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Oral and dental considerations in pediatric cancers

Priyanshi Ritwik[1] · Tammuella E. Chrisentery-Singleton[2]

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Abstract
Oral health care is an integral component of interprofessional collaborative care for children and adolescents diagnosed with cancer. The current review highlights the phases of cancer therapy when dental interventions and palliative care are necessary for children diagnosed with cancer. Contemporary research and review articles pertinent to the oral and dental complications during pediatric cancer therapy and late effects in pediatric cancer survivors were identified by PubMed/MEDLINE search. Best practice guidelines set forth by specialty organizations were also included. The literature search was limited to articles published in the English language. Baseline oral and dental health assessment should occur before initiation of cancer therapy to prevent debilitating complications during the immunosuppressed phase. Counseling on preventive oral health practices is imperative during cancer treatment. Ideally, all dental treatment should be completed before initiation of immunosuppressive therapy. Palliative care and treatment for mucositis, opportunistic oral infections, pain, and other oral complications associated with cancer therapy should be provided as necessary. Survivors of childhood cancers present with unique craniofacial and dental anomalies, dependent on the type of cancer treatment and age at the time of treatment. Pediatric dentists and pediatric oncology teams work collaboratively to screen for and treat dental and oral diseases. As the survival rates of childhood cancers improve, it is essential for the dental profession to provide the individualized care necessary for this vulnerable population. The oral health profession also reinforces health practices congruent with cancer prevention and cancer screening.

Keywords Pediatric cancer · Pediatric dentistry · Pediatric cancer survivors · Dental complications

1 Introduction

Across all ages, ethnicities, and socioeconomic groups, childhood cancer remains the leading cause of death by disease in children. It is estimated that approximately 15,000 children (hereafter defined as ages 0–14 years) and adolescents (hereafter defined as ages 15–19 years) are diagnosed with cancer in the USA each year [1–3]. Survival rates are similar for children and adolescents and approach 85% overall but vary among the two groups for certain cancers. For example, the current 5-year relative survival rate for leukemia is 86% for children but only 72% for adolescents [4]. In contrast, survival for brain and other nervous system tumors is lower in children than in adolescents [4].

✉ Priyanshi Ritwik
Priyanshi.ritwik@uth.tmc.edu

[1] Department of Pediatric Dentistry, School of Dentistry, The University of Texas Health Science Center at Houston, 7500 Cambridge Street, Ste 5301, Houston, TX 77054, USA

[2] Hemophilia Treatment Center, Mississippi Center for Advanced Medicine, 2053 Gause Blvd, East – Ste 200, Slidell, LA 70461, USA

In children, the most common types of cancer are leukemias, followed by brain and other central nervous system tumors, soft tissue sarcomas (half are rhabdomyosarcomas), neuroblastoma, and renal tumors [5]. The most common types of cancer in adolescents are gonadal tumors, thyroid carcinoma, germ cell tumors, lymphomas, brain and other central nervous system tumors, leukemias, soft tissue sarcomas, bone sarcomas, and melanoma [5].

Genetic syndromes such as Down syndrome and environmental factors such as previous ionizing radiation exposure are associated with a small percentage of childhood cancer cases [6–9]. Additionally, children with AIDS and other immunodeficiencies have an increased risk of developing certain cancers, predominantly non-Hodgkin lymphoma and Kaposi sarcoma [10]. However, the cause of most childhood cancers remains largely unknown, and thereby there are no current strategies for the prevention of these cancers [11, 12].

More than 40,000 children undergo treatment for cancer each year [13]. Treatment is complex and usually occurs in very specialized institutions that participate in well-established collaborative networks, like the Children's

Oncology Group, resulting in a relatively high proportion of children enrolling in clinical trials [13, 14]. Approximately 60% of children with cancer enroll into clinical trials (therapeutic and observational), while others receive standard therapy established by recent clinical trials [13]. Treatment modalities include surgery, chemotherapy, radiation therapy, immunotherapy, and stem cell transplant. Most children with cancer are treated using chemotherapy or a combination of two or more of these modalities. Childhood cancers tend to respond well to chemotherapy as they are fast-growing and thus more susceptible to chemotherapy [15]. Many improvements in childhood cancer survival have come from switching from monotherapy to multimodality therapy with lower individual drug dosing [15].

Although therapeutic regimens in pediatric cancer are specific to the cancer type, site, staging, histology, and other prognostic factors, tremendous success has been seen in the treatment of acute lymphoblastic leukemia (ALL). Specifically, ongoing pediatric leukemia clinical trials at St. Jude Hospitals called for the maximum tolerated dose of chemotherapy, aggressive supportive care, and better CNS prophylaxis (with the delivery of methotrexate intrathecally) [16]. The standard treatment plan in ALL includes several treatment phases, specifically an induction, consolidation, interim maintenance, delayed intensification, and maintenance phases (Table 1) [17].

Over the past 50 years, the overall survival rate of childhood cancer has improved from 10% to nearly 90% [18]. However, the survival rate can be lower for certain cancers, and the number of diagnosed cases annually has not declined in nearly 20 years [19]. Moreover, 60% of children who survive cancer suffer late-effects such as infertility, heart failure, and secondary cancers [20–23]. Awareness of the possible late effects in pediatric cancer survivors is important for pediatric and adult providers, physicians, and dentists caring for this population. There are approximately 400,000 adult survivors of children's cancer in the USA [17].

2 The role of dentistry in the management of pediatric cancers

Professional oral and dental supervision are critical components of patient-centered care in pediatric cancer therapy [24]. Accredited pediatric cancer centers must have pediatric dentists as team members [14]. The engagement of an oral health specialist, such as a pediatric dentist, commences at the time of cancer diagnosis and continues through the patient's lifetime as a cancer survivor [25]. When a new pediatric cancer diagnosis is established, pediatric dentists screen for dental problems that can arise during cancer therapy [24]. The various ways in which dental care intersects with pediatric cancer is shown in Fig. 1.

3 Dentistry in new cancer diagnosis

3.1 Oral screening

Children with a new cancer diagnosis should receive a comprehensive oral and dental examination prior to commencement of oncology treatment [24, 26]. This establishes a relationship between the dentist and the child before the onset of oral complications related to cancer treatment. A clinical and radiographic evaluation of the oral cavity is performed by the dentist to diagnose diseases of the oral hard and soft tissues, including but not limited to dental caries, to establish caries prevention strategies, and to provide anticipatory guidance related to the oral effects of the cancer and its treatment [24].

Interprofessional communication between the dentist and the oncology team ensures best patient-related outcomes [14]. The severity of dental caries and/or periodontal disease, necessary dental treatment, and the presence of any new pathologic lesions should be discussed between the dentist and the oncology team [24]. Expeditious dental treatment should be provided with medical clearances and precautions in place before cancer therapy commences. A team-based approach between the dentist and oncology team facilitates dental treatment without delaying cancer therapy. Building a partnership with the patient is also important. Often children and families who have received a new cancer diagnosis are emotionally distraught with the implications of the diagnosis [27], and these experiences may elevate dental fear and anxiety in the child [28]. Conducting an initial, noninvasive dental appointment enables the dentist to perform a thorough oral assessment utilizing basic behavior guidance techniques while building patient trust.

3.2 Prevention

The most obvious and prevalent disease in the pediatric oral cavity is dental cavities or caries [29, 30]. New and untreated carious lesions can become a debilitating problem once cancer treatment has commenced [24]. Moreover, neutropenia and/or thrombocytopenia resulting from cancer therapy present complications in performing dental treatment [24, 25]. Educating caregivers on the preventable pathogenesis of dental caries and providing techniques to ensure routine oral care during cancer therapy are essential in preventing new carious lesions [24]. Anticipatory guidance provided at this stage should address oral hygiene techniques, age-appropriate quantity of fluoridated toothpaste, and a low-cariogenic diet [24, 31, 32].

Periodic professional application of fluoride in the form of fluoride varnish, fluoride gel, or fluoride foam in the dental office should be scheduled on a risk-based frequency [33, 34]. Prescription high-strength fluoride toothpastes containing 5000 ppm of fluoride should be prescribed to patients who can reliably expectorate toothpaste [33]. Fluoride trays can

Table 1 Format of a basic treatment plan for pediatric acute lymphoblastic leukemia (ALL)

Treatment phase	Duration	Chemotherapies used	Route of administration
Induction	29 days	ARA-C	IT
		MTX	PO/IT
		DEX*, PRED	IV/PO
		VCR	IV
		ASP, PEG-ASP	IM/IV
		DAUN*	IV
Consolidation	4–8 weeks	MTX	IT
		6-MP	PO
		VCR	IV
		CPM	IV
		ARA-C	IV
		PEG-ASP	IM/IV
Interim maintenance (IM)	8 weeks#	MTX	IT
		6-MP	PO
		VCR	IV
Delayed intensification (DI)	8 weeks#	MTX	IT
		DEX, PRED	PO
		6-TG	PO
		VCR	IV
		DOXO	IV
		PEG-ASP	IV
		CPM	IV
		ARA-C	IV
Maintenance	Each cycle lasts for 84 days. Cycles are repeated until the duration of therapy, which is ~2 years for girls and ~3 years for boys	MTX	IT
		VCR	IV
		PRED	PO
		6-MP	PO

Formulation of a basic treatment plan for pediatric ALL, according to standard protocols [13, 15–17]. *ARA-C* cytarabine, *MTX* methotrexate, *DEX* dexamethasone, *PRED* prednisone, *VCR* vincristine, *ASP* asparaginase; *PEG-ASP* pegylated asparaginase, *DAUN* daunorubicin, *6-MP* mercaptopurine, *CPM* cyclophosphamide, *6-TG* thioguanine, *IT* intrathecal, *PO* oral administration, *IV* intravenous, *IM* intramuscular.

* Treatment is reserved for high-risk ALL patients

Repeat course as needed in high-risk patients

be provided for patients who will tolerate wearing them [26]. If the child cannot expectorate, a casein phosphopeptide and amorphous calcium phosphate (CPP-ACP) containing product such as MI Paste® may be recommended to maintain surface mineralization of enamel [35]. Flossing is further recommended to minimize plaque biofilm [24]. Fluoridated alcohol-free mouth rinses are an adjunct to brushing and flossing if the child can swish and spit [24]. Children with plaque-induced gingivitis or periodontal disease should be prescribed an alcohol-free chlorhexidine mouth rinse (0.12% chlorhexidine gluconate) [24].

Dietary counseling is another key component of oral health care in pediatric cancers and should provide education on low cariogenic foods with minimal fermentable carbohydrates [34]. Consumption of sweetened beverages such as juices and sodas must be limited. Snacks between meals should not contain added sugar [34]. Given the emotional circumstances of having a child with cancer, parents may be tempted to provide the child with comfort foods that are typically rich in sugar or fermentable carbohydrates. Patients and their families should be educated on the importance of avoiding these foods in their diet in order to prevent dental caries and minimize cancer treatment-related complications.

Radiation introduces new dental care considerations for children. Children who receive radiation therapy to the head and neck region may develop trismus (painful spasm of muscles of mastication) [36–38]. Physical therapy in the form of stretching exercises for masticatory muscles should ideally be commenced prior to the initiation of radiation therapy and continued beyond its completion [24]. Additionally, the feasibility of salivary gland sparing techniques in should be discussed with the radiation oncologist [24].

3.3 Dental treatment

Should a child who is about to commence cancer therapy need dental procedures such as restorative treatment, periodontal therapy, or extractions, the pediatric dentist and oncology team must discuss the patient's anticipated tolerance to dental treatment [24]. Medical parameters which influence dental procedures are absolute neutrophil count (ANC), platelet count, coagulopathies secondary to cancer or treatment, and absolute hemoglobin (Hgb) level [24, 26]. An ANC > 2000/mm^3 does not require antibiotic prophylaxis to perform dental treatment [24]. By contrast, an ANC of 1000–2000/mm^3

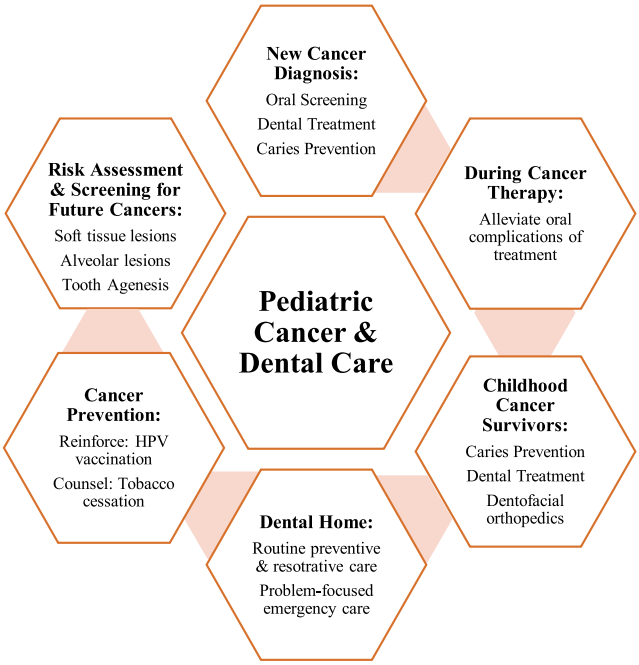

Fig. 1 The role of dentistry in pediatric cancer therapy, prevention, and screening. A new cancer diagnosis warrants dental screening, treatment, and cavity prevention measures. Routine dental care during cancer treatment is important to manage oral side effects. Children in remission require continued cavity prevention measures and routine dental care, as well as potentially dentofacial orthopedic care. The dental home is the ongoing relationship between the dentist and the patient, inclusive of all aspects of oral health care delivered in a comprehensive, continuously accessible, coordinated, and family-centered way. Components of cancer relapse prevention related to dental care include reinforcing the HPV vaccine and encouraging smoking cessation. Future screenings are necessary, as survivors of childhood cancer are at increased risk for soft tissue lesions, alveolar lesions, and tooth agenesis

should trigger a consultation with the pediatric oncologist to ascertain the need for antibiotic coverage. An ANC < 1000/mm^3 indicates an elevated risk for infection from dental procedures, and in these cases, dental treatment should be deferred until the ANC is within the desired range [24]. In the case of dental emergencies, children may need prophylactic antibiotics and hospitalization to complete the necessary treatment [24].

Platelet count identifies the risk for bleeding. Dental extractions as well as anesthetic injections increase the risk of bleeding and/or hematoma formation in thrombocytopenic patients [24, 26]. The risks are significant if the platelet count is < 75,000/mm^3 [24]. In such situations, a consultation with the pediatric oncologist is necessary to determine the need for platelet transfusions and arrange hospitalization to monitor hemostasis [24]. Should the child's hemoglobin (Hgb) level be below 10 g/dL, the oncologist should be consulted prior to dental treatment [26]. In general, red blood cell transfusion may be necessary for children whose Hgb levels are below 7 g/dL [26]. If the dental treatment is being provided under general anesthesia, the Hgb level should be at least 10 g/dL [26].

Primary teeth in exfoliative stages should be allowed to naturally exfoliate [24]. Infected teeth, non-restorable teeth, root tips, and periodontally compromised teeth should be extracted 1–2 weeks before initiation of cancer therapy to allow adequate time for healing [24]. Root canal treatment for permanent teeth should be completed at least 1 week prior to initiation of cancer treatment to ensure healing of the periapical periodontal tissue [24].

Advances in adhesive dentistry provide the benefit of minimally invasive conservative restorations for small carious lesions [24]. Susceptible grooves and fissures should be sealed to decrease risk for future decay [39]. A contemporary technique for arresting dental caries is the application of 38% silver diamine fluoride (SDF) [40]. Repeated applications of SDF can arrest decay without the need to administer local anesthesia or mechanically prepare the tooth [40]. However, its application results in black discoloration of carious lesions, and the esthetic outcomes must be discussed with the guardians during informed consent. Multiple applications of topical SDF are a noninvasive caries management option for medically fragile pediatric patients who may not be medically clear to receive traditional dental treatments [24].

Ideally, all necessary dental treatment should be completed prior to commencement of cancer treatment [24]. If this is not feasible due to urgency to begin cancer therapy, the dentist will have to prioritize the treatment of dental infections, extractions, periodontal therapy, and elimination of sources of mucosal irritation [24].

Some children may have existing orthodontic appliances or space maintainers. Intraoral appliances should be removed if they have the potential to cause mucosal or gingival irritation, if the potential for mucositis exists, or if oral hygiene is poor [24]. Removable appliances can be worn if the patient can tolerate them and is able to maintain good oral hygiene [41]. A patient undergoing orthodontic treatment at the time of cancer diagnosis should have the appliance removed expeditiously and use removable orthodontic retainers [24, 41]. Orthodontic treatment may be resumed after a 2-year event-free survival period [24, 42].

Appliances with metal components should be removed in children who require multiple magnetic resonance images (MRIs) of the head and neck region (such as children with intracranial tumors) to prevent scatter and artifacts on the MRIs [43]. For this reason, metal restorations such as silver amalgam restorations and stainless steel crowns are not placed in children who require repeated MRIs of the head and neck for cancer surveillance.

4 Role of dentistry during cancer treatment

4.1 Mucositis

Oral mucositis is likely to develop in 40% of children receiving standard-dose chemotherapy, in 80% of patients receiving radiation therapy for head and neck cancers and in 75% of patients undergoing bone marrow transplantation [24, 26, 44]. Oral mucositis is graded as mild, moderate, or severe based on the patient's symptoms and clinical presentation. The World Health Organization Oral Toxicity Scale, shown in Table 2, is a grading tool which can be used to monitor the severity of mucositis during cancer treatment [45]. On this scale, grade 3 and grade 4 mucositis are considered severe. Oral mucositis interferes with patient nutrition, functioning, and tolerance for cancer therapy [46]. Patients report it as the most debilitating side effect of cancer treatment [47]. Children are thrice more likely than adults to develop mucositis, xerostomia, and infections during cancer treatment [48]. The clinical image in Fig. 2a exemplifies the onset of Grade 2 mucositis in an infant receiving cancer therapy.

The mainstay of management of oral mucositis is palliative care [24, 47]. Maintaining good oral hygiene is important to prevent and reduce the severity of oral mucositis [49, 50]. Gingival and mucosal tenderness are deterrents to brushing. Softening toothbrush bristles in warm water for a few minutes may facilitate comfort during brushing [24]. Patients who have severe mucositis and cannot tolerate a toothbrush may use foam brushes as a last resort [24, 26]. Oral cryotherapy, recombinant human keratinocyte growth factor-1, low-level laser therapy, sodium bicarbonate rinses, and benzydamine mouthwash have evidence-based support for management of oral mucositis in patients with cancer [47]. Analgesic medications can be used to treat pain associated with oral mucositis [24, 47]. Topical anesthetics obtund pain for a short duration but do not treat the mucositis [24, 47]. Undesirable effects on cardiovascular and central nervous systems can arise from systemic absorption of the anesthetic from the oral mucosa, and they should be used judiciously in young children [25].

4.2 Oral infections

Children receiving cancer therapy easily develop opportunistic oral infections (fungal, bacterial, and viral) [49]. The clinical manifestations of these infections may be atypical because of underlying neutropenia [26]. Oral candidiasis and herpetic infections are often seen in these children [26]. Figure 2b shows candidiasis on the tongue of a 5-year-old child who was receiving cancer treatment. Prophylactic nystatin is ineffective in preventing oral candidiasis [51]. When oral candidiasis develops in children receiving cancer therapy, nystatin is the first line of medication to be tried, although it may not always resolve the infection [25, 26]. Systemic antifungal agents such as amphotericin B may be necessary [51]. Clinicians must keep in mind that the sugar content of the oral suspension of nystatin is high, and frequent use can increase caries susceptibility [25, 26].

Bacterial infection of the oral mucosa or gingiva should be identified and promptly treated to prevent the onset of fever or systemic bacteremia [26]. Localized infections can be managed with chlorhexidine mouthwash and diligent oral hygiene [26]. If systemic bacteremia from an odontogenic source is suspected, an infectious disease specialist should be consulted to institute appropriate antibiotic therapy [26].

Table 2 WHO Oral Toxicity Scale [45]

Mucositis Grade	Features
1	Soreness and/or erythema
2	Erythema, ulcers; patient is able to swallow food
3	Ulcers, extensive erythema; patient is unable to swallow food
4	Mucositis to the extent that alimentation is not possible

4.3 Neuropathic pain

Children who receive plant alkaloid chemotherapeutic agents such as vincristine and vinblastine are likely to develop neuropathic pain, especially in the mandible [24, 26]. These children complain of deep pain in the jaw and teeth in the absence of an odontogenic source of pain [24, 26, 52]. Such neuropathic pain is usually transient in children and diminishes or resolves after completion of chemotherapy [24]. In the absence of a definitive cure for chemotherapy-induced neuropathic pain, palliative care may be provided with over-the-counter pain medications or patient-controlled analgesia [25, 26].

4.4 Xerostomia

Children who receive cancer chemotherapy and/or head and neck radiation therapy develop xerostomia during and beyond the active treatment phase [24, 26, 53]. Damage to salivary glands from medications or ionizing radiation is the underlying cause of xerostomia. Xerostomia increases caries risk, exacerbates mucositis, and increases risk for oral infections [24, 26]. Use of sugar-free gum, sugar-free mints and lozenges, saliva substitutes, alcohol-free mouthwash, and oral moisturizers help alleviate xerostomia [24, 26]. Patients with xerostomia should also be encouraged to sip water frequently through the day [24, 26, 53].

4.5 Lip care

Children receiving chemotherapy and/or radiation therapy often develop chapped lips and angular cheilitis. Figure 2C

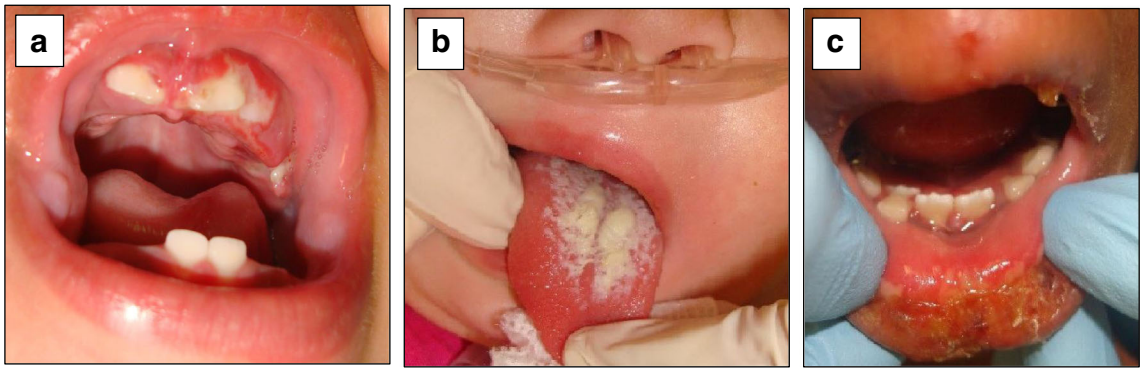

Fig. 2 (**A**) Image depicts mucositis in a child receiving cancer treatment. (**B**) Candidiasis on the tongue of a 5-year-old child following treatment with cancer therapy. (**C**) Swelling, ulceration, and crusting of the lower lip in an 8-year-old child actively receiving cancer therapy

shows swelling, ulceration, and crusting of the lower lip in an 8-year-old child receiving cancer therapy. Lanolin-based creams and ointments are more effective in moisturizing the lips for these patients than petrolatum-based products [24].

5 Role of dentistry for childhood cancer survivors

5.1 Craniofacial skeleton

Exposure to ionizing radiation in childhood can lead to aberrations in the developing craniofacial complex and malocclusion with a skeletal etiology [26, 54]. The orthodontic problems may be compounded by dental anomalies (tooth agenesis, microdontia, and blunted roots) [41]. During their teen years, pediatric cancer survivors may desire orthodontic treatment. However, elevated caries risk from xerostomia and enamel hypoplasia may prevent implementation of an ideal orthodontic treatment plan. If the teeth have blunted roots, orthodontic movements can further exacerbate root shortening and cause unfavorable crown-root ratios. The use of light orthodontic forces and compromised orthodontic results should be discussed with the patient and guardians [42]. Figure 3A a shows dental crowding, malocclusion, pulp chamber obliteration, and severe shortening of the roots of all permanent teeth in an 18-year-old who is a 16-year neuroblastoma survivor. Orthodontic treatment plans for childhood cancer survivors should take these limitations into consideration.

5.2 Dentition

Children and adolescents are at elevated risk for developing long-term dental complications from cancer treatment because childhood is the most active stage of dental development [55]. Since development of primary teeth starts *in utero* and continues over the next 3 to 4 years, primary tooth germs are rarely damaged during cancer therapy [56]. However, the development of permanent teeth starts soon after birth and is completed around the age of 14 to 16 years with the root completion of second molars [56]. This leaves a long window of opportunity for cancer treatment to adversely affect the developing permanent dentition. Specific dental manifestations of childhood cancer treatment include elevated risk for dental caries, xerostomia, tooth agenesis, microdontia, enamel hypoplasia, and blunting of roots [57–59]. Microdontia and blunting of roots can be seen in the patient shown in Fig. 3A. Figure 3B shows dental decay in a child who received radiation therapy for maxillary rhabdomyosarcoma when she was 10 years old.

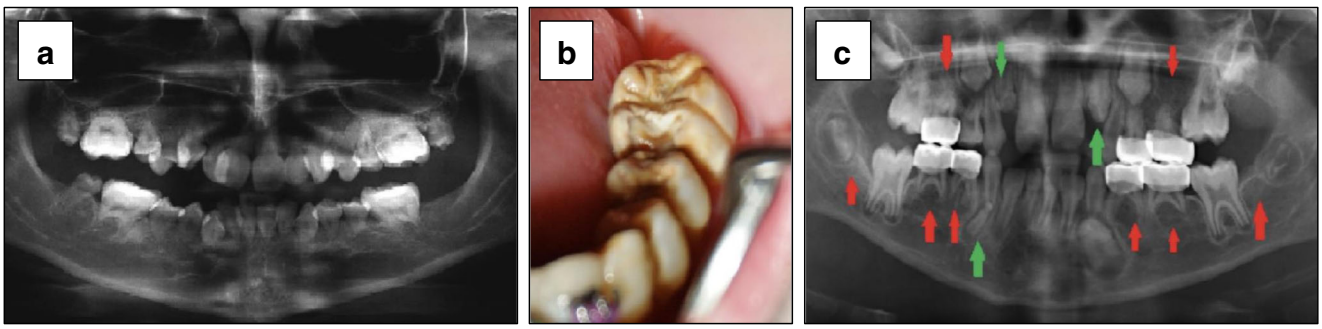

Fig. 3 (**A**) Malocclusion, pulp chamber obliteration, and blunted roots of all permanent teeth in an 18-year-old who is a 16-year neuroblastoma survivor. (**B**) Dental decay in a child who received radiation therapy for maxillary rhabdomyosarcoma when she was 10 years old. (**C**) An 8-year-old male with history of Diamond-Blackfan anemia, chemotherapy, and hematopoietic stem cell transplant at the age of 3 years. Tooth agenesis is shown by red arrows, and microdontia is shown by green arrows

The permanent teeth impacted, the severity of dental anomalies depend on the age of the child and stage of dental development at the time of cancer chemotherapy and/or radiation therapy, as well as the intensity of cancer therapy [60, 61]. A higher incidence of dental anomalies and developmental dental defects is anticipated in children who receive cancer therapy before the age of 3 years [61]. A history of hematopoietic stem cell transplantation, use of multiple classes of chemotherapeutic agents (more than 4), and the use of heavy metal agents significantly increase the risk for dental disturbances [55]. Figure 3 c is a panoramic radiograph of an 8-year-old male with Diamond-Blackfan anemia who received chemotherapy and hematopoietic stem cell transplant at the age of 3 years. His radiograph shows agenesis of multiple teeth, indicated by red arrows, and microdontia of multiple teeth, indicated by green arrows. All the affected teeth would be in early formative stages at the age of 3 years based on standard dental developmental norms.

5.3 Trismus and xerostomia

Trismus can persist in patients even after completion of radiation treatment [54]. Continuity of stretching exercises can help minimize the oral restrictions due to trismus. Exposure of salivary glands to radiation therapy causes hypofunction and decreased long-term saliva production. Saliva that is produced is thick and ropey. All these factors contribute to elevated caries risk in the long-term survival phase as well [54]. The effects of xerostomia can be alleviated with frequent use of alcohol-free mouth rinses and sugar-free mints and lozenges. Patients will need to continue use of prescription fluoride products.

5.4 Oral cancer screening

Oral cancer screenings are imperative for survivors of pediatric cancer, as the oral cavity remains a prominent site for future neoplastic lesions in these patients [24, 54]. Suspicious soft tissue lesions should be referred to an oral and maxillofacial pathologist and surgeon for biopsy.

5.5 Graft *versus* host disease

After hematopoietic stem cell transplant (HSCT), some children may develop graft *versus* host disease (GVHD). In the past, GVHD was classified as acute or chronic, based on the onset of symptoms before or after 100 days from stem cell transplant respectively [26]. With the utilization of different stem cell sources and advances in therapy, this temporal distinction is no longer accurate [62]. In contemporary care, it is preferable to recognize acute GVHD by the clinicopathological constellation of inflammatory dermatitis, enteritis, and hepatitis [62]. Acute GVHD is a cause of major morbidity and mortality in children with HSCT [62].

Chronic GVHD tends to be lower in children than in adults [63]. Its occurrence leads to significant morbidity, diminished quality of life, and decreased overall survival [63]. The median time of onset is 6 months from HSCT, but the onset is invariably within 3 years post-transplant [63]. The oral cavity is commonly, involved and erythema, mucositis, xerostomia, ulcer, mucoceles, and elevated dental caries levels are the prominent findings [26, 63]. The first line of treatment is high-dose steroids, tapered over time to the lowest allowable dose without GVHD flare-ups [63].

6 Role of dentistry in cancer prevention

Exposure of the oral cavity and oropharynx to human papillomavirus (HPV) can result in an asymptomatic, transient oral infection which is cleared by the body's immune system [64]. However, a small percentage of these oral infections can persist in a dormant state and may lead to benign or malignant disease in the future [64]. High-risk HPV types 16 and 18 can cause oropharyngeal squamous cell carcinoma (SCC) and have been reported to be the leading cause of oral SCC in

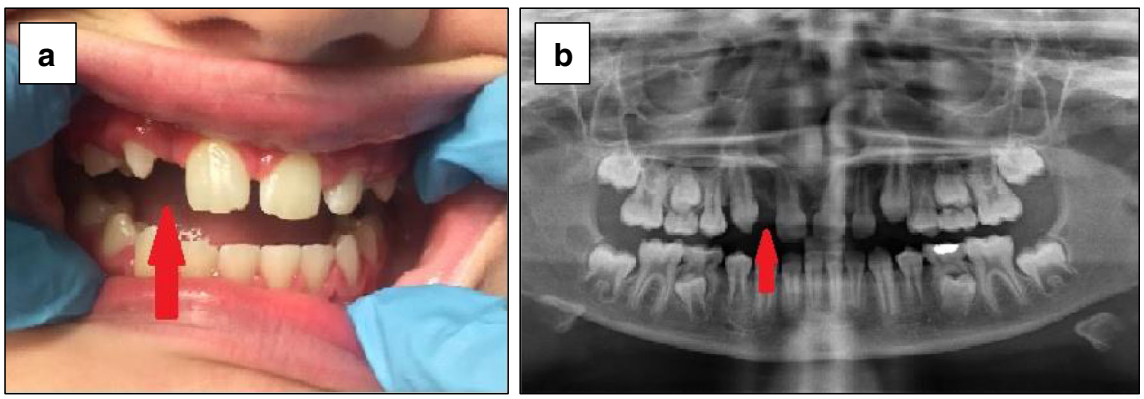

Fig. 4 Image (**A**) and radiograph (**B**) of excessive spacing in the dentition of an 11-year-old child and the dental radiograph confirming the congenital absence of the right maxillary lateral incisor highlighted by red arrow

North America [64–66]. The American Dental Association [67], the American Academy of Pediatric Dentistry [68], and the American Academy of Pediatrics [69] support the administration of the HPV vaccine as a safe and effective method to reduce HPV-related oral infections and cancer. Reinforcing HPV vaccination for boys and girls according the CDC immunization schedule of two doses at age 11 or 12 years [70] is important not only to prevent cervical and other cancers of the reproductive system but also for preventing oropharyngeal cancer. Dental visits for adolescents also incorporate discussions and counseling on cessation of tobacco products, alcohol, and other substances for potential of abuse for overall health and cancer prevention.

7 Role of dentistry in screening for cancer risk factors

Oral health professionals are uniquely poised to evaluate abnormalities in oral soft tissue, alveolar bone, and teeth in children which can indicate an elevated risk for neoplasia in later life. Communicating these findings with physicians is important to establishing a lifetime risk for future neoplastic lesions.

Oral cancer screening is an integral component of all dental examinations and includes assessment of precancerous oral lesions as well, such as leukoplakia, erythroplakia, oral submucous fibrosis, and lichen planus [71]. A history of radiation therapy to the head and neck for treatment of cancer, unfortunately, also increases the risk for oral cancer and salivary gland tumors in the future [72]. The cumulative risk is positively associated with radiation dose and underscores the importance of regular dental appointments in childhood cancer survivors [72].

Identifying tooth agenesis (TA) is of particular interest in pediatrics, which is the congenital absence of one or more teeth [73]. TA can involve primary and/or permanent dentitions [73]. TA is suspected if there is excessive spacing in a child's dentition or a tooth is clinically absent. It is confirmed by absence of tooth/teeth on dental radiographs [74]. Figure 4 shows excessive spacing in the dentition of an 11-year-old child, with the dental radiograph showing the congenital absence of the right maxillary lateral incisor highlighted by a red arrow.

Genetic mutations in key genes regulating odontogenesis result in TA [75–77]. These mutations have also been shown to be associated with neoplasms diagnosed later in life [75–78]. The processes of odontogenesis and tumorigenesis may initially seem unrelated. However, there is overlap of molecular pathways such as those controlled by MSX1, PAX9, and AXIN2 genes and epithelial neoplasms [75, 76, 79]. Colorectal neoplasms [80], epithelial ovarian cancer [81, 82], breast cancer [83, 84], prostate cancer [84], and cancers of the central nervous system [84] have been associated with TA. TA can be detected within the first decade of life and enables health-care providers to discuss future neoplastic risks and need for active surveillances [74].

8 Conclusion

Oral health care is imperative for children who have been diagnosed with cancer. Resolution of untreated dental caries, periodontal problems, and oral pathologic lesions should be achieved before commencement of cancer therapy. Oral complications such as mucositis and infections should be anticipated during cancer treatment. As the survival rates of childhood cancers improve, it is important for these patients to have an established dental home where long-term oral and dental complications of cancer treatment, such as dental anomalies, orthodontic problems, and risk for oral cancer and salivary gland tumors, can be appropriately managed. The oral health profession plays an important role in reinforcing cancer prevention strategies and in screening oral and systemic factors for future risk for cancers. Interprofessional collaborative care between the dental and medical team is imperative in all phases of care for children diagnosed with cancer and for children diagnosed with risk factors for future neoplasia.

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