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INTERNATIONAL SOCIETY
for
ORAL ONCOLOGY

Newsletter 2005-2006

Editor: Andrei Barasch Scientific Editor: Rajesh V. Lalla

Geneva was the site for the 2005 MASCC/ISOO annual meeting. In addition to the famous Jet d'Eau (above), the heat and prices were also memorable. Sincere thanks to Dr Aapro for hosting this excellent meeting.

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Some format changes to the newsletter

Andrei Barasch, Editor

Call for articles, news items and larger participation

This issue of the ISOO newsletter comes to you with a changed format, complete with a new editor, chief over a crew of one. I have received this task from the capable hands of Kathryn Damato who did a splendid job with the past issues. However, discussions about format changes have started before my coronation and came to pass after consultations with members of our society's leadership.

The philosophy here consists of our desire to make this publication a forum for scientific exchange, information, opinion and relevant news. We would like these pages to speak for, and to the ISOO members, as well as to the MASCC membership at large. We need the audience to become authors and vice-versa, with the distinct purpose of advancing scientific communication and cooperation among the many capable researchers and clinicians who form our ranks.

As these pages will be open to all who would like to contribute, I will make a personal plea to my friends and colleagues to forward to me items of interest that are apt for this forum. In particular editorials, scientific advances, developing research, clinical cases and reviews will be most welcome. Also, please forward professional and personal items of interest that you would like the readership to discover. I understand the time

limitations most of us face on a daily basis. However, this is OUR newsletter, OUR voice and means to stay in touch, and OUR way to hear and be heard. We are a vigorous, energetic group and can make our vitality permeate the pages of our publication.

I hope you enjoy reading this edition and will find it informative. If so, help me keep it that way. If not, I challenge you to make it better and more relevant to all of us. Either way, this is a chance to show temerity for the benefit of the entire group.

Note

Please send all your communications electronically to Andrei Barasch at abarasch@uab.edu

Editorial : Is Oral Oncology taken seriously outside teaching hospitals?

. **Andrei Barasch, DMD, MDSc**

Associate Professor, University of Alabama at Birmingham

Most of us have had this experience: when explaining to an audience of physicians what we do for a living, a voice typically coming from a puzzled face will incredulously ask what a dentist can do for cancer. Is there a cancer of the teeth? After a more detailed presentation aided by thoroughly prepared visual props, most physicians will understand, appreciate and applaud our efforts. Or do they?

There are no data available to inform us of the impact of Oral Oncology in the larger Oncology community. Furthermore, there is no validated tool to assess our perceived usefulness in the Oncology service, no Oral Oncology-related Quality of Care, if you will. We all have our anecdotes to relate, and can describe the working environment at our respective institutions. With the (dubious) distinction of having worked at five

academic centers, I have had my fair share of experiences. I have certainly seen some significant progress over the years, yet my perception is that dentists in general and Oral Oncologists in particular are still hospital second class citizens, particularly outside of teaching institutions. Many Oncology teams do not include an oral specialist, and dental and oral clearance is optional at many institutions that treat cancer patients. Attitudes displayed by physicians range from warmth, to benevolent tolerance, to outright aggression. Moreover, when funds fall short in the Cancer Center or the Bone Marrow Transplantation Unit, dental is among the first services to be cut.

There can be endless discussion (at least I hope there will be **some**) about the reasons for this situation, but at least one question begs to be asked: What is the true value that we provide to cancer care? Work by Drs. Sonis and Elting has placed a dollar value on the impact of mucositis. That is a great beginning but we still have much to achieve, and even more to prove. Members of our society must adopt a proactive stance in educating both physicians and the population at large about our role and position in cancer care. Our research must continue to make a sizable difference in the body of knowledge. More than anything though, our clinical work and experience must continue to expand in scope and importance, such that the oral specialist will become indispensable to the practice of oncology.

Can we, Oral Oncologists treat oral cancer? Most medical specialties maintain some involvement in treating malignant diseases of their area of expertise. Unfortunately, the vast majority of dental schools and dental residency programs do not train their students in cancer treatment. Even Oncology-oriented dental teaching programs place their focus on supportive care only. Yet, when the medical community faced an impasse

with oral Kaposi's sarcoma (KS) in AIDS patients, a few inspired colleagues experimented with intralesional vinblastine, which soon became the palliative treatment of choice (1,2). Yes, that treatment was not with therapeutic intent, but some complete remissions were achieved with that method. This is but one successful example of what may be endless possibilities for local treatment of oral malignancy. One can cogently argue that we have the best training with regards to oral structures and treatment of oral disease. We can have a significant influence in bringing treatment and prevention of oral cancer to a local level and thus expand the practice of Oral Oncology. The Oral Oncologist can become the primary specialist for oral cancer care and assume the leading role in this area of clinical research and practice.

References

1. Epstein JB. Management of intraoral Kaposi's sarcoma and a proposal for clinical staging. Oral Dis 1997; 3:S124-8.
2. Flaitz CM, Nichols CM, Hicks MJ. Role of intralesional vinblastine administration in treatment of intraoral Kaposi's sarcoma in AIDS. Oral Oncol Eur J Cancer 1995; 31B:280-5.

ISOO News

"Hellenic Association of Supportive Care of the Oral Cavity in Cancer (HASCOCC)" was founded in Greece.

Under the leadership of Ourania Nicolatou-Galitis, DDS, MS, Dr Dent, Associate Professor of Oral Pathology & Medicine In charge of the Dental Oncology Unit School of Dentistry, University of Athens, the HASCOCC came into existence on 27 September 2005. The young organization includes 72 oncology specialists from various fields and is currently awaiting official recognition from the Greek government.

The establishment of this association follows the opening of the Dental Oncology Unit at the National and Kapodistrian University of Athens. Dr. Steven Sonis was the invited lecturer for the event which took place on 10 May 2005.

After the Dedication, May 10th, at the entrance of the School of Dentistry. Professor Sonis and his wife are in the middle surrounded by Prof. G. Vougiouklakis, Dean, Prof. S. Papanicolaou, Head of the Dept. of Oral Medicine & Pathology, asst. Prof. O. Nicolatou-Galitis, and some of the radiation oncologists.

PhD Degree for Monique Stokman

Monique Stokman has recently completed her PhD studies, becoming the first dental hygienist in the Netherlands to do so. The title of her thesis (defense took place in December 2005) is *New Options for Evaluation and Intervention of Cancer Therapy Induced Oral Mucositis*. The dissertation consists of 9 chapters of which 3 are evaluation, and 3 are intervention studies. Six articles based on this work have been published or accepted for publication in various peer-reviewed journals. Among Dr. Stokman's advisors are fellow members Dr. Fred Spijkervet, Dr. Joel Epstein and Dr. Isaac van der Waal. A copy of the thesis publication can be obtained by contacting Monique at m.a.stokman@kchir.umcg.nl. Congratulations Monique!

Recognition awards

Loree Oberle-Edwards RDH, MS and Kathryn Damato, RDH, MS accepted the beautiful inscribed time pieces in recognition for their efforts on behalf of the Society. The Swiss sponsor of the photograph will remain unnamed. The time of the awards was precisely 10:10, which was too early for some participants to be fully awake.

ISOO Continuing Education—A Great Success

In conjunction with the annual meeting in Geneva, our continuing education course has been well-attended by the Swiss dental community. This year's topic was Head and Neck Cancer, which was aptly presented by two of the towering figures in this topic, Dr. Sol Silverman Jr,, and Professor Isaac van der Waal. Translated instantaneously into three Swiss languages, the course was both interesting and entertaining.

Our thanks are directed to Dr. Dominic Ettlin for his help with organizing the course, to the Swiss Cancer Society for their generous support and to Noble Biocare Co. for their help with marketing this course.

Numerous backs with the heads in upright position demonstrate the success of the ISOO continuing education course in Geneva. Drs. Isaac van der Waal and Sol Silverman Jr. lectured.

MASCC/ISOO—the Oral Care Study Group

Michael Brenan, DDS, MHS, Director of Oral Medicine, Carolinas Medical Center, Charlotte, NC, co-chair of the Oral Care Study Group

The Oral Care Study Group of MASCC/ISOO has had an active 2005, with major initiatives underway. During the first half of the year, a group of 9 members of ISOO completed a preliminary literature review of the most common oral complications associated with cancer therapies. A total of 528 articles were identified by a literature search, with 176 clinical trials that reported oral

complications. Of these reviewed articles, 48 evaluated oral complications associated with chemotherapy, while 128 evaluated complications of radiotherapy with or without chemotherapy. Only 13% of these articles were randomized controlled trials, and 73% of all studies were prospective. The five most commonly reported oral complications in order of incidence included xerostomia, dysphagia, fungal infection, osteoradionecrosis, and dysgeusia. The preliminary results were presented at a planning meeting of the Oral Care Study Section members prior to the annual MASCC/ISOO meeting in Geneva, Switzerland in June, 2005.

The results from this initial review of the literature provided a stepping stone for a recent NIH grant application submitted in October, 2005 with numerous members of ISOO as co-investigators. Funding from this NIH initiative would provide the means to complete a more thorough systematic review of the epidemiology and treatment of the various oral complications from cancer therapies. These findings will provide the basis for future projects with a strong collaborative base of ISOO members. More exciting possibilities to follow!

Oral Oncology, a constant focus of the Israeli Society of Oral Medicine

Sharon Elad, DMD, Lecturer, Hadassah University, Jerusalem

At the end of 2005, the Israeli Society of Oral Medicine (ISOM) looked back at a fruitful year of advancing issues in oral oncology.

Educational activity directed at the professional community concentrated on raising awareness of bisphosphonate-related osteomyelitis/necrosis. Dr. Noam Yarom lectured on this

topic at the ISOM session of the annual meeting of the Israeli Dental Association, attended by over 1,000 professionals. In his lecture, global data and the suspected pathogenesis of bisphosphonate-related osteomyelitis/necrosis were reviewed. The audience heard about current guidelines for the dental management of patients treated with bisphosphonates. Dr. Yarom also presented the results of a new collaborative study between Tel-Hashomer Medical Center and Hadassah University Medical Center.

Another aspect of this collaborative study was presented by Dr. Sharon Elad to the Oncology Department at Tel-Hashomer Medical Center. Her aim was to increase awareness of this bisphosphonate-induced adverse event among oncologists. Additionally, she addressed the practical aspects of this pathologic entity at the "Amen" (Israeli branch of the International Multiple Myeloma Foundation) meeting. The audience consisted of multiple myeloma patients and their families and the scientific program for the evening also included lectures about the epidemiology and new treatments of multiple myeloma. The lectures were followed by intense discussions with the audience regarding the bisphosphonate issue.

During 2005 the ISOM introduced an official brochure for oncology patients. This colorful information sheet will provide essential information to oncology patients about common oral complications and promote oral care. The content was written by Drs. Noam Yarom, Esther Scheuer and Sharon Elad. Sponsorship of production and distribution was secured from a large Israeli pharmaceutical company.

The Mucositis Resource Center

Rajesh V. Lalla, BDS, PhD, Asst. Professor, University of Connecticut, Farmington, CT

Have you visited the MASCC/ISOO website recently? If not, you're missing out on some great content. The website has been extensively revamped. An exciting new feature of this re-design is the Education and Resource Centers. There are currently 14 such online Centers, ranging from Antiemetic to Quality of Life. Of particular interest to ISOO members might be the Oral Care Resource Center and the Mucositis Resource Center. I am currently serving as Editor of the Mucositis Resource Center.

The Mucositis Resource Center has content divided into the following five sections: *Morbidity & Economic Costs, Pathogenesis, Management Guidelines, Recent Advances and Patient Education*. This content currently includes mucositis-related presentations (slides plus audio) from the Miami meeting, with presentations from Geneva to be added shortly. So if you ran off to go to the beach in Miami or were not able to make it to Geneva, here's your chance to catch up on what you missed. The Mucositis Resource Center also includes links to free full text of the two papers in the 2004 Cancer supplement on mucositis as well as a table with the 2005 Guidelines update.

To get to the Resource Centers, go to "www.mascc.org" and click on "Education and Resource Centers" in the menu on the left. If you have any suggestions for content or improvements to the Mucositis Resource Center, please send me an email at "lalla@nso2.uchc.edu".

Happy Surfing!

State of the Mouth: Oral Mucositis and Other Supportive Care Issues

Judith Raber-Durlacher, DDS, PhD, Andrei Barasch, DMD, MDSc & Douglas E. Peterson, DMD, PhD

Oral mucositis induced by cancer chemotherapy is a morbid complication that can negatively impact quality of life (Öhrn , Wahlin and Sjoden, 2001) and significantly increase cost of care (Sonis et al 2001); this complication can also contribute to increased mortality. Pretreatment oral assessment and intervention followed by individualized oral care and patient education provided during (and after) cancer treatment may reduce the adverse impact of oral mucositis, and are strongly recommended in patients scheduled for intensive chemotherapeutic and head and neck irradiation regimens (Consensus Monograph 1990).

Recent scientific efforts have improved our understanding of the mucosal damage process and led to progress in development of new prophylactic and therapeutic pharmaceutical interventions. Some of the more promising drugs emerging to combat mucositis include topical L-glutamine (Saforis) and intravenous recombinant human keratinocyte growth factor (KGF, palifermin). Amifostine (Ethyol) has been approved by the FDA for salivary gland protection and is currently undergoing further trials to establish its efficacy in preventing mucositis. Promising products that are currently under investigation include N-acetyl-L-cysteine (a potent antioxidant) and Isegartan, an analog of protegrin-1 (broad-spectrum antimicrobial).

Undoubtedly, knowledge in this area of supportive care should continue to be systematically expanded. It is critically important to further elucidate the pathogenesis of mucositis and identify risk factors, since this will provide us with better tools for prevention and treatment. Similarly, effects of chemotherapy on salivation, including epidemiologic aspects and duration of salivary changes,

should be assessed. Management recommendations will follow a better understanding of its pathogenesis and role in mucosal protection.

Nevertheless, there seems to be a significant gap between our present knowledge and what has been translated into standards of care. In a recent survey among supportive care providers, integrated dental services were reported to be available in only about 25% of the institutions (Barker et al 2004). In addition, successful implementation of oral care regimens is still relatively rare (McGuire 2003). These deficiencies may be primarily associated with a lack of recognition of the medical necessity for oral and dental care, a lack of translational research related to oral complications, and the fact that oral complications may be under-reported by patients, and under-diagnosed, and under-treated by care providers (Trotti et al 2003). It is therefore essential that educational programs continue to be developed for supportive care providers and cancer patients.

The field of oncology is dynamic and new evidence in diagnosis and treatment of malignant diseases is associated with shifts in the scope and magnitude of oral complications. As the management of other supportive care issues in oncology has improved (e.g. nausea and vomiting, febrile neutropenia, etc), the importance and impact of the unresolved issue of oral complications of cancer therapy is coming into sharper focus. Selected aggressive chemotherapy regimens are accompanied by more severe oral mucositis and infection. At the same time, less toxic, non-myelosuppressive conditioning regimens are likely to induce less severe mucositis and reduced rates of infection, but may be associated with other significant oral problems.

Interaction between medical and dental professionals can facilitate early identification of oral complications. For instance, concern has been raised recently on a potential association of osteonecrosis involving the jaws and the use of bisphosphonates, especially pamidronate and zoledronate (Marx 2003, Pogrel and Miller 2003, Wang et al 2003). These drugs are potent inhibitors of osteoclast-mediated bone resorption and may also affect angiogenesis. Since

bisphosphonates are increasingly being used for the management of bone metastases and hypercalcemia in cancer patients, information on possible adverse side effects is relevant for medical oncologists and dentists (Migliorati 2005). Although we consider it too early to make any recommendations other than preventive dental care prior to treatment, increased awareness of this putative oral complication seems justified and collaborative studies should be performed in the future.

Taken together, providing oral supportive care in cancer patients treated with high-dose chemotherapy or ionizing radiation requires close cooperation between multiple disciplines. Education in basic as well as oncology-specific oral care should be part of the curriculum of all health care providers who treat cancer patients in their clinical practice. Studies on the pathogenesis of oral complications may provide a key to prevention and treatment. Clinical research including significant numbers of patients should be performed in order to develop evidence-based recommendations, and form a solid base for the recognition of the medical necessity of oral and dental supportive care and secure reimbursement by third party payers. In addition, new cancer treatment strategies warrant continuous adaptation of oral care regimens to the changing scope of oral complications.

Surviving Oral Cancer

Eva Grayzel Cohen

Editor's Note: Eva Grayzel Cohen is a storyteller in Lehigh Valley, PA. Her husband and her father are both physicians, so Eva is neither a stranger to medical lingo nor an underprivileged person with no access to care. Due to its length, her story will be published in three sections. Presented below is the first part.

LIFE WITH ORAL CANCER, BEFORE I KNEW IT

At age 33 I was diagnosed with stage IV squamous cell carcinoma on the lateral tongue. I never smoked, and rarely drink.

Two years prior to my diagnosis, I had an excisional biopsy of an 8-week old "canker sore" on my lateral tongue. What could the biopsy possibly show? A virus or bacteria? I was just glad to get that thing off my tongue. I received a call that the biopsy showed nothing, so I thought nothing of it. Now I know that it was read by a **general** pathologist who missed the atypical cells. He called it 'hyperkeratosis'. I never thought to question the biopsy and why a sore was determined to really be a 'callous'. I was happy and free of symptoms for two years while the tumor was growing.

The canker sore returned on the side of my tongue. After a month I got really tired of the constant discomfort. My dentist told me to see an oral surgeon. I returned to the OS who told me that since it is developing over the biopsy site from two years ago, it is probably the same thing, a hyperkeratotic lesion. 'Try salt water rinses,' he said. 'And, come back to see us, if it doesn't get better.' The latter direction was very vague, unhelpful advice for an optimistic, naïve person. I wanted to believe it was getting better. Living with it every day, it was hard to notice the subtle changes. And subtle they were. Some days it didn't hurt so much. It felt better for a while, but after another month passed, I realized it really didn't look much better. When I returned to the OS I was told to try a gel called Ambesol. 'If it doesn't get better, let us know.'

Well, I really believed it was getting better. Until one day, I was feeling the gnawing pain in my tongue, took a look under a bright light and realized that it is definitely not getting better; if anything, it looked worse. Yet one more month had passed at that point. Convinced that it was caused by trauma, the OS told me to return to my dentists to have my back teeth smoothed to lessen the irritation it is causing my tongue. It took a couple of weeks to get the appointment…and, another couple of months before I believed that I did not see ANY improvement.

"You must be biting your tongue…maybe you are talking too much…could you be gnawing at your tongue during your sleep?" I assured them that my tongue hurt so much that if I bit it, or gnawed at it, it would send me through the roof in a manner I would not forget. But they still insisted it was traumatic in nature and told me to return to the dentists for a mouth guard, a plastic device to cover my teeth so they would no longer irritate my tongue.

It took a couple of weeks before I could get the appointment with the dentist to make the impression, a month for it to come in, and another few visits before it fit comfortably. Then I waited even longer to see if it helped. I was dieing to believe it would help.

The pain increased with time. "The tongue is small and we don't want to unnecessarily cut it further," my oral surgeon told me. It was the killer earache that led to some concern among my treating physicians. Sometimes I would wake up during the night, crying in pain. I told my general physician that every time my

tongue hurts, my ear hurts. But I was told I had some water on my eardrum and was given antibiotics. The pain did not go away and I was desperate. No one knew what to do with me.

In my small town in Pennsylvania during the time I had this nasty tongue lesion, I had seen two dentists, two oral surgeons, an endodontist, a general doc and several docs unofficially. All of them had no idea what they were looking at. Well, that just says two very important things: One: oral care providers need more education on oral cancers. Two: We, the general public, need to be aware about oral cancer. If it can happen to me, it can happen to anyone!

I called a family friend who worked at Mt Sinai Hospital in New York City. He was a plastic surgeon specializing in cleft palette. I described the situation and he proclaimed "What are you doing in your little town there? Get yourself to a medical center! If one doc doesn't know what it is, another will." When I asked where and whom I should see, he recommended Dr Mark Urken at Mt Sinai Hospital. All I knew was that he specialized in lumps and bumps in the head and neck region. I got in to see Dr Urken within two weeks. At this point, nine months had passed since the second lesion appeared. He recommended a biopsy right away.

I took the bus into NYC for my biopsy on April 1st, 1998. Why the bus, you think, when this could be serious? Well, I had no idea, not an inkling that my condition was even remotely serious. My mother met me at the hospital to take me home. She knew something was up when the doctor waited for her to be by my side when he spoke to me. April Fools jokes were rampant all around, yet the news I heard was no joke.

At first, Dr Urken used some enigmatic words to describe my condition. I was still a little out of it from the anesthesia. Maybe that was a good thing. He used the word 'carcinoma' but I did not know that meant malignant. When he looked down and answered in the affirmative, I squeezed my mom's hand and don't remember another thing after that. The moment I comprehended what the doctor was telling me, it felt like a truck was barreling up my body and crashing into every organ and bone, crashing inside my head leaving shards of glass everywhere. The shock alone could have killed me. God help those people who do not have someone to accompany them. Mom and I planned that she would drive me home. I could not sit in a car for 1.5 hours. I was completely incapacitated by my fear and devastation. Aside from the excruciating pain of the extensive biopsy, emotionally I couldn't go home to my children. I couldn't even face my husband.

My mother cradled me all night and got me cold packs every couple of hours. We did not have many words. That is because there are no words; no words to explain why something like this could happen to a young person who has dedicated so much time to helping others. What could a mother say to a daughter who was just

told that the cancer had spread to the lymph nodes and the surrounding lymphatic tissue?

Dr Urken called my husband who is a radiologist. "Your wife has cancer in her tongue. It has spread to the lymph nodes and possibly the lymphatic tissues. I will have a pathologist work by my side so I do not need to remove more than necessary. With each slice, it will be read to check for clean borders. I will reconstruct her tongue with tissue from her forearm and thigh. I will remove an artery from her forearm to feed blood to the graft site. Also, I will remove all the lymph nodes on the left side of her neck since it is clear that at least one node is enlarged and infected."
Ken asked Dr. Urken not to share with me the advanced stage I had entered. So, I believed I was stage II-III, when Ken knew it was stage IV. My survival chance was 15%, but I did not know that.

(Continued in the next issue)

Sincere thanks to MGI Pharma for their generous support of this Newsletter

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