INTERNATIONAL COLLABORATION TOWARDS PREVENTION OF ORAL CANCER: MY TWENTY YEARS EXPERIENCE UP TO THE MYANMAR PROJECT

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1. Prologue

The five-year survival rate in Japanese patients with oral cancers, which are mostly squamous cell carcinoma (SCC), still remains no more than 60%. This prognostic situation is not always better than that of the other organ cancers, though oral cancers can be detected directly by naked eyes because of their locations in the oral cavity. This is partly because (i) 70% of the patients visit firstly hospital with their oral cancers in T2 stages or more than half of them in stages III and IV in case of Niigata University Hospital (delayed detection), and partly because (ii) oral borderline malignancies, especially carcinoma in-situ (CIS), are not precisely diagnosed by pathologists (incomplete diagnostic criteria). For the latter issue, responsible are we pathologists as I will describe later, while the former issue is a matter of public health for residents to be dissolved from some cancer awareness campaigns by the cooperation between medical/dental professionals and governments or municipalities. Based on the concept above mentioned, I have started international collaboration research projects on oral cancer towards macroscopic or social understanding of prevalence and lifestyle or habitual backgrounds of oral cancer, in addition to laboratory investigation on oral cancer at tissue, cell, molecule, and gene levels. As Romanian said, “Prevention is better than cure” could be applicable to cancers including oral cancer. Since cancer is one
fieldwork on chewing-related oral cancer. Dr. Faleh Sawair from University of Jordan joined my expedition to Yemen, and we were successful in collecting new data on chewing-related oral cancer. In Yemen and its neighboring countries, people do not chew betel quid but chew Qat leaves, which I had come to know in Madagascar where there were many other kinds of chewing staffs like cola. Through these fieldworks, I became confident that oral mucositis is the basic causative factor of oral cancer, which is common to chewers even if their ways of chewing are different as well as wearers of prosthodontic appliances.

4. Oral CIS diagnostic criteria from the Japanese Society of Oral Pathology

The second strategy for oral cancer prevention was left up to the histopathologists’ side as mentioned in the prologue section. Until then, pathologists had not been aware that the histopathological diagnosis of oral CIS was challenging and that their diagnoses were performed by subjective criteria, which were different from hospital/pathologist to hospital/pathologist. Unfortunately, clinicians were not always critical either to such a situation that was inconvenient for patients. To resolve this situation, I wanted to perform accurate diagnosis of oral borderline malignancies and organized a working committee for formulating new criteria of oral CIS as one of the Japanese Society of Oral Pathology (JSOP) projects in 2005. As their fruits of efforts, the committee has published a monograph named *Oral CIS Catalog* and an original paper to explain more in detail their concept introduced in the monograph. What I would like to have emphasized in these publications was that oral CISs are histologically well differentiated as their invasive counterparts SCCs are well differentiated and that oral CIS cannot be diagnosed only based on the classic concept of cellular or nuclear atypia: there are some important histopathological which had never been recognized prior to our criteria. To support the significance of these histological characteristics of CIS, I have tried to explain biologically how each of those histological phenomena is resulted from intracellular or intercellular events, respectively. I believe that the criteria have been certified scientifically. Histopathological diagnoses should be science-based but not only experience-based.

5. Cohort study in Myanmar

I visited Myanmar firstly in December, 2005 to attend the first Myanmar-Japan Biomedical Workshop held in Yangon, which was organized by Dr. Makoto Naito and his academic colleagues in Myanmar. In this occasion, I saw again Dr. Yi Yi Myint, who had just moved to the Department of
of the most representative lifestyle-related diseases, it is one and only way towards prevention to detect causative environmental factors of oral cancer.

2. Epstein-Barr virus (EBV)-related salivary cancer

I happened to look at histopathological specimens of lymphoepithelial carcinoma among those of so-called lymphoepithelial lesion of the salivary gland, which were brought from Shanghai Ninth People’s Hospital by Dr. Jun Cheng 25 years ago. Until then I had been ignorant about the fact that the disease also arises in the stomach and salivary gland, though I just understood that it is a nasopharyngeal tumor. Since I heard that there are many patients with salivary lymphoepithelial carcinoma in China, I started a collaboration research on this particular salivary cancer with Chinese pathologists. I visited more than ten areas of China to collect lymphoepithelial carcinoma cases. This project was enabled by support of Dr. Cheng, who is now associate professor in my lab. During more than ten years period of collaboration, I have broadened my acquaintance among Chinese pathologists from the old generation such as Drs. Airu Liu, Zhiyu Zhou, and Shifeng Yu to the young generation such as Drs. Jiang Li, Lanyan Wu, and Yan Gao. Not only China but later I also visited and contacted with Taiwan, Korea, Malaysia, Canada, and Russia for collecting cases to broad my acquaintance over the world. As a result, our collection of lymphoepithelial carcinoma cases reached more than 160 cases, from which we found the association of EBV in its pathogenesis, the presence of some special genotypes, which are tumorigenic, among EBV specimens of patients from such endemic areas as Guangdong and Sichuan. These projects were supported by grants-in-aid from the Ministry of Education, Japan and from the Japan Society of Promotion for the Promotion of Science (JSPS). From this experience, I have become aware of the importance as well as pleasure in working in an international situation.

3. Oral submucous fibrosis

In the next step, I visited Sri Lanka because I was again ignorant about the disease of oral submucous fibrosis, which I had to talk about in teaching dental students in my oral pathology class. In the town of Candy, I saw for the first time betel quid stands on streets, in which betel leaves, areca nuts, tobacco leaves, and lime paste were being sold and bought by many customers. Their business looked very busy. In collaboration with Dr. Tilakaratne at University of Peradeniya, I have come to understand the histopathogenesis of betel quid chewers’ mucosa or oral submucous fibrosis. With these communications a trigger, my lab was involved in a JICA project on Dental Education in Sri Lanka.

To see more actual situation of betel quid chewing, I visited again Taiwan, where the habit was also very popular, to come to be acquainted with Dr. Chun-Pin Chang at Taiwan National University. He hosted several times international conferences related oral pathology or oral cancer in Taipei. I also visited Malaysia, Indonesia, India, Bangladesh, Pakistan, Yemen, Jordan, Madagascar, Sudan, and Morocco for the
Medical Research (Central Myanmar) at Nay Pyi Taw, a new Capital of the country, to which it took nine hours by car from Yangon at that time. Why again? Because I remembered that we met many years ago when I asked some questions at her poster on op/op mice presented at a meeting of the Japanese Society of Pathology. We discussed a possibility of collaboration on oral cancer in Myanmar, and I actually visited her at Nay Pyi Taw next year to discuss a preliminary survey on oral cancer frequencies in Yangon and Mandalay. In 2007, Dr. Htun Naing Oo, Director General of the institute and Dr. Myint visited us in Niigata to discuss how to carry out the survey as well as how to extend the research to the second stage. Dr. Oo suggested his idea on a cohort study in some appropriate areas in Myanmar. The first fruit from the collaboration was published in 2010, in which we found that oral cancer (squamous cell carcinoma) is not so frequent in Myanmar as in the other countries where betel quid chewing is widely performed.24

The cohort study in Chauk and Taungoo areas has started on our hypothesis that oral cancer should be unintentionally prevented in Myanmar by their lifestyle, especially nutrient situations. This project designed by Drs. Oo and Myint was fully supported by the Department of Medical Research, the Ministry of Health, and local hospitals or governmental offices. In Taungoo, we collected cytology and blood samples, which are now under investigation. In the process, Dr. Myint has moved to the Department of Medical Research (Upper Myanmar) at Pyin Oo Lwin as Director General. The project has been supported by the Japanese Society for the Promotion of Science and is expected to extract some achievements toward the direction of oral cancer prevention.

6. Epilogue

This article is to celebrate the 15th anniversary of the Department of Medical Research (Upper Myanmar). I am looking forward to visiting again Pyin Oo Lwin in February, 2015.

References


