MINI-REVIEW

Histopathological Classification of Nasopharyngeal Carcinoma

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Abstract

This article reviews all related research and reports on nasopharyngeal cancer (NPC) histopathological classifications worldwide. Despite continuous advance of Chinese and international NPC histopathological classification research, it was difficult to unify previous with current China classifications, and the China with World Health Organization (WHO) classifications. For example, non-keratinizing and undifferentiated carcinoma of the WHO NPC classification does not coincide with poorly-differentiated squamous cell carcinoma of the previous China classification. In addition, the incidence rates of different NPC pathological types show obvious regional discrepancies. It suggested that for facilitating Chinese and international NPC research and exchange, NPC histopathological classifications worldwide should be effectively unified.

Keywords: Nasopharyngeal carcinoma - histopathology - diagnostic classification

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Introduction

Nasopharyngeal primary cancer is the cancer occurring in the mucosa lining epithelium (squamous, columnar and transitional epithelium) and the minor salivary glands of nasopharynx (Hong and Guo,2003;Zong et al.,2001). Although many research on NPC has been carried out at home and abroad, very few were population-based studies on NPC histopathology especially on its temporal trends, most were hospital–based researches on NPC pathological proportions (Huang et al., 2000; Luo et al., 2001; Xie et al., 2003; Zhou et al., 2009). Before exploring the epidemiological law especially the secular trend of different NPC pathological types, NPC histopathological classifications should be thoroughly analyzed. To further in-depth study the epidemiological characteristics and the time trends of different NPC pathological types, and to provide scientific information for its prevention and control, current status of and developments on NPC histopathological classification studies were reviewed.

International and WHO NPC Histopathological Classifications

NPC histopathology was first described and named as "the skull base cancer" in 1845 by Michaux, the name of "endothelioma" was raised by Trotter in 1911, and the name of "Lymphoepithelial carcinoma" was brought forward by Reverchon et al respectively in 1921. Quick and Culter in 1927 put forward the name of "transitional cell carcinoma" which was also called "Ringert's tumor". In 1929, Ewing divided NPC histopathologically into five types, which were squamous cell carcinoma, transitional cell carcinoma, lymphoepithelial carcinoma, malignant adenoma and cystic adenoid basal cell carcinoma respectively. In 1938, Cappell divided Lymphoepithelial carcinoma into Schimincke and Regaud two subtypes. In 1953, Willis thought all NPC belonged to epidermoid carcinoma. Bloom in 1961 raised the name of "embryonal carcinoma". Yeh in 1967 divided NPC histopathology into typical (or classic) epidermoid carcinoma, clear cell carcinoma, spindle cell carcinoma, transitional cell carcinoma, lymphoepithelial carcinoma, pleomorphic carcinoma and mixed cell carcinoma subtypes in the UICC (Union for International Cancer Control) NPC Symposium, while Shanuugaratnam divided NPC histopathology into squamous cell carcinoma and undifferentiated carcinoma two types, in which squamous cell carcinoma included typical (or classic) carcinoma, clear cell carcinoma and spindle cell carcinoma three subtypes, and undifferentiated carcinoma included vesicular nucleus cell carcinoma, fused type and mixed type three subtypes(Li et al.,1983).

Two kinds of NPC pathological classifications had been existed. One was simplified classification, another was detailed classification based on its differentiated degree, tumor cell morphology, clinical and prognosis. For example, Weiland in 1977, according to the biopsy results of 464 NPC cases in Mayo Hospital in the United States, put forward a simplified classification which only divided NPC histopathology into well-differentiated keratinizing squamous cell carcinoma (accounted for 25%) and poorly-differentiated non-keratinizing squamous cell carcinoma (accounted for 75%) two types. While Sauaki from Japan divided NPC into squamous cell carcinoma and adenocarcinoma two major types, which were further divided into subtypes (Li et al., 1983).

UICC affiliated with WHO held its first NPC symposium in Kyoto, Japan on 4-6 April 1977 and published a monograph which its first part was about NPC pathology (Li et al., 1983). In 1978, WHO (Shanmugaratnam et al.,

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1978) divided NPC histopathology into three major types: type I (squamous cell carcinoma), type II (non-keratinizing carcinoma) and type III (undifferentiated carcinoma), but this is not used any longer (Fletcher, 2009). In 1981, a NPC seminar sponsored by WHO Western Pacific Region was held in Guangzhou. In the seminar it was suggested that type II and type III NPC be combined as one, and only type I (squamous cell carcinoma) and type III NPC (undifferentiated carcinoma) be retained. But as this kind of classification was too simple, most China experts did not accepted it (WHO regional office for the western pacific, 1982). Except for description on NPC histological classification was supplemented in the seminar summary, it was also made clear in the seminar that the abbreviation of "NPC" was only applicable for the nasopharyngeal cancer with squamous differentiation under the light microscope (WHO regional office for the western pacific, 1982).

In 1991, a monograph was co-edited by the experts of Chinese University of Hong Kong, in which their achievements on NPC pathological studies were included (Van and Gibb, 1991). In the same year, WHO modified its NPC histopathological classification, and re-divided it into two major types: keratinizing squamous cell carcinoma and non-keratinizing carcinoma, in which keratinizing squamous cell carcinoma contained well-and moderate-differentiated, poorly-differentiated two subtypes, and non-keratinizing carcinoma included differentiated and undifferentiated two subtypes. Keratinizing squamous cell carcinoma of new WHO classification retained keratinizing squamous cell carcinoma of type I (Squamous cell carcinoma) in 1978 WHO classification, while non-keratinizing carcinoma of new WHO classification included type II, type III and part of type I (non-keratinizing squamous cell carcinoma) in 1978 WHO classification (Shanmugaratnam et al., 1991).

Based on the second edition in 1991, the 3rd edition of WHO NPC histopathological classification in 2003 increased basaloid squamous cell carcinoma type and divided NPC into three types which were keratinizing squamous cell carcinoma, non-keratinizing carcinoma and basaloid squamous cell carcinoma respectively (Barnes et al.,2005;2006).

Although the nasopharyngeal primary tumor is the tumor of mucosa lining epithelium (squamous, columnar and transitional epithelium) and the minor salivary gland of nasopharynx, Fletcher (Fletcher,2009) believed that WHO so-called NPC was only the cancers occurring in the nasopharyngeal mucosa epithelium and showing squamous differentiation under the light and electron microscopy or tested by immunohistochemistry, did not include the cancers occurring in the nasopharynx but without squamous differentiation such as adenocarcinoma (arising from minor salivary glands and non-minor salivary gland).

China NPC Histopathological Classification

Cheng (1935) in 1935, Qin and Si (1940) in 1940 had reported NPC Lymphoepithelial carcinoma respectively. Since 1950s, many China pathological experts had published a number of research papers about NPC pathological classification, such as Gui et al (1956) in 1956 published the article titled Analysis on the Clinic and Pathology of 138 Cases of Nasopharyngeal Malignant Tumor, in which they made preliminary study on NPC histopathological type and its relation with clinic. In 1959, Teaching and Research Group of Pathological Anatomy of Zhong shan Medical College (1961) divided NPC pathology into 4 types, which were Squamous cell carcinoma, transitional cell carcinoma, Lymphoepithelial carcinoma and adenocarcinoma respectively. Liang et al (1962) in 1962 first presented NPC international histopathological classification, and divided NPC histopathology into undifferentiated, poorly- and well-differentiated three major categories. In his classification undifferentiated carcinoma was actually pleomorphic cell carcinoma, and poorly-differentiated carcinoma included large round cell carcinoma, spindle cell carcinoma and squamous cell carcinoma grade III (equivalent to poorly-differentiated squamous cell carcinoma), well-differentiated included squamous cell carcinoma grade Iand II, basal cell carcinoma and columnar cell carcinoma (adenocarcinoma).

During 1961-1976, four NPC conferences were successively held in China, many studies on NPC pathology were reported and issues on NPC histopathological classification was raised in these meetings (Li et al., 1983; Zong et al., 2000). In 1975, Zong (1975) considered all NPC cells had different degrees of squamous differentiation, the difference of different NPC pathological types was actually the difference of squamous differentiation degrees of its cancer cells, and the NPC histopathological classification was just the classification being made artificially.

In 1978, a pilot classification program was raised in Fujian conference on NPC histopathological classification (Chen and Zong, 1978). According to the program NPC pathology was divided into carcinoma in situ and invasive carcinoma two major types. Invasive carcinoma was re-divided into micro-invasive carcinoma (invasive scope not beyond a light microscope visual field with 400 times amplification), well-differentiated carcinoma (including squamous cell carcinoma and adenocarcinoma), poorly-differentiated carcinoma (including squamous cell carcinoma and adenocarcinoma), undifferentiated carcinoma and other rare cancers such as cystic adenoid basal cell carcinoma and muco-epidermoid carcinoma. In this classification carcinoma in situ and micro-invasive carcinoma were particularly listed out and well-differentiated, poorly- differentiated adenocarcinoma and some rare cancers were added in. And these rare cancers were actually salivary gland cancer of Zong et al 2000 classification.

In the Nanning film reading meeting on NPC pathological classification and the China NPC conference held in Changsha in 1978 and 1979 respectively, large round cell carcinoma was renamed as vesicular nucleus cell carcinoma.

The 5th Meeting of China NPC Prevention Collaborative Group in 1979 (Tang, 2000) recommended that NPC histopathology be divided into carcinoma in situ

and invasive carcinoma two major types, while invasive carcinoma be re-divided into well-differentiated cancer (including adenocarcinoma and squamous cell carcinoma), poorly-differentiated cancer (including adenocarcinoma, squamous cell carcinoma and vesicular nucleus cell carcinoma), undifferentiated carcinoma and other rare cancers such as column tumor-type adenocarcinoma, mucoepidermoid carcinoma, malignant mixed tumor, basal cell carcinoma etc. The 1979 classification was similar to 1978 classification, the only difference was that vesicular nucleus cell carcinoma was added into the type of poorly- differentiated carcinoma in 1979 classification.

In 1991, NPC was divided into carcinoma in situ and invasive carcinoma two major types in the book titled the Norms of China Common Cancer Clinical Diagnosis and Treatment, while invasive carcinoma was re-divided into micro-invasive carcinoma, squamous cell carcinoma, adenocarcinoma, vesicular nucleus cell carcinoma and undifferentiated carcinoma five categories, among them squamous cell carcinoma and adenocarcinoma included well-differentiated, moderately-differentiated and poorly-differentiated three subtypes. This classification was similar to the China classifications of 1962, 1978 and 1979, but more detailed, and increased moderately-differentiated squamous cell carcinoma and adenocarcinoma, and listed vesicular nucleus cell carcinoma as an independent category (as of its unique shape, good prognosis to radiation therapy). But listing vesicular nucleus cell carcinoma as an independent category may be wrong, as it was clearly pointed out in 1991 WHO classification (Shanmugaratnam et al., 1991) vesicular nucleus cell carcinoma belonged to undifferentiated carcinoma, and thereafter related data in China also believed that undifferentiated carcinoma included vesicular nucleus cell carcinoma (Zong et al., 2000; 2001; Zhang and Xu, 2005).

In 2000, Zong et al(2000;2001) raised a new NPC pathological classification consistent with international classification as follows: 1. Precancerous lesions; 2. Carcinoma in situ and micro-invasive carcinoma; 3. Keratinizing squamous cell carcinoma or squamous cell carcinoma which could be re-divided into well-, moderately- and poorly-differentiated three grades, and included pleomorphic or anaplastic squamous cell carcinoma, papillary squamous cell carcinoma, adenoid squamous cell carcinoma, basal cell-like squamous cell carcinoma and clear cell squamous cell carcinoma; 4. Non-keratinizing carcinoma, part of them also known as lymphatic epithelial carcinoma, which could be re-divided into differentiated type (including spindle-cell non-keratinizing carcinoma), undifferentiated type (also known as nasopharyngeal undifferentiated carcinoma and once called as large round cell carcinoma and vesicular nucleus cell carcinoma) and mixed type three subtypes; 5. Nasopharyngeal adenocarcinoma which could be divided into traditional and salivary gland two types. Traditional adenocarcinoma, including adenocarcinoma with focal squamous metaplasia, adenosquamous carcinoma, papillary adenocarcinoma, intestinal-type adenocarcinoma and signet ring cell carcinoma, could be re-divided into well-, moderately-and poorly-differentiated three grades. The most common adenocarcinoma of salivary gland was adenoid cystic carcinoma, followed by mucoepidermoid tumor. The framework of Zong et al classification was different from those of previous China classifications, but similar to that of WHO classification, based first on if its tumor cell with keratinizing or not, other than first based on its tumor cell differentiation or cell type. In addition, Zong et al classification did not fully elucidated its corresponding relationship with the previous China classifications, thus some problems arose when trying to link them.

Unification of Different China Pathological Classifications

As of now, China has adopted several NPC pathological classifications, such as the classification of 1962 Liang et al, the 5th China NPC Collaborative Group Meeting in 1979, the Norm of China Common Cancer Diagnosis and Treatment in 1991, 2000 Zong et al, 1991 WHO and 2003 WHO, so, different NPC pathological terms such as lympho-epithelial carcinoma, large round cell carcinoma, vesicular nucleus cell carcinoma, undifferentiated carcinoma, spindle cell carcinoma, well-differentiated squamous cell carcinoma, moderately-differentiated squamous cell carcinoma, poorly-differentiated squamous cell carcinoma, keratinizing squamous cell carcinoma, non-keratinizing squamous cell carcinoma, differentiated non-keratinizing carcinoma etc had appeared in China pathological diagnoses of NPC in different time.

How can we unite all these different terms when analyzing the time trends of different NPC pathological types? As the consistency existed among the China classifications of the 1962 Liang et al, the 5th China NPC Collaborative Group Meeting in 1979 and the Norm of China Common Cancer Diagnosis and Treatment in 1991, so it was not difficult to unite the above three classifications. The point was how the above three classifications unite with the Zong et al classification. Table 1 shows how we did the link according the available data about NPC pathological classification. Some errors might exist, especially for the unification of poorly-differentiated squamous cell carcinoma.

Unification of Chinese and WHO NPC Pathological Classifications

The corresponding of China and WHO NPC pathological classifications mainly involved two aspects, one aspect was the correspondence between Zong et al and WHO classification, another was the correspondence between other China except Zong et al classifications and WHO classification.

Although most usually so-called NPC cancer cells with varying degrees of squamous differentiation under the electric microscope (Zong,1975; Muir and Shanmugaratnam, 1967), nasopharyngeal primary cancer can also be adenocarcinoma (some cancer cells of poorly-differentiated adenocarcinoma with squamous metaplasia) (Zong et al.,2000). Nasopharyngeal cancer in WHO classification only referred the cancer whose cells with squamous metaplasia under light microscopy and

Table 1 Unification of the NPC Pathological Classification of Zong et al 2000 and other Chinese Classifications

2000 Zong et al		Other Chinese Classification
Keratinizing SCC	Well-differentiated	Well-differentiated SCC
	Moderately-differentiated	Moderately-differentiated SCC
	Poorly-differentiated	Others[a]
Non-keratinizing carcinoma (also known as lymphoepithelial carcinoma)	Differentiated	Poorly-differentiated squamous carcinoma ?
		Spindle cell carcinoma
		Pleomorphic cell carcinoma
		Papillary non-keratinizing carcinoma
	Undifferentiated	Poorly-differentiated squamous carcinoma?
		Vesicular nucleus cell carcinoma
		Large round cell carcinoma
		Undifferentiated
		Small cell carcinoma
		Neuroendocrine small cell carcinoma
	Mixed	
Adenocarcinoma (gland carcinoma)	Traditional Well-differentiated	Well-differentiated gland carcinoma
	Moderately-differentiated	Moderately-differentiated gland carcinoma
	Poorly-differentiated	Poorly-differentiated gland carcinoma
		Others[b]
	Salivary gland type	Adenoid cystic carcinoma
		Mucinoepidemoid tumor
		Others[c]

SCC, squamous cell carcinoma; [a]including pleomorphic or anaplastic SCC, papillary SCC, adenoid SCC, basal cell-like SCC and clear cell SCC; [b]including adenocarcinoma with focal squamous metaplasia, adenosquamous carcinoma, papillary adenocarcinoma, intestinal-type adenocarcinoma, mucinous adenocarcinoma and signet ring cell carcinoma; [c]including acinar cell carcinoma, and cancer in the pleomorphic adenoma, malignant basal cell adenoma, malignant myoepithelial carcinoma, epithelial - myoepithelial carcinoma and clear cell carcinoma

electric microscopy or tested by immunohistochemistry, did not include nasopharyngeal adenocarcinoma without squamous metaplasia (Hong and Guo, 2003; Shanmugaratnam et al.,1991), while nasopharyngeal cancer in all China classifications included all primary cancer occurred in nasopharyngeal mucosa lining epithelium and minor salivary gland no matter if its cancer cell with squamous metaplasia or not. That's the most significant difference between China and WHO classifications.

Although Zong et al classification had the same basic structure as that of WHO, the differences between them, except for the above difference, also included: 1) A mixed subtype was added in the non-keratinizing type of Zong et al classification; 2) Basal cell-like squamous cell carcinoma was classified as the subtype of keratinizing squamous cell carcinoma in Zong et al classification, but listed as an independent type in WHO classification; 3) WHO type I NPC only referred keratinizing squamous cell carcinoma, and non-keratinizing squamous cell carcinoma was included in the non-keratinizing type, while Zong et al classification didn't elucidated clearly if non-keratinizing type included non-keratinizing squamous cell carcinoma or not.

The comparison between other China NPC pathological classifications and WHO was actually similar to the comparison between other China NPC pathological classifications and Zong et al Some Chinese experts compared 1991 WHO NPC classification with the classification of the Norm of China Common Cancer Clinical Diagnosis and Treatment in 1991, such as the comparison by Li (2002) in her book tilted Newly-Edited

Table 2. Comparison between 1991 WHO and Chinese NPC Pathological Classification

WHO Classification		Chinese Classification
Li's Comparison	Keratinizing squamous cell carcinoma	Well-differentiated sqamous cell carcinoma
		Moderately-differentiated sqamous cell carcinoma
	Non-keratinizing carcinoma(differentiated)	Poorly-differentiated sqamous cell carcinoma
		Vesicular nucleus cell carcinoma
	Undifferentiated	Undifferentiated
Hong and Guo's Comparison	Keratinizing squamous cell carcinoma	Well-differentiated sqamous cell carcinoma
		Moderately-differentiated sqamous cell carcinoma
	Non-keratinizing carcinoma(differentiated)	Poorly-differentiated sqamous cell carcinoma
	Undifferentiated	Vesicular nucleus cell carcinoma
		Undifferentiated
Zhang and Xu's Comparison	Keratinizing squamous cell carcinoma	Well-differentiated sqamous cell carcinoma
		Moderately-differentiated sqamous cell carcinoma
	Non-keratinizing carcinoma(differentiated)	Poorly-differentiated sqamous cell carcinoma
		Vesicular nucleus cell carcinoma
	Undifferentiated	Poorly-differentiated sqamous cell carcinoma
		Undifferentiated

Head and Neck Oncology published in 2002 (see Table 2), the comparison by Hong and Guo (2003) in their book titled Nasopharyngeal Carcinoma published in 2003(see Table 2) and the comparison by Zhang and Xu (2005) in their book titled Oncology published in 2005 (see Table 2).

Although Zong et al (1991; 2000; 2001) considered there was no principle difference between 1991 China and WHO classification, only were the terms used somewhat different, in fact from Table 2 we could see some discrepancy did exist between them. Undifferentiated and non-keratinizing types in 1991 WHO classification could not unify well the corresponding types in 1991 China classification. Hong and Guo (2003) thought poorly-differentiated squamous cell carcinoma in1991 China classification was equal to the non-keratinizing type in 1991 WHO classification, while Li (2002) thought non-keratinizing type in 1991 WHO classification should included both vesicular nucleus cell carcinoma and poorly-differentiated squamous cell carcinoma in 1991 China classification, Zhang and Xu (2005) thought it should include vesicular nucleus cell carcinoma and part of poorly-differentiated squamous cell carcinoma in 1991 China classification. As to the undifferentiated carcinoma of 1991 WHO classification, Li believed it was actually equal to the undifferentiated carcinoma of 1991 China classification, while Hong and Guo thought it should also included vesicular nucleus cell carcinoma of 1991 China classification, Zhang and Xu thought it should also included part of poorly-differentiated squamous cell carcinoma in stead of vesicular nucleus cell carcinoma of 1991 China classification.

What pathological types on earth could undifferentiated and non-keratinizing types of 1991 WHO classification unite with 1991 China classification? Wu et al (2002) considered undifferentiated carcinoma could be divided into four subtypes according to its morphological features, which were: 1) Vesicular nucleus cell carcinoma; 2) Undifferentiated carcinoma; 3) Poorly-differentiated squamous cell carcinoma; 4) Mixture of vesicular nucleus cell carcinoma and squamous cell carcinoma respectively. So-called "large round cell carcinoma " and "vesicular nucleus cell carcinoma" in the past were considered as the subtype of undifferentiated carcinoma with most distinguished characteristic, the next were relatively uncommon small-cell undifferentiated carcinoma and small cell neuro-endocrine carcinoma (Liang et al., 1962; Zong, 1975; Chen et al., 1978).

Li (2007) believed vesicular nucleus cell carcinoma was essentially a type of undifferentiated carcinoma, but with different shape, WHO (Shanmugaratnam et al., 1991) thought so too. If all above points be combined together, it might be safely to consider that undifferentiated carcinoma in 1991 WHO classification should included undifferentiated carcinoma, large round cell carcinoma, vesicular nucleus cell carcinoma, small cell undifferentiated carcinoma, small cell neuro-endocrine carcinoma and part of poorly-differentiated squamous carcinoma in 1991 China classifications, and non-keratinizing differentiated carcinoma in 1991 WHO classification should only included part of poorly-differentiated squamous cell carcinoma in 1991 China classification. Unification like this also tallied with the previous research results about the NPC pathological proportions. If all poorly-differentiated squamous cell carcinoma in 1991 China classification were included in the non-keratinizing differentiated carcinoma of 1991 WHO classification, then the proportion of non-keratinizing differentiated carcinoma would exceed 90%, and the proportion of undifferentiated carcinoma would be greatly reduced, which was obviously inconsistent with the previous findings. If so, new problem was also created. It was which part of the poorly-differentiated squamous cell carcinoma of 1991 China classification should belong to non- keratinizing differentiated carcinoma of 1991 WHO classification and which part of the poorly-differentiated squamous cell carcinoma of 1991 China classification should belong to undifferentiated carcinoma of 1991 WHO classification? Right now it seems that except re-reading the original slide there are no other ways to distinguish it.

Proportions of Different NPC Pathological Types

According to the classification in the Norms of China Common Cancer Clinical Diagnosis and Treatment in 1991, the squamous cell carcinoma of NPC in China accounted for 98 percent with the highest proportion, and poorly-differentiated squamous cell carcinoma accounted for 95 percent of squamous cell carcinoma (Zhang and Xu.2005). Cao et al (2006) reported that 97.6 percent of 1,142 in-hospital NPC cases of Guangdong registered residents were poorly-differentiated squamous cell carcinoma, 1.7 percent undifferentiated carcinoma and 0.5 percent well-differentiated squamous cell carcinoma. Zong et al (2000;2001) believed that NPC high-incidence areas were actually the areas with high incidence of non-keratinizing carcinoma, which accounted for more than 95 percent of all NPC cases, its subtypes of differentiated, undifferentiated and mixed accounted for about 10 percent, 70 percent and 20 percent of non-keratinizing carcinoma respectively, while there were no difference for the squamous cell carcinoma incidence all over the world, which accounted for 3 percent to 5 percent, and adenocarcinoma was extremely rare.

Hong and Guo (2003) considered keratinizing type of NPC in 1991 WHO classification was relatively rare, accounting for 5 percent to 10 percent, more common in older people, while non-keratinizing type of NPC accounted for more than 95 percent. Li (2007) thought well- and moderately-differentiated subtypes of keratinizing squamous cell carcinoma in 1991 WHO NPC classification were rare in NPC high incidence areas, such as in Zhongshan of Guangdong where accounted only for 1.67 percent, but relatively more common in NPC moderate to low incidence areas, such as in Tunisia 7.8 percent, but in the United States as high as 25 percent. Luo et al (2001) re-read the original pathological slides of 2,610 NPC cases diagnosed in 1999-2000 in the pathological department of Cancer Center affiliated with Sun Yat- Sen University, and found that keratinizing squamous cell carcinoma accounted for 2.3 percent of all NPC cases (of which poorly-differentiated squamous

cell carcinoma accounted for 85.45 percent of keratinizing squamous cell carcinoma), non-keratinizing 96.7 percent, among which differentiated and undifferentiated subtype accounted for 8.9 percent and 91.1 percent of non-keratinizing type respectively. Her result was similar to the results of Hong and Guo (2001) and Li (2002).

Barnes (2001) thought that keratinizing NPC could account for 25 percent of all NPC cases, and was rare under the age of 40, while the differentiated non-keratinizing subtype was the least common, and accounted about for 12 percent of all NPC cases. Hording et al (1994) considered that undifferentiated NPC accounted for about 60 percent of all NPC cases, and was the most common cancers in child group.

Tao and Chan (2007) believed that differentiated keratinizing squamous cell carcinoma of new WHO classification accounted for 25 percent of all NPC cases in North America, but less than 2 percent in southern China, differentiated non-keratinizing carcinoma accounted for 12 percent in North America, but less than 3 percent in southern China, undifferentiated carcinoma accounted for 63 percent in North America, but 95 percent in Southern China.

From above data we could see, although the incidence of non-keratinizing NPC was significantly higher than that of keratinizing NPC, the incidence of different NPC pathological types in different regions varied greatly, the proportions of Keratinizing squamous cell carcinoma in the NPC high, moderate and low incidence areas were about 2 percent, 5 percent to 10 percent and 25% respectively, but the proportions of non-keratinizing carcinoma in NPC high and low incidence areas were 95 percent and 75 percent respectively. Thus, what Zong et al believed there were no significant difference worldwide for the incidence of squamous cell carcinoma was obviously questionable.

Suggestions

China had adopted several NPC pathological classifications before, and these classifications were difficult to link with WHO classification except for the classification of Zong et al, which blocked NPC international academic exchange and the analyses on the time trend of different NPC pathological types. So the following suggestions were made: 1) Improving China NPC pathological classifications, so that not only can it integrate completely with the WHO classification, facilitate international exchange, but also can retain our own characteristics; 2) The previous China NPC pathological classifications should be unified with current China classification, so the study on the time trend of different NPC pathological types can be carried out; 3) If the China classifications can not be unified and integrated with WHO classification, then use WHO classification, because only this can international exchanges be smoothly carried through.

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