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Review Article

PEDIATRIC NEOPLASMS OF HEAD AND NECK - A REVIEW

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ABSTRACT

Neoplasms occurring in the pediatric population contribute significantly to mortality and morbidity in this age group. Those neoplasms occurring in the head and neck are of special interest to dentists. Most of them respond well to therapy and exhibit a better prognosis than those neoplasms occurring in the adults. Certain neoplasms occur specifically in the pediatric population while some adult neoplasms also occur in children rarely. This article focuses on those neoplasms that show peak incidence in the pediatric population. It also provides a brief note on the basic differences between adult and pediatric neoplasms.

Keywords: Pediatric, Neoplasms, Risk factors, Prognosis, Head and neck, Children.

INTRODUCTION

The Greek words 'pedia' meaning child, 'iatrike' meaning treatment and 'ics' meaning branch of science form the English word 'pediatrics'. "Pediatrics is the branch of medicine that deals with the care of children from conception to adolescence in health and illness"¹. According to Indian academy of pediatrics, the upper limit of pediatric age group is 18 years.

The principal cause of mortality in children is trauma, followed by cancer². Among the various neoplasms that occur in the pediatric age group, leukemia and neoplasms of brain and central nervous system account for more than half of the cases³. In India, cancer ranks 9th position among the causes of mortality in children between 5 – 14 years of age⁴.

Predisposing risk factors for pediatric neoplasms:

Ionizing radiation exposure, Down syndrome and other specific chromosomal and genetic abnormalities explain the etiology of cancer in few cases. Other risk factors proposed include early life exposure to infectious agents, parental, fetal or childhood exposure to pesticides, solvents or other household chemicals, family history of childhood cancer, maternal medical conditions during pregnancy or before conception and maternal diet during pregnancy^{2, 3}. Also, children with AIDS possess an increased risk of developing certain cancers like Kaposi's sarcoma³.

Pediatric neoplasms vary from that of adults in various aspects, of which few general differences are listed in Table 1.

HEAD AND NECK PEDIATRIC NEOPLASMS:

Neoplasms of the head and neck constitute 2.5% of all pediatric tumors⁶. Head and neck neoplasms in the pediatric age group pose a challenge because of the potential adverse effects of both the disease process and the treatments employed on developing head and neck structures. One-fourth of the malignant lesions have ensuing manifestation in the head and neck region². The neoplasms presenting in the oral cavity and those affecting the salivary glands are of special interest to the dentists and will be discussed in this article.

The pediatric neoplasms occurring in the head and neck region can be classified as given in Table 2.

I. BENIGN NEOPLASMS:

CONGENITAL GRANULAR CELL TUMOR (CGCT):

CGCT, also called as congenital epulis (or) Neumann's tumor, is a rare benign tumor present at birth with female predominance. Odontogenic epithelial, pericytic and fibroblastic origin have been proposed⁷.

It occurs almost always in alveolar mucosa, more frequently in anterior maxilla⁸ with tongue involvement in some cases⁷. It may be sessile or pedunculated and is characteristically seen protruding from the oral cavity. It can cause airway obstruction and difficulty in feeding. Surgical excision is the treatment of choice⁸. However, spontaneous regression has been observed in occasional cases⁷.

MELANOTIC NEUROECTODERMAL TUMOR OF INFANCY (MNTI):

MNTI is an extremely rare pigmented benign neoplasm of neural crest origin⁹. Vast majority of cases arise in infants less than 1 year of age¹⁰.

It usually presents as a rapidly growing, painless mass typically in the premaxilla. Lesions affecting mandible have also been documented^{11, 12}. It can result in nasal obstruction or feeding difficulties². Complete surgical excision is the recommended treatment. Multifocality results in recurrence in 10% to 15% of cases².

HEMANGIOMA:

Haemangioma is a benign vascular tumor that can be divided into two types: infantile and congenital type. The infantile type usually appears few weeks after birth, proliferates rapidly as the child grows and attains a stable phase, after which it undergoes involution. The less common congenital type is present at birth and may or may not involute¹³.

Around 60% of haemangiomas occur in head and neck region¹⁴. Most common sites include facial skin, lips, parotid gland, gingiva and palatal mucosa. They may also occur intramuscularly or centrally within jaw bones¹⁵. Initially it presents as a flat, pink lesion, but as it proliferates, it becomes bright red and elevated with cobblestoned surface. Ulceration can occur in few cases¹³.

Conservative observation is the recommended treatment since most of the lesions resolve by 9 years of age. In cases complicated by ulceration, massive growth or disfigurement, early intervention is indicated using either systemic or intralesional corticosteroids, sclerosing agents, chemotherapeutic agents, and surgery or lasers¹³. The efficacy and safety of using recombinant interferon- α 2b in the treatment of life-threatening cases is being explored¹⁶.

LYMPHANGIOMA:

Lymphangioma is a congenital benign lesion, consisting of localized centres of abnormal development of lymphatic system. It commonly presents in the head and neck region. Three types of lymphangioma are capillary lymphangioma, cavernous lymphangioma and cystic hygroma¹⁷.

Intraorally, lymphangioma occurs on lips, tongue and floor of the mouth and presents as soft, non-tender mass. It may cause marked disfigurement, malocclusion, respiratory obstruction and dysphagia¹⁸. Surgical excision and intralesional injection of sclerosing agents is recommended¹⁹. Complete excision is not always possible, which may result in recurrences²⁰.

JUVENILE OSSIFYING FIBROMA (JOF):

JOF is an aggressive bone-forming neoplasm, most often seen between 5 and 15 years of age showing male predilection²¹. The microscopic subtypes include psammomatoid juvenile ossifying fibroma and trabecular juvenile ossifying fibroma. Psammomatoid type more commonly affects sinonasal and orbital bones of the skull while trabecular type affects mostly gnathic bone, particularly maxilla²².

Clinically, the lesion often causes rapid painless expansion of the affected bone. Depending upon the location, it may cause nasal obstruction, exophthalmos or swelling²³. En bloc resection with free surgical margins is recommended²⁴. Reported rate of recurrence is 30 – 58% due to failure of

complete removal in these areas due to presence of important anatomical structures²¹. It is considered to be aggressive due to its clinical behaviour and high recurrence rate.

AMELOBLASTOMA:

Ameloblastoma, a benign odontogenic tumor rarely seen in the pediatric age group, account for about 10 – 15% of all reported cases²⁵. It is classified into three types: solid/multicystic, peripheral and unicystic. Unicystic ameloblastoma, a less aggressive type is considered to more common in the younger age group than adults, with about 50% of cases occurring in the second decade²⁶.

Approximately 90% of cases of unicystic ameloblastoma occur in mandible, frequently associated with an impacted tooth²⁶. It manifests as painless swelling, producing facial asymmetry, displacement or mobility of tooth and root resorption²⁷. Due to its slow growth, sometimes, it is diagnosed only in the adult age²⁸.

Unicystic ameloblastoma shows better prognosis than solid/microcystic and peripheral types²⁸. Surgery is more difficult as the lesion grows rapidly with extensive destruction attributed to more amount of cancellous bone present in children²⁹. Conservative management by enucleation followed by Carnoy's solution and peripheral osteotomy are the recommended treatment options³⁰.

ADENOMATOID ODONTOGENIC TUMOR (AOT):

AOT is an uncommon benign odontogenic tumor which occurs more commonly in the second decade³¹. Females are affected twice more frequently than males. It shows predilection for maxilla, especially anterior part of maxilla³². Clinicopathologic types include follicular, extrafollicular and peripheral forms³¹.

Follicular type, the predominant form of AOT, occurs in association with an unerupted tooth, mostly canine. Extrafollicular type arises between the roots of the adjacent erupted teeth and peripheral type occurs in the gingival tissue. AOT is usually asymptomatic except in case of large lesions which present as painless swellings³³.

Conservative surgical enucleation is recommended. Recurrence of AOT is very rare and prognosis is excellent³².

AMELOBLASTIC FIBROMA (AF):

AF and related lesions are defined by WHO as 'neoplasms composed of proliferating odontogenic epithelium embedded in a cellular ectomesenchymal tissue that resembles dental papilla, and with varying degrees of inductive change and dental hard tissue formation'³⁴. The related lesions are ameloblastic fibro-dentinoma (AFD) and fibro-odontoma (AFO)³⁵.

AF is considered as a neoplasm of childhood/adolescence. It affects mandible more commonly, especially posterior region³⁶. The tumor grows slowly, producing painless expansion of the jaws. In some cases, it may impede the eruption of teeth³⁷. Conservative surgical procedures like enucleation, curettage and simple excision are adequate³⁶. Recurrences of AF and AFO may show malignant transformation into ameloblastic fibrosarcoma during later period of life³⁸.

ODONTOMA:

Odontomas are hamartomas consisting primarily of enamel and dentin and variable amounts of cementum and pulp³⁸. The

two types of odontomas are compound and complex. Compound odontoma consists of dental tissues arranged in more orderly pattern while complex odontoma is represented by well-formed tissues in a disorderly pattern³⁹.

Of the two types, compound odontoma is a pediatric lesion, with majority of cases occurring before the age of 20. It frequently presents in the maxillary anterior region and is often associated with an unerupted permanent tooth³⁸. It is usually asymptomatic though it can alter or hinder the eruption of associated teeth. Spontaneous eruption of compound odontoma into oral cavity has also been reported. Treatment consists of surgical removal followed by histopathological analysis⁴⁰.

CEMENTOBLASTOMA:

Cementoblastoma is a true benign neoplasm of cementum or cementum-like tissue formed by cementoblasts. About 50% of the cases occur in the second decade of life. Almost all the lesions get attached or surround a root or roots of an erupted permanent tooth⁴¹. They rarely occur in relation to deciduous tooth⁴².

Cementoblastoma shows predilection for mandible, with permanent molars and premolars being the most frequently involved teeth⁴². It produces cortical bone expansion resulting in facial asymmetry and dental crowding. Simple enucleation of the lesion along with the tooth and curettage is the treatment⁴³.

TERATOMA:

Teratoma is a tumor which consists of tissues from all three germ layers. They occur particularly in neonates. Most of the tumors occurring in neonates are benign while malignant elements are seen in adults⁹. Head and neck neoplasms account for 5% of cases, frequently involving neck, oropharynx, nasopharynx, orbit and paranasal sinuses. Oropharyngeal teratomas have been reported exclusively in neonates and young infants².

Oral teratomas involving tongue and floor of the mouth have been described⁴⁴. In case of children, though metastasis and malignant potential are rare². There is increased morbidity due to respiratory difficulties in these patients⁹.

II. MALIGNANT NEOPLASMS:

LEUKEMIA:

Leukemia is the most common neoplasm occurring in the pediatric age group. Most frequently occurring types include acute lymphocytic leukemia (ALL), followed by acute myeloid leukemia (AML). Peak incidence of ALL is seen at 4 years of age⁴⁵. During the first year of life, girls shows higher incidence of leukemia. Ionizing radiation is considered as the most significant environmental risk factor⁴⁶.

Head and neck manifestations of leukemia include lymphadenopathy, sore throat, laryngeal pain, gingival enlargement and oral ulceration⁴⁵. Chemotherapy and radiotherapy instituted can induce numerous complications like thrombocytopenia, anemia and granulocytopenia leading to tendency to bleeding, susceptibility to infections, mucositis, taste alteration, xerostomia, dysphagia, trismus, osteoradionecrosis and so on⁴⁷. Dental abnormalities like delayed dental development, microdontia, hypoplasia, agenesis, V-shaped root and shortened root have also been reported⁴⁸.

It is preferable to complete all dental care procedures before the initiation of therapy to reduce the risk of oral complications. Maintaining meticulous oral hygiene is recommended⁴⁵. Any emergency dental treatment during the course of therapy can be provided if absolute neutrophil count exceeds 1000/mm³ and platelet counts are appreciable⁴⁷.

LYMPHOMA:

After leukemia, lymphoma is the second most common pediatric malignancy, accounting for 20.3% of cases in India⁴⁹. Non-Hodgkin's lymphomas comprise 60% of the pediatric lymphomas, among which precursor T-cell lymphoblastic lymphoma was found to be common in Indian population⁵⁰. Low grade follicular lymphoma seen in adults is extremely rare in children⁵¹. Extra-nodal sites are more frequently involved in children than adults⁴⁹. Since pediatric lymphomas are rapidly growing and aggressive, they mostly present with widespread dissemination at the time of diagnosis⁵¹. Treatment involves chemotherapy given over 12 – 32 months.

In developing countries, pediatric Hodgkin's lymphomas occur at a younger age than Western countries. It shows a strong male predilection. The common subtype in India is mixed cellularity. Majority of the cases show detectable Epstein-Barr virus genome. Painless cervical and supraclavicular lymphadenopathy is the usual clinical presentation. Multiagent chemotherapy alone or in combination with radiotherapy result in better survival rates⁵². Lymphomas may involve extra-nodal sites in oral cavity and oropharynx, primarily located in Waldeyer's ring, causing dysphagia and sore throat. Oral lymphomas are frequently seen in gingiva, palate and tongue and grow rapidly resulting in bone destruction. Lesions in oral cavity are commonly seen in HIV-infected individuals. Lymphomas of salivary glands mostly involve parotid gland and are commonly associated with Sjogren's syndrome⁵³.

RHABDOMYOSARCOMA:

Rhabdomyosarcoma is the most common sarcoma in the paediatric population, contributing 50% to 70% of all paediatric sarcoma². Majority of cases are diagnosed between 1 and 15 years⁹. Head and neck is the most common site of involvement, accounting for 35% to 40% of paediatric rhabdomyosarcoma². Oral lesions are rare, though cases involving buccal mucosa, alveolus, tongue and hard palate have been reported in children^{54,55}.

There are three histological types: embryonal, alveolar and pleomorphic. Embryonal rhabdomyosarcoma usually affects children, mostly less than 10 years of age⁹.

Botryoid and spindle cell type, variants of embryonal rhabdomyosarcoma exhibit favourable prognosis while embryonal type has intermediate prognosis. Compared to adults, children have better survival rates⁵⁵.

INFANTILE FIBROSARCOMA:

It is a cellular, active neoplasm, accounting for 5% of all malignancies of head and neck in children. It is seen in infants under the age of 1 year^{6,56}. Distal parts of extremities are frequently affected, although few cases have been reported affecting jaws and soft tissues of oral cavity^{6,57,58}. It exhibits rapid growth but the chances of metastasis are low⁵⁷.

Surgery is the principal treatment. Neoadjuvant chemotherapy has also been shown to be effective since the tumor is chemosensitive and spontaneous regression can occur⁵⁹. It shows favourable prognosis with limited biologic potential than adult fibrosarcoma⁵⁶.

PRIMITIVE NEUROECTODERMAL TUMOR (PNET):

PNET is a group of neoplasms developing from migrating embryonal cells of the neural crest⁶⁰. It mainly affects children and young adults. It can occur in soft tissues or bone with very few cases being reported in jaws and oral cavity⁶⁰⁻⁶². It is a highly aggressive tumor with rapid rate of local spread and metastasis. Treatment consists of multiagent chemotherapy and surgery⁶³.

MUCOEPIDERMAL CARCINOMA (MEC):

Salivary gland tumors are rare in children, accounting for about 10% of all pediatric neoplasms of head and neck⁶⁴. MEC is the most common salivary gland tumor occurring in children, representing 50% of malignant salivary gland tumors in this age group. The age range varies from 5 – 15 years. Most of the cases arise in parotid gland while few have been reported in minor salivary glands of palate, buccal mucosa and lips. Those cases occurring in children have good prognosis as most of them are well-differentiated^{64,65}.

Complete removal of tumor with adequate margins is the treatment of choice. Elective neck dissection is not recommended in case of low-grade tumors and clinically negative nodes. The use of radiotherapy is considered in selected cases keeping in mind the long-term adverse effects in children⁶⁴.

ACINIC CELL CARCINOMA (ACC):

Next to MEC, ACC is the second most common salivary gland malignancy in children. Slight female predilection has been noted⁶⁶. Vast majority of cases arise in parotid gland. It commonly presents as a slowly growing painless mass without any symptoms. It may show local invasion with propensity for recurrence and distant metastasis. Surgery is the treatment while radiotherapy is given only in selected cases⁶⁷.

OSTEOSARCOMA:

Osteosarcoma is the most common primary malignancy of bone. 6 – 30% of osteosarcoma of maxillofacial area occurs in first and second decades⁶⁸. Rapid bone growth during adolescence is considered as a cause for the development of this lesion. They show predilection for occurrence in mandible. Pain in the involved region of bone, sometimes with a soft tissue mass is the usual clinical presentation⁶⁹. Mucosal ulceration and loosening of teeth can also occur⁶⁸.

Treatment involves surgery with wide resection. Obtaining clear surgical margins is difficult in case of maxillary lesions due to complexity of the region. Radiotherapy is indicated in cases with positive or questionable surgical margins. Lesions occurring in the younger age have better prognosis⁶⁸.

EWING’S SARCOMA (EWS):

EWS is the second most common primary bone malignancy in children and adolescents⁷⁰ and is rare in the head and neck. About 95% of the patients possess (11;22) (q24;q12) translocation⁷¹.

EWS most commonly occurs in the age range of 4 to 15 years. Among the jaws, it shows predilection for ramus of mandible, although few cases have been reported in maxilla^{71,72}. Pain and localized swelling are the common complaints. Patient can also present with systemic symptoms like fever, anemia and weight loss². Gnathic EWS may mimic odontogenic inflammation⁷².

Multimodality treatment including surgery and/or radiotherapy followed by chemotherapy is advocated. It exhibits rapid growth and the possibility of micrometastasis at diagnosis is high⁷². 10-year survival rate for pediatric cases of head and neck have been reported to be more than 60%⁷³.

CONCLUSION

“A child is a unique individual; he or she is not a miniature adult, not a little man or woman”. Pediatric neoplasms vary from that of adults in various aspects like clinical behaviour, site predilection, rate of metastasis and survival rates. Hence, the diagnosis and treatment of these neoplasms should take the differences into account.

TABLE 1: DIFFERENCES BETWEEN ADULT AND PEDIATRIC NEOPLASMS: [3, 5]

	PEDIATRIC NEOPLASMS	ADULT NEOPLASMS
Origin	Deeper visceral structures and from parenchyma of organs	Epithelial layers that line the ducts and glands of organs and compose the skin
Etiology	Mostly due to changes in DNA that take place very early in life, sometimes even before birth	Mostly due to environmental or lifestyle risk factors
Common types	Lymphohematopoietic cancers, nervous system cancers and sarcomas	Epithelial tumors
Metastases	Present at diagnosis in approximately 80% of cases. It is attributed to rapid proliferation of cells and lack of recognition of abnormal cells essential for apoptosis in children.	Present at diagnosis in approximately 20% of cases
Chemotherapy	More frequently used in children because children better tolerate the acute adverse effects. Also, the neoplasms in children are more responsive to chemotherapy when compared to adults	Less frequently used comparatively.
Radiotherapy	Sparingly used in children because they are more vulnerable than adults to its late adverse effects	Commonly used treatment modality

TABLE 2: CLASSIFICATION OF PEDIATRIC NEOPLASMS AFFECTING HEAD AND NECK

BENIGN NEOPLASMS	MALIGNANT NEOPLASMS
<p><u>Soft tissue neoplasms:</u></p> <ul style="list-style-type: none"> • Mesenchymal tumors: <ul style="list-style-type: none"> ○ Giant cell lesions ○ Myxoma ○ Aggressive fibromatosis and desmoplastic fibromas ○ Congenital granular cell tumor • Neurogenic tumors: <ul style="list-style-type: none"> ○ Neurofibroma ○ Neurilemmoma ○ Neuroma ○ Ganglioneuroma ○ Melanotic neuroectodermal tumor • Vascular lesions: <ul style="list-style-type: none"> ○ Hemangioma ○ Lymphangioma • Salivary gland tumors: <ul style="list-style-type: none"> ○ Pleomorphic adenoma ○ Warthin's tumor 	<p><u>Soft tissue neoplasms:</u></p> <p>A. Connective tissue origin:</p> <ul style="list-style-type: none"> • Hematopoietic and reticuloendothelial tumors: <ul style="list-style-type: none"> ○ Leukemia ○ Lymphoma ○ Burkitt's lymphoma • Mesenchymal tumors: <ul style="list-style-type: none"> ○ Rhabdomyosarcoma ○ Fibrosarcoma • Neurogenic tumors: <ul style="list-style-type: none"> ○ Primitive neuroectodermal tumor ○ Neuroblastoma ○ Granular cell myoblastoma <p>B. Epithelial origin:</p> <ul style="list-style-type: none"> • Salivary gland tumors: <ul style="list-style-type: none"> ○ Mucoepidermoid carcinoma ○ Acinic cell carcinoma ○ Adenoid cystic carcinoma ○ Congenital parotid salivary carcinoma or sialoblastoma
<ul style="list-style-type: none"> • <u>Hard tissue neoplasms:</u> • Fibro-osseous lesions: <ul style="list-style-type: none"> ○ Juvenile ossifying fibroma • Odontogenic tumors: <ul style="list-style-type: none"> ○ Ameloblastoma (unicystic) ○ Calcifying epithelial odontogenic tumor ○ Adenomatoid odontogenic tumor ○ Ameloblastic fibroma ○ Ameloblastic fibro-dentinoma ○ Ameloblastic fibro-odontoma ○ Odontoma 	<p><u>Hard tissue neoplasms:</u></p> <ul style="list-style-type: none"> ○ Osteosarcoma ○ Chondrosarcoma ○ Ewing's sarcoma
<p>Miscellaneous:</p> <ul style="list-style-type: none"> ○ Teratoma 	

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