AKADEMIJA NAUKA I UMJETNOSTI BOSNE I HERCEGOVINE
АКАДЕМИЈА НАУКА И УМЈЕТНОСТИ БОСНЕ И ХЕРЦЕГОВИНЕ
ACADEMY OF SCIENCES AND ARTS OF BOSNIA AND HERZEGOVINA

RADOVI

KNJIGA XCIII

Odjeljenje medicinskih nauka

Knjiga 33

Centar za medicinska istraživanja

Knjiga 3

SARAJEVO 2004

ORAL SEQUELS OF POSTRADIATION SYNDROME

Berislav Topić
Academy of Sciences and Arts of Bosnia and Herzegovina

Abstract
The treatment of malignancies includes surgical therapy, radiotherapy, chemotherapy and combinations of these methods. Head and neck cancer accounts for a high percentage of radiotherapeutic casuistics. Orofacial region is an important area of nuclear medicine. Radiotherapy side effects cause systemic and local reactions known as postradiation syndrome. Radiation induces multiple effects that manifest at various levels, i.e. cellular, tissue, organ and systemic level. Oral sequels of head and neck radiotherapy can cause pathologic lesions of oral mucosa (mucositis), salivary glands and their function (salivation), teeth (cervical caries), jaws (osteoradionecrosis), and functional disorders of mastication, swallowing, taste, appetite and speech. Therefore, every patient scheduled for head and neck radiotherapy should undergo dental examination and receive appropriate and strictly individualized dental treatment. That is why the oncologic team should also include a dental medicine specialist. The procedures and treatments are described, which should be performed before and after head and neck radiotherapy to prevent the occurrence of such oral complications and to ensure the highest possible postradiation quality of life for the patient.
Key words: oral cavity, cancer, radiotherapy, postradiation syndrome

Introduction

In medicine, radioactive beams are used for experimental, diagnostic and therapeutic purposes. Orofacial region is one of the most common radiation areas of nuclear medicine, reflecting radiation casuistics of the following specialties:

- neurosurgery,
- ophthalmology,
- otorhinolaryngology,
- cervicofacial surgery,
- maxillofacial surgery,
- oral surgery,
- oral medicine,
- dermatology and
- endocrinology (parathyroid, thyroid and pituitary glands).

Epidemiologic data on head and neck cancer without lymphoma and skin carcinoma show their prevalence to be 14% in men and 5% in women (1-5). The following methods are used in the treatment of malignancies:

- surgical,
- radiation,
- chemotherapy,

- hormone,
- immunologic, and
- combinations of these (6).

Radiotherapy entails multiple effects on the cells, tissues, organs and body as a whole. At the cellular level, mitotic activity is reduced. The morphological and functional structure of the cell in the phase of mitosis is destroyed, thus preventing its further replication and ultimately resulting in cell death. The involved epithelium becomes atrophic and susceptible to irritation to cause its lesions. Local impairments of the circulation and metabolic activity occur due to the effect of radiation on vascularization (endarteritis) (7).

Radiation sensitivity of various tissues and organs varies:

- highest sensitivity – lymphatic tissue, bone marrow, gonads, intestinal epithelium
- high sensitivity – skin, cornea, gastrointestinal tract, oral mucosa
- moderate sensitivity – connective tissue, vasculature, salivary glands, cartilage, developing bone
- low sensitivity – kidneys, liver, adult thyroid, adult cartilage, adult bone
- lowest sensitivity – muscle, central nervous system (CNS), nerves (8,9).

Ionizing radiation causes systemic and local reactions, depending on the radiation intensity and intervals. Systemic reaction may manifest as acute radiation syndrome (10,11), the latent period lasting from several hours to several weeks, depending on the radiation dose. The prodromal symptoms include nausea, vomiting and diarrhea.

A radiation dose of 2 to 10 Gy causes hematologic alterations, i.e. hematologic syndrome. A radiation dose of 10 to 50 Gy causes gastrointestinal syndrome, whereas a radiation dose of >50 Gy leads to CNS syndrome.

Postradiation lethality is due to infection, dehydration, hemorrhage and electrolyte disbalance.

The radiation side effects can be:

- early, which occur immediately upon radiation and persist for several days. They include fatigue, exhaustion, and skin lesions in the area exposed to radiation; and
- late, which are diverse and occur several months to years after radiation, and may be permanent. These can develop as the sequels of the disease and radiation, and include exhaustion, fatigue, asthenia, insomnia, pains, inappetence, and blood count alterations.

Radiotherapy side effects in the head and neck region include the following:

- oral mucosa is red, sensitive, painful, dry and covered with sores, presenting in a variety of clinical pictures of alterated oral epithelium, e.g., cheilitis, stomatitis, gingivitis and glossitis, indicating a common diagnosis of mucositis (12), frequently additionally complicated by *Candida albicans* infection (13);
- salivary glands are altered and their secretory function is impaired (14,15), the amount of saliva is reduced and qualitatively changed, i.e. viscous, thick and sticky. Mastication and swallowing are difficult, the taste and smell are impaired (16) and accompanied by disgust and inappetence;
- the teeth are affected with cervical caries (17);
- restricted movement of the jaws, which may progress to ankylostoma. Postradiation osteoradionecrosis (PRON) may develop (18,19). The mandibular spongiosa is gradually reduced, while the compact structures are highly developed and less vascularized than the maxilla, which shows abundant collateral vascularization. Therefore, the mandible suffers more severe lesions due to radiation than the maxilla;
- radiation dermatitis occurs on the face and neck skin (20). The skin turns darker, dry and susceptible to injuries; also, total alopecia develops on the capilli.

For all this, a patient scheduled for radiotherapy in the head and neck region should first undergo dental examination and specific dental treatment. Thus, a dental doctor should be included in the oncologic team.

The oncologic team should consist of the following specialists: oncologist, pathologist, radiologist – roentgenologist, radiation physicist, dosimetrist, radiotherapist (technician), radiotherapy nurse, physiotherapist (technician), psychologist, dietitian, social worker and respective specialist (21).

Responsibilities and duties of dental doctor as oncologic team member

Dental doctor participates in the oncologic team activities before and after the patient's exposure to radiotherapy.

Before radiotherapy

- oral clinical examination including x-ray finding of the teeth and jaws (orthopantomograph or panoramix and retroalveolar images)
- patient education, instruction and motivation for oral hygiene during and after radiotherapy
- complete treatment of the teeth and jaws

- radical approach in dental therapy
- extraction of any tooth with a predictable prognosis without treatment of <5 years (22)
- indications for tooth extraction:
  - all pulpless teeth
  - apical periodontitis
  - teeth requiring endodontic treatment
  - teeth with true periodontal pockets
  - teeth with crown destruction
  - retained root (*radix relicta*)
  - impacted tooth (*dens impacta*)
- a dilemma between extraction and apicoectomy is not acceptable
- tooth extraction should be performed at least 14-20 days (mimimum 10 days) before radiotherapy
- alveolar extraction should not leave sharp edges or prominences; alveoloplasty should be performed if necessary
- upon tooth extraction, the extraction wound should be sutured to allow it to heal *per primam*
- fresh coagulum is sensitive to radiation
- antibiotics should be prescribed for 7-10 days
- cystectomy should be performed in case of jaw cysts
- removable appliances should not be worn during and 2 years after radiotherapy

After radiotherapy

- efforts should be invested in appropriate care of the teeth, gingiva, oral cavity and throat (20,23)
- teeth should be cleaned with soft toothbrush after each meal and at bedtime
- abrasive-free toothpaste with fluoride should be used
- tooth neck (cervical caries) and interdental space (interdental stimulants) hygiene requires special attention
- mouthwash with NaCl and sodium bicarbonate solutions during the day
- mouthwash with graded pressure water pick
- in most cases, postradiation xerostomia occurs (15); the patients are instructed to:
  - sipping some fresh beverage will alleviate discomforts, whereby cold drinking water is preferred over carbonated beverage; a thermos bottle with water and ice should be brought along in the morning
  - sugar-free chewing gums may help

- when oral mucosa is not burning, application of olive oil with lemon juice can help, especially before meals

- artificial saliva should be prescribed (Glandosan spray, Oral Balance gel, Xero-Lube)
- a sialagogue should be prescribed (pilocarpine hydrochloride solution, Salagen tablets, teas)

Maxillomandibular complications

The most severe postradiation sequel involving oral cavity is the maxillomandibular complication manifesting with a clinical picture of osteomyelitis, postradiation osteoradionecrosis and sequestration (18,19). The preventive measures mentioned above should be taken before radiotherapy to prevent these complications, as it is well known that prevention is better than treatment.

A bone exposed to radiation has a reduced ability of regeneration, its vascular supply is impaired, and the osteocyte-osteoblast count is reduced. The manidble is more of a problem than the maxilla. May these complications occur, the following therapeutic regimen should be introduced, in this sequence:

- high-dose antibiotics, according to antibiotic sensitivity report, followed by
- oxygenation in hyperbaric chamber; therapy with hyperbaric oxygenation increases tissue oxygenation, thus stimulating angiogenesis, and osteoblast and fibroblast function (24), and finally
- operative treatment.

Dietary regimen

- diet should be predominated by protein, containing enough calories, vitamins, minerals and water (20,21)
- spices, raw food, fresh vegetable, cookies, zwieback, nuts, hazelnuts and between-meal sweets should be avoided (cervical caries)
- acidic food and irritating drinks should be avoided
- cigarette smoking and alcohol consumption are forbidden
- mouthwash should not contain alcohol, because alcohols results in mucosa drying-up
- food should be taken when the patient is hungry, not waiting the mealtime. More than 3 main meals should be taken during the day in the form of snacks. If the patient eats very small amounts of food, the diet can be calorie enriched (butter, creams, cheese, sweet fruit)

- the food should be tasteful, soft and chopped, nicely served in cosy atmosphere with some fine music on, and in the company of caring persons
- the patient should be kind on ordering food and demanding some recipe modifications
- one should remember the old folk's saying that 'strength enters the body through the mouth'
- attention should be paid to the patient's free time organization.

Conclusion

Oral care provided by dental doctor is an important part of all steps in the dignosis and treatment of patients with head and neck cancer. If confirmed, an early suspicion of the potential diagnosis of oral cancer (5) is of utmost importance for improved patient survival rate, reduction of therapeutic complications, and prevention of visible mutilating procedures. The patient's quality of life can be improved by timely, skilful and knowledgeable support invested by dental doctor for the prevention of oral complications that may develop during or after radiotherapy. Dental doctor should be included as member of the oncologic team in the management of patients with head and neck cancer scheduled for radiation therapy. This poses the need of including the respective subjects in dental medicine undergraduate education, whereas the specialists to be oncologic team members should continuously keep informed about up-to-date scientific and professional advances in the fields of epidemiology, pathogenesis, etiology, prevention, diagnosis, therapy and follow-up of patients with head and neck cancer, with special reference to the maxillofacial region.

Apstrakt

ORALNE SEKVELE POSLIJERADIJACIJSKOG SINDROMA

Liječenje malignoma provodi se kirurški, radijacijski, kemoterapijom i kombinirano. Malignomi glave i vrata čine visok postotak radijacijske kazuistike. Orofacijalna regija je značajno područje nuklearne medicine. Nuspojave zračenja izazivaju sistemske i lokalne reakcije koje se svrstavaju kao postradijacijski sindrom. Učinci zračenja su višestruki, a odražavaju se na razini stanice, tkiva, organa i organizma. Radijacijska terapija u području glave i vrata može u usnoj šupljini izazvati patološke promjene na oralnim sluznicama (mukozitis), žlijezdama slinovnicama i njihovoj funkciji (slina), zubima (cervikalni karijesi), čeljustima (osteoradionekroza), kao i funkcionalne smetnje žvakanja, gutanja, okusa, apetita, govora. Zbog toga svaki bolesnik kojega se namjerava podvrgnuti radijacijskoj terapiji u području glave i vrata treba proći stomatološki pregled i dobiti odgovarajuću strogo individualiziranu stomatološku obradu. Zato stomatolog treba biti uključen u onkološki tim. Detaljno se navode postupci i obrada koje treba provesti u bolesnika prije i poslije radijacijske terapije u području glave i vrata, kako ne bi došlo do navedenih komplikacija u usnoj šupljini, čime bi život bolesnika u poslijeradijacijskom razdoblju bio što prihvatljiviji i snošljiviji.

Ključne riječi: Usna šupljina, karcinom, radioterapija, postradiacioni sindrom

Literature

1. Zavod za statistiku federacije BiH. Uzroci smrtnosti u Federaciji BiH 2000. Demografski podaci 2001.
2. Zavod za statistiku R. Hrvatske. Uzroci smrtnosti u R. Hrvatskoj. Demografski podaci 2000.
3. Hrvatski zavod za javno zdravstvo. Novi slučajevi raka usta u R. Hrvatskoj 1999. Bilten 2000; 24.
4. Topić B, *et al.* Oralna medicina. Sarajevo: Stomatološki fakultet, 2001;67-90.
5. Topić B. The prevalence of precancerous lesions in primary dental health care. Radovi ANUBiH 2003; 31:61-71.
6. Dautović S. Tumori. In: Topić B, *et al.*, eds. Oralna medicina. Sarajevo: Stomatološki fakultet, 2001;371-404.
7. Squier CA. Mucosal alterations. Natl Cancer Inst Monogr 1990;9:169-72.
8. Miles DA, Van LM, Razmus TF. Basic principles of oral and maxillofacial radiology. Philadelphia: WB Saunders Co., 1992;28-33.
9. Peterson DE, D'Ambrosio JA. Nonsurgical management of head and neck cancer patients. Dent Clin North Am 1994;38:425-45.
10. Jansma J, Vissink A, *et al.* Protocol for the prevention and treatment of oral sequelae resulting from head and neck radiation therapy. Cancer 1992;70:2171-80.
11. Ang KK, Brock WA. Radiotherapy for head and neck neoplasms. Curr Opin Oncol 1998;5:502-7.
12. Spijkervet FKL, Van Saene HKF, *et al.* Effect of selective elimination of the oral flora on mucositis in irradiated head and neck cancer patients. J Surg Oncol 1991;46:167-73.
13. Rossie KM, Taylor J, *et al.* Influence of radiation therapy on oral *Candida albicans* colonisation: a quantitative assessment. Oral Surg Oral Med Oral Pathol 1987;64:698-701.
14. Greenspan D. Management of salivary dysfunction. Natl Cancer Inst Monogr 1990;9:159-61.
15. Fox PC. Management of dry mouth. Dent Clin North Am 1997;41:863-75.
16. Borthoshuk LM. Chemosensory alterations and cancer therapies. Natl Cancer Inst Monogr 1990;9:179-84.
17. Epstein JB, Loh R, *et al.* Chlorhexidine rinse in prevention of dental caries in patients following radiation therapy. Oral Surg Oral Med Oral Pathol 1989; 68:401-5.

18. Epstein JB, Wong FLW, Stevenson-Moore P. Osteoradionecrosis: clinical experience and proposal for classification. J Oral Maxillofac Surg 1987;45:104-10.
19. Epstein JB, Rea G, *et al.* Osteoradionecrosis: study of the relationship of dental extractions in patients receiving radiotherapy. Head Neck Surg 1987;10:48-54.
20. Silverman S Jr. Oral cancer, 3rd ed. Atlanta: American Cancer Society, 1990.
21. Haagedoorn EML, *et al.* Essential oncology for health professionals. Assen Van Gorcum, 1994.
22. Lynch MA. Burket's oral medicine – diagnosis and treatment, 7th ed. Philadelphia: Lippincott, 1977;279.
23. Sonis ST, Fazio RC, Fang L. Principles and practice of oral medicine, 2nd ed. Philadelphia: WB Saunders Co., 1995;416-54.
24. Myers RA, Marx RE. Hyperbaric oxygen in postradiation head and neck surgery. Natl Cancer Inst Monogr 1990;9:151-7.