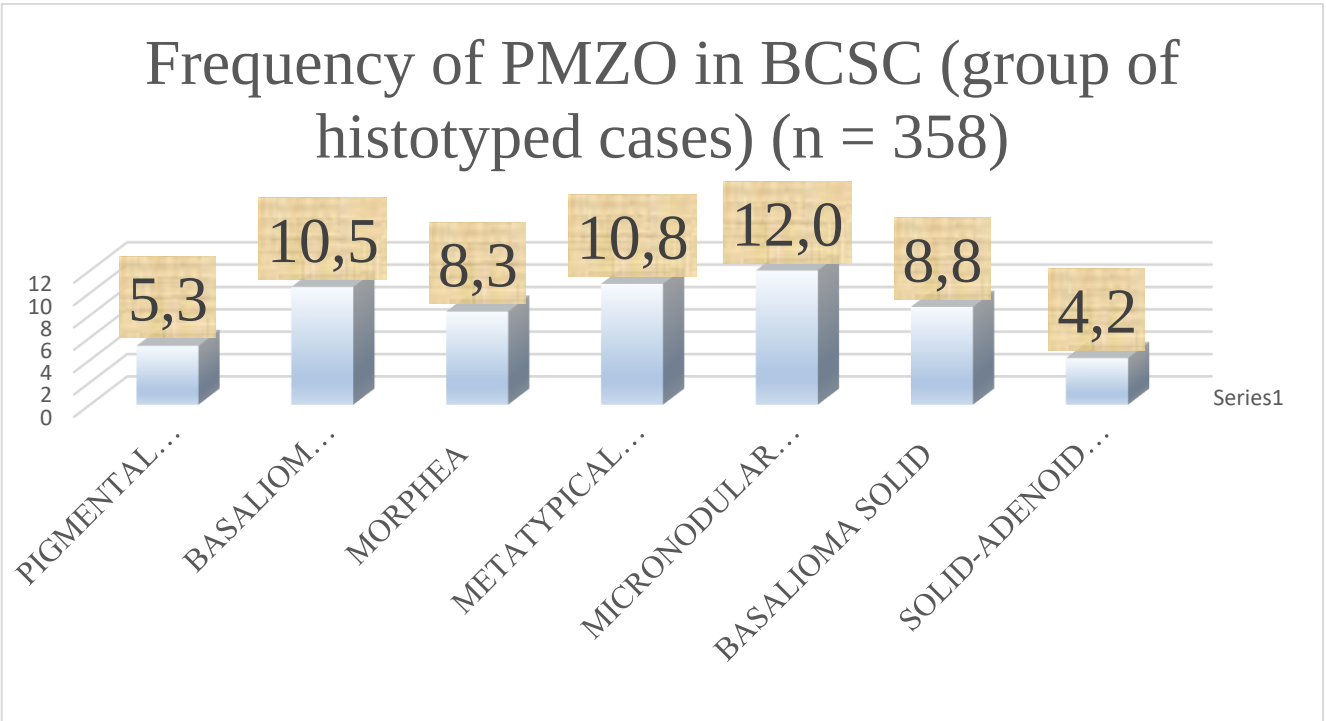

Figure №7. The incidence of PMMT in BCSC (a group of histotyped cases) (n = 358).

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CONCLUSIONS:

Thus, we analyzed the combination of primary multiple malignant disease with BCSC, and the sensitive part of them is represented by the combination of BCSC of the micronodular histotype - 12.0%. Patients with primary BCSC must be carefully examined not only during the initial diagnosis with the establishment of the BCSC histotype, but also with regular dispensary observation to exclude PMMT, more often in the early preclinical stage, thereby greatly facilitating the prognosis of diseases of each patient with PMMT in the future.

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