Review Article

Pediatric soft tissue tumors of head and neck – An update and review

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ARTICLE INFO

Article history:
Received 01-12-2020
Accepted 17-12-2020
Available online 30-12-2020

Keywords:
Pediatric
Sarcoma
Soft tissue
Tumor

ABSTRACT

Pediatric malignancies especially sarcomas are the most common and predominant cause of mortality in children. Such ongoing efforts are crucial to better understand the etiology of childhood cancers, get better the survival rate for malignancies with a poor prognosis, and maximize the quality of life for survivors. In this review article we authors aim to discuss relatively common benign and malignant connective tissue tumors (soft tissue tumor), focusing on current management strategies and new developments, as they relate to the role of the otolaryngologist– head and neck surgeon. Other rarer paediatric head and neck tumors beyond the scope of this review

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1. Introduction

Pediatric cancers differ from the adult malignancies in both prognosis and distribution by histology and tumor site. The incidence pattern in adults the cancer rates tend to increase rapidly with increasing age unlike in children. In children relatively wide age range exists, with two peaks – the first in early childhood and the second in adolescence.¹

Most of the pediatric tumors of maxillofacial region are benign, hemangioma being the most common benign tumor of infancy and childhood.² Although childhood cancer is relatively uncommon, it remains a significant cause of mortality in this population and is second only to accidents as a cause of death in children over 5 years of age. Data from the United States National Cancer Institute database suggest that the head and neck are involved in 12% of all childhood malignancies.³ In literature, neoplasms of the head and neck region account for approximately 5% of all childhood malignancies.⁴

Ionising radiations, genetic factors, rays, chemotherapeutic agents, family history, infections, immuno deficiencies and congenital anomalies are the most commonly involved risk factors for these paediatric cancers. Even though many genetic conditions are associated with increased risks for childhood cancer, but they are thought to occur in only less than 5% of the conditions. Extremely small fraction of paediatric cancer is to arise due to environmental exposures compared to adult epithelial tumor.¹

Curative therapy with chemotherapy, radiation and surgery may unfavourably affect a child’s development & result in serious long term medical & psycho social effects in both childhood & adulthood. Probable undesirable delayed side effects include subsequent malignancy, early mortality infertility, reduced stature, cardiomyopathy, osteoporosis, pulmonary fibrosis, neurocognitive impairment affective mood disorders & altered social functioning. The core objective in this matter is to enhance the survival rate of a lot of children with cancer by coordinated participation and research trials.¹

https://doi.org/10.18231/j.achr.2020.059
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Most common Paediatric tumors of head and neck are as follows (Table 1)

Vascular anomalies are congenital errors in vascular development. They frequently involve the head, neck, and oral cavity. They are subdivided into vascular tumors (haemangioma) and vascular malformations.\(^5\)\(^-\)\(^7\)

However, the factors that have not changed are the complexity of vascular anomalies and the importance of a multidisciplinary approach, or therapeutic center, for the treatment and long-term follow-up of these patients. Under the global heading of vascular anomalies, these lesions predominately occur within the head and neck and affect approximately one in 22 children.\(^5\)\(^,\)\(^7\)

Haemangiomas are the most common soft tissue tumors of infancy occurring approximately 5 to 10 % of 1yr old infant. The risk of haemangioma is 3 to 5 times more in girls than boys. Haemangiomas can be present at birth but usually arise shortly after birth and grow rapidly during the first year of life, but in next five yrs. there is slowing of growth & involution by 10 to 15yr of age.\(^1\)

In 1982, Mulliken & Glowacki defined haemangiomas as vascular tumors with a growth phase marked by endothelial proliferation & hypercellularity and involution phase.\(^8\)

Haemangiomas originate from the reticular dermis or subcutaneous tissues and appear as bluish or relatively colourless masses (previously called cavernous haemangioma). Compound haemangiomas have superficial and deep components and were previously called cavernous haemangiomas. Compound haemangiomas have superficial and deep components and were previously called capillary cavernous haemangiomas.\(^9\)

Active intervention should be considered in all disfiguring haemangiomas, to prevent potential psychosocial trauma and cosmetic deformity. The first line drug of choice for the treatment of life or sight-threatening haemangiomas is prednisolone. The response rate varies from 30% to 90% and depends on the dose, duration and age at start of treatment. Steroids are useful only in the proliferative phase. Interferon are also been used, but because of their potentially serious side effects, it is suggested that they are used only in steroid-resistant life and sight-threatening lesions.\(^8\)

Lymphangioma is a congenital malformation of the lymphatic system, frequently found at birth, with 90% diagnosed before the age of 2 years. A sub-type of lymphangioma is called cystic hygroma. It is composed of large lymph-containing cysts.\(^10\) More than 90% of lymphangiomas occurs in the cervical region. In the oral cavity most commonly it can arise in larynx, orbit, tongue, floor of the mouth, and the cheek region.\(^11\) Lymphatic malformations have a tendency to grow with the age of the child and rarely regress. The symptoms and complications depend on the location of the lesion. The most life-threatening complication of lymphangioma is acute airway obstruction. Lymphangioma can be diagnosed clinically, but imagistic studies are important for the confirmation of the diagnosis.\(^12\)

Prenatal ultrasound, MRI especially a fetal MRI are used to detect cystic hygroma and vascular malformations. Surgical excision is the usual treatment of lymphangioma.\(^13\) Awareness of potential airway involvement and possible complications is necessary to provide a safe anaesthetic to a patient with lymphangioma. Anesthetic concerns include bleeding, difficulty visualizing the airway, extrinsic and intrinsic pressure on the airway causing distortion, and enlarged upper respiratory structures, including the lips, tongue, and epiglottis.\(^14\) This aspect is very important when a child is undergoing serial extraction or any other surgeries under general anaesthesia.

Tumors of neurogenic origin are a small but significant portion of head and neck masses in children. Neurofibromas and schwannomas are the most common nerve sheath tumours of the peripheral nerves in the head and neck region.\(^15\)

Plexiform neurofibromas are pathognomonic of NF1. These lesions usually occur in early childhood and precede cutaneous neurofibromas.\(^16\) Sudden and rapid enlargement of an existing neurofibroma should be considered a sign of malignant transformation, until proved otherwise. There is a 4% chance of transformation into a malignant peripheral nerve sheath tumour in NF-1.\(^17\)

Neurofibromatosis type 1 (NF-1), also known as Von Recklinghausen’s disease, is a multisystem genetic disorder, characterized by increased cell proliferation and tumor development. It affects 1 out of 3000 to 4000 live births. Characteristically the pigmented skin lesions (due to the focal melanosis in the epidermis), cafe au lait spots and freckling, are the hallmarks features of NF1. These lesions may be present at birth or become obvious during the early years of life.\(^18\)

Rhabdomyosarcoma (RMS) is an aggressive malignant skeletal muscle neoplasms arising from embryonal mesenchyme. In records it accounts for over 50% of all pediatric soft tissue sarcomas. The head and neck region is the most common site for this tumor in children.\(^19\) The period between 1975 and 2002, it was found that the 5-year survival rate for rhabdomyosarcoma has increased from 53% to 65% for children younger than 15 years and from 30% to 47% for adolescents aged 15 to 19 years.\(^20\) Horn and Enterline, subdivided rhabdomyosarcomas into botryoid, embryonal, alveolar, and pleomorphic subtypes depending on morphologic features, without the benefit of immunohistochemical or genetic confirmation.\(^21\)

The advent of collective combined contemporary, multi-agent chemotherapy, radiotherapy, and surgery has made the five-year survival rate is approximately 85% for this RMS subtype.\(^22\) For patients with embryonal tumors, high
birth weight and large size for gestational age are associated with an increased incidence of rhabdomyosarcoma. Genetic conditions associated with rhabdomyosarcoma include Li-Fraumeni cancer susceptibility syndrome, neurofibromatosis type I, Beckwith-Wiedemann syndrome and Basal cell nevus syndrome. The prognosis for a child or adolescent with rhabdomyosarcoma is associated to the age of the patient, site of origin, widest diameter of the tumor, resectability, presence of metastases, number of metastatic sites or tissues involved, presence or absence of regional lymph node involvement, histopathologic subtype (alveolar vs. embryonal), and delivery of radiation therapy in selected cases. Children aged 1 to 9 years have the best prognosis, the prognosis worsens in younger and older patients. In recent Intergroup Rhabdomyosarcoma Study Group (IRSG) trials, 5-year failure-free survival (FFS) was 57% for patients younger than 1 year, 81% for patients aged 1 to 9 years, and 68% for patients older than 10 years. Five-year survival for these groups was 76%, 87%, and 76%, respectively. In addition; infants younger than 1 year may be less likely to receive radiation therapy for local control, because of concern about the high incidence of complications in this age group.

The embryonal subtype is the most frequently observed subtype in children, accounting for approximately 60% to 70% of rhabdomyosarcomas of childhood. An increased frequency of this subtype is noted in adolescents and in patients with primary sites. Pleomorphic rhabdomyosarcoma affect all ages and are more common in adolescents and young adults. In adults, pleomorphic rhabdomyosarcoma is associated with a worse prognosis.

The embryonal and alveolar histologies have distinctive molecular characteristics that have been used for diagnostic confirmation, and may be useful for assigning therapy and monitoring residual disease during treatment. Unique translocations between the FKHR gene on chromosome 13 and either the PAX3 gene on chromosome 2 or the PAX7 gene on chromosome 1 are found in 70% to 80% of patients with alveolar histology tumors. Translocations involving the PAX3 gene occur in approximately 59% of alveolar rhabdomyosarcoma cases, while the PAX7 gene appears to be involved in about 19% of cases. Patients with metastatic rhabdomyosarcoma having the PAX7-FKHR fusion gene appear to have a substantially better prognosis than those with the PAX3-FKHR. Embryonal tumors they exhibit loss of allelic heterozygosity and abnormalities in parental imprinting. Loss of allelic heterozygosity particularly affects loci at chromosome 11p15, and consistent loss of genomic material from the chromosome 11p15 region in embryonal tumors has been observed.

Even though RMS has shown marked improvement in survival over the past decades, in addition to a poor prognosis for patients over ten-years old, diagnostic delay can have a profusely unfavorable impact on prognosis.

Table 1: Most common Pediatric tumors of head and neck

| Soft tissue tumors in head and neck region in children |
|-------------------------------------------------------|
| 1. Fibrous tissue tumors                               |
| 2. Lipomatous tumor                                   |
| 3. Skeletal muscle tumors                             |
| 4. Endothelial tumors of blood & lymph vessels        |
| 5. Neural tumors                                       |
| 6. Cartilage & bone tumors                            |
| 7. Multiple hereditary exostosis                      |
| 8. Enchondroma                                         |
| 9. Chondroblastoma                                    |
| 10. Chondromyxoid fibroma                             |
| 11. Osteoid osteoma                                   |
| 12. Osteoblastoma                                     |
| 13. Fibromas (non ossifying fibroma, fibrous cortical defect) |
| 14. Unicameral bone cyst                              |
| 15. Aneurysmal bone cyst                              |
| 16. Fibrous dysplasia                                 |
| 17. Eosinophilic granuloma                            |
| 18. Osteosarcoma                                      |
| 19. Ewing's sarcoma                                   |
| 20. Miscellaneous                                     |
| 21. Granular cell tumor of infancy                    |
| 22. PNET of infancy                                   |

Fibrous dysplasia was first described by Lichtenstein in 1938 as a disorder characterized by progressive replacement of normal bone elements by fibrous tissue. Fibrous dysplasia (FD) is a sporadic benign skeletal disorder that can affect one bone (monostotic form), or multiple bones (polyostotic form), and the latter may form part of the McCune-Albright syndrome (MAS) or of the Jaffe-Lichtenstein syndrome (JLS). Malignant transformation is rare, and is usually precipitated by radiation therapy. Malignant degeneration occurs in less than 1% of cases of fibrous dysplasia. Malignancies are almost exclusively osteosarcoma Sudden increase in the level of alkaline phosphatase is one of the symptoms for malignant transformation and for that reason its amount should be periodically observed. Usually the prognosis is good although the bad outcomes occur more frequently among young patients or those with polyostotic forms of the disorder.
The radiotherapy increased malignant transformations more than 400 times.  

Severity and extent of Gsα mutation-associated diseases are not related to the stage of embryogenesis when the mutation occurred, but rather are functions of survival of mutated cells within the clone during migration, growth and differentiation, and of the ratio of mutated to normal cells at the affected anatomical site.  

Gender prevalence of FD is equal. The monostotic form is more common and affects the 20 to 30 years age group: polyostotic FD has its onset mainly in children younger than 10 years of age.  

In fibrous dysplastic bone, the increased expression of cAMP by the mutated lesional cells is associated with abnormal osteoblast differentiation and formation of defective bone.

However, after surgical reduction of fibrous dysplastic lesions, particularly in younger subjects and when the lesions are more immature, is high (50%) so a conservative surgical approach will often require more than one intervention to control the clinical signs and symptoms.

Osteosarcoma is the most common primary malignant neoplasm of bone. Osteosarcomas of the head and neck represent a small percentage of osteosarcomas with studies reporting occurrences of less than 10%. Though compared to incidence of osteosarcomas of long bones, the number of craniofacial osteosarcomas is very low, the prevalence of jaw osteosarcoma is in fact 10 times greater than that of osteosarcoma in the total body skeleton, considering that jaws represent only 0.86% of total body volume. The incidence of head and neck osteosarcoma is observed to be even more uncommon if only the pediatric patient population is examined (age<18 yrs), accounting for less than 1% of all head and neck malignant tumor. Radiation therapy, hereditary retinoblastoma, Paget’s disease of bone, a history of fibrous dysplasia, or trauma are some of the factors known to predispose to the development of osteosarcoma.

Osteosarcoma of the head and neck, including osteosarcoma of the jaw, typically occurs after the second decade, in contrast to osteosarcoma of the long bones, which usually occurs in the first and second decades of life. Although osteosarcoma can occur in different anatomic sites, in pediatric patients mandible is most commonly involved site followed by the maxilla/maxillary sinus, and other sinuses (sphenoid, ethmoid sinuses). It has been hypothesized that because the mandible retains growth centers for more than 30 years, osteosarcomas of the head and neck could occur more commonly in this location.

The classic radiologic appearance of long-bone osteosarcomas called as ‘sunburst’ appearance is not pathognomonic for jaw osteosarcomas. The radiologic appearance of jaw osteosarcomas depends on the interplay of three processes: bone formation and mineralization, bone destruction, and periosteal bone formation. Radiologically, the lesions may range from predominantly radiolucent to radio-opaque lesions depending on the degree of ossification.

Histologically, osteosarcoma can be of different subtypes including conventional osteoblastic osteosarcoma, chondroblastic, fibroblastic, anaplastic, telangiectatic, giant-cell rich, and small cell osteosarcomas. The fibroblastic subtypes have the best response to chemotherapy and the chondroblastic subtypes have the worst response. Osteogenic sarcomas, predominantly osteoblastic subtype, with one chondroblastic subtype has been reported in one of the study of 22 cases of head and neck osteosarcomas in pediatric population.

Wide surgical excision and adjuvant treatment with radiotherapy and/or chemotherapy are the recommended treatment for osteosarcomas. Diagnosis of tumor in its early stages and complete resection are the most important factors in increasing prognosis of jaw osteosarcoma. Anatomical limitations in face cause some difficulties in achievement of uninvolved margins and for this reason local recurrence of the lesion is high (33%-69% percent). Mandibular osteosarcomas have a better prognosis than maxillary tumors because of easier resectability, and the ability to obtain negative surgical margins. A poorer outcome for maxillary tumors is expected, related to the difficulty in obtaining adequate resection margins, leading to increased incidence of local recurrence, residual disease, and death. Distant metastases have been reported in 10–20% of patients with HNOS, compared with 53–75% of patients with disease arising outside the head and neck.

Ewing’s family of tumours (Ewing tumour) includes Ewing’s sarcoma of bone and soft tissues, primitive neuroectodermal tumours (PNET), Askin tumour and other less frequent neoplasms. PNET and Ewing’s sarcoma were initially regarded as distinct clinicopathological entities, but it has more recently been argued that they actually represent the same tumour type, diverging only by a higher degree of neural differentiation in PNET's. Considering both clinical and morphological evidence along with recent data provided by molecular genetics, Ewing’s sarcoma and PNET most likely represent, respectively, the poorly and well-differentiated ends of a spectrum of round-cell sarcomas exhibiting a partial neuroectodermal phenotype, which can be collectively termed as Ewing’s family of tumours. Ewing’s sarcoma/PNET is the second most frequent bone tumour in the paediatric age group after osteosarcoma. It accounts for 4-6% of primary malignant bone tumors, peaks in the second decade of life, slightly more common in males. Ewing tumours of bone usually appear in the diaphysis of long tubular bones, the femur and tibia being the most frequent sites. About one-third of cases...
appear in the axial skeleton, mainly in the pelvis and the ribs. 

Involvement of the head and neck in Ewing’s Sarcoma is rare, accounting for approximately 1 to 4% of cases. In the head and neck region, the mandible and skull base are the two most common primary sites, followed by the orbit, and nasal cavity with or without the paranasal sinuses. The maxilla is also reported as the most common site of presentation. It is most commonly seen in second decade of life with the age of presentation ranging from 7.5 to 14 year and also 5 months to 22 years. The most common clinical presentation of this tumor is painful swelling.

Histopathologically, the neoplastic lobules are composed of small round cells exhibiting round or ovoid vesicular nuclei, a distinct nuclear membrane, small nucleoli, finely granular chromatin and poorly defined, scanty cytoplasm. The mitotic activity tends to be quite variable. Necrosis is almost always present and can be extensive, sometimes leaving collars of viable tumour cells around the richly ramified capillary network. There are usually extensive deposits of cytoplasmic glycogen; the PAS stain is positive in more than half of the tumours. Histopathological assessment of tumour necrosis after therapy using various grading systems correlates with overall survival.

Strong expression for CD99, a cell-surface glycoprotein (the product of the MIC2 antigen) has been observed for Ewing’s sarcoma which plays a key role in the differential diagnosis of round-cell sarcomas. CD99 is considered as a sensitive but non-specific marker for Ewing sarcoma. Genetic analysis is important in the diagnosis of Ewing’s sarcoma. The central karyotypic anomaly is a t(11;22) translocation, with other variants found in about 15% of cases: a t(21;22), a t(7;22) and a t(17;22) and t(2;22). Because of t(11;22), fusion of the Ewing’s sarcoma (EWS) gene with the transcription factor FLI1 (friend leukaemia virus integration site 1) on chromosome 11q24 belonging to the ETS (avian erythroblastosis virus transforming sequence) family occurs in the molecular level which leads to the oncogenic conversion of the EWS gene. Antibodies to the FlI-1 gene product as a sensitive marker of Ewing’s family of tumors has been studied. ESW gene ‘split apart’ probes coupled with morphological findings can improve the diagnostic accuracy of ES/PNET.

The multidisciplinary treatment including surgery, radiotherapy and chemotherapy is the ideal approach for the treatment of Ewing’s sarcoma. Complete resection of Ewing’s sarcoma of head and neck region is difficult to achieve because of the anatomic location and also the extension of tumor to adjacent structures. Multimodality therapy consisting of an initial biopsy, aggressive combination chemotherapy and localized radiotherapy can be the treatment of choice for Ewing’s sarcoma of the head and neck region and may result in long-term survival. In lesions that are initially unresectable and/or show a poor response to chemotherapy, radiation is used for local control. A good prognosis can be expected if the disease has not metastasized. Large tumors were found to be associated with poorer outcome than those with smaller tumors. Tumor volume has been shown to be an important prognostic factor in Ewing’s sarcoma. In Ewing’s sarcoma of head and neck which are locally advanced and/or surgically irresectable, it is difficult to consider tumor size and volume.

The multimodality treatment surgery, radiotherapy and chemotherapy has significantly improved the 5-year survival ratio, now reaching 40% to 75%. The most common location for metastases in ES is the lungs, followed by bones and the bone marrow. The presence of metastasis is the main adverse prognostic factor and is associated with significantly worse relapse-free survival and only about 20% long term survivors. Radical radiotherapy in the pediatric age group can lead to other complications in the pediatric patients. The use of high doses of radiation for tumors in the head and neck region may produce functional squeal and local complications, including fibrosis, contractures, anklyosis of the temporomandibular joint and also secondary malignancy. Combining surgery and postoperative radiotherapy can expose the patients to the sequel of both treatments.

2. Conclusion

Very limited information is available about the clinical behavior and management of soft tissue tumors of the head and neck in children as most series describe pediatric and adult patients together. To better understand the natural history, clinical course of these tumors and to establish management recommendations for children, more case reports and case series are required in this field.

3. Authors contribution and declaration

We hereby declare that all the authors have contributed sufficiently in the intellectual content, conception, planning and designing the work and interpretation of the data (when applicable) and construction of the manuscript.

4. Source of Funding

None.

5. Conflict of Interest

None.

References

1. Kliegman B, Jenson S. Nelson’s textbook of paediatrics. In: 18th Edn., vol. 2; 2007. p. 2097–162.
2. Bleyer. Cancer statistics review Cancer; 1993.
3. Albright JT, Topham AK, Reilly JS. Pediatric head and neck malignancies: US incidence and trends over 2 decades. Arch
Otolaryngol Head Neck Surg. 2002;128:655–9.
4. Dickson PV, Davdoff AM. Malignant neoplasms of the head and neck. Semin Pediatr Surg. 2006;15(2):92–8.
5. Drolet BA, Esterly NB, Frieden IJ. Hemangiomas in Children. N Engl J Med. 1999;341(3):77–81.
6. Greene AK, Kim S, Rogers GF, Fishman SJ, Olsen BR, Mulliken JB, et al. Risk of Vascular Anomalies With Down Syndrome. Pediatr 2008;121(1):e135–40.
7. Buckmiller LM, Richter GT, Suen JY. Diagnosis and management of hemangiomias and vascular malformations of the head and neck. Oral Diseases. 2010;16(5):405–18.
8. Mulliken JB, Glowacki J. Hemangiomas and Vascular Malformations in Infants and Children. Plast Reconstr Surg. 1982;69(3):412–22.
9. Ethanandam M, Mellor TK. Haemangiomas and vascular malformations of the maxillofacial region—A review. Br J Oral Maxillofac Surg. 2006;44(4):263–72.
10. Kennedy TL. Cystic hygroma-lymphangioma: a rare and still unclear entity. Laryngoscope. 1989;99:1–10.
11. Thompson DM, Kasperbauer JL. Congenital cystic hygroma involving the larynx presenting as an airway emergency. J Natl Med Assoc. 1994;86:629–32.
12. Lahwani AK, Engel TL. Teratoma of the tongue: a case report and review of the literature. Int J Pediatr Otorhinolaryngol. 1992;24(3):261–8.
13. Yonesu K, Nakayama E, Kawazu T. Value of contrast – enhanced magnetic resonance imaging in differentiation of hemangiomas from lymphangiomas in the oral and maxillofacial region. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1999;88(4):496–500.
14. Bettina MT, Welna JO, Do. Childhood airway manifestations of lymphangioma: A case report. AANA J. 2004;72:280–3.
15. Egelhoff JC, Lanzieri CF, Gilkeson RG. Pediatric head and neck imaging. CT and MR Imaging of the Whole Body. In: 4th Edn. St. Louis; Mosby; p. 691–721.
16. Visrutaratna P, Oranratanachai K, Singhavejsakul J. Clinics in diagnostic imaging. Singapore Med J. 2004;45(96):188.
17. Hrehorovich PA, Franke HR, Maxinin S, Caracta P. Malignant Peripheral Nerve Sheath Tumor. Radio Graphics. 2003;23(3):790–4.
18. Korf BR. Diagnosis and management of neurofibromatosis type I. Curr Neurol Rep. 2001;1(2):162–7.
19. Chigumucuaria R, Alfatoua A, Myulla RWI. Orofacial rhabdomyosarcoma in neonates and young children: a review of literature and management of four cases. Oral Oncol. 2002;38(5):508–15.
20. Smith MA, Seibel NL, Altekruse SF, Ries LA,G, Melbert DE, O’Leary M, et al. Outcomes for Children and Adolescents With Cancer: Challenges for the Twenty-First Century. J Clin Oncol. 2010;28(15):2625–34.
21. Horn RC, Enterline HT. Rhabdomyosarcoma: A clinico-pathological study and classification of 39 cases. Cancer. 1958;11(1):181–99.
22. Stiller CA, Stevens MC, Magnani C, Corazziari I. Eurocare Working Group. Survival of children with soft-tissue sarcoma in Europe since 1978: results from the Eurocare study. Eur J Cancer. 2001;37:767–74.
23. Oglinovanov S, Carozza SE, Chow EJ, Fox EE, Horel SJ. Magnetic resonance imaging in differentiation of hemangiomas from lymphangiomas in the oral and maxillofacial region. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1999;88(4):496–500.
24. Parham DM, Ellison DA. Rhabdomyosarcomas in adults and children: an update. Arch Pathol Lab Med. 2006;130(1):1454–65.
25. Crist W, Gehen EA, Ragab AH, Dickman PS, Donaldson SS, Fryer C, et al. The Third Intergroup Rhabdomyosarcoma Study. J Clin Oncol. 1995;13(3):610–30.
26. Maurer HM, Gehen EA, Belfangady M. The Intergroup Rhabdomyosarcoma Study-II. Cancer. 1993;71(5):1904–22.
27. Breneman JC, Lyden E, Pappo AS. Prognostic factors and clinical outcomes in children and adolescents with metastatic rhabdomyosarcoma—a report from the Intergroup Rhabdomyosarcoma Study IV. J Clin Oncol. 2003;21(1):78–84.
28. Punyko JA, Mertens AC, Baker KS, Ness KK, Robison LL, Gurney JG, et al. Long-term survival probabilities for childhood rhabdomyosarcoma. Cancer. 2005;103(7):1475–83.
29. Malempati S, Rodeberg DA, Donaldson SS. Rhabdomyosarcoma in infants younger than 1 year: a report from the Children’s Oncology Group. Cancer. 2011;117(5):3493–501.
30. Joshi D, Anderson JR, Paidas C, Breneman J, Parham DM, Crist, et al. Age is an independent prognostic factor in rhabdomyosarcoma: A report from the soft tissue sarcoma committee of the children’s oncology group. Pediatr Blood Cancer. 2004;42(1):64–73.
31. Ferrari A, Casanova M, Bisogno I, Zecchetto G, Bernardi BD, et al. Rhabdomyosarcoma in infants younger than one year old. Cancer. 2003;97(10):2597–604.
32. Barr PG, Smith LM, Lynch JC, Stitzelecki D, Parham DM, Qualman SJ, et al. Examination of Gene Fusion Status in Auralveolar Rhabdomyosarcoma Entered on the Intergroup Rhabdomyosarcoma Study—III Trial. J Mol Diagn. 2006;8(2):202–8.
33. Sorensen PH, Lynch JC, Qualman SJ. PAX3-FKHR and PAX7-FKHR gene fusions are prognostic indicators in alveolar rhabdomyosarcoma: a report from the children’s oncology group. J Clin Oncol. 2002;20(11):2672–9.
34. Neville BW, Damm DD, Allman CM. Bouquet JE: Bone Pathology. In: In Oral and maxillofacial pathology. 2nd edn; 2002. p. 635–40.
35. Ogusalu CO, Lewis A, Dooungul L. Benign fibro-osseous lesions of the jaw bones in Jamaica: analysis of 32 cases. Oral Dis. 2001;7(3):155–62.
36. Cholakova R, Panasirskia K, Kanziriski N. Dysplasia in the maxillomandibular region- case report. Jofmed. 2010;16(4):10–3.
37. Parekh SG, Donthrani-Rao R, Ricchetti E, Lackman RD. Fibrous Dysplasia. J Am Acad Orthop Surg. 2004;12(5):305–13.
38. Riminucci M, Saggio I, Robey PG, Bianco F. Fibrous Dysplasia as a Stem Cell Disease. J Bone Min Res. 2006;21(52):P125–31.
39. Feller L, Wood NH, Khammasia RAG, Lemmer J, Raubenheimer EJ. The nature of fibrous dysplasia. Head Face Med. 2009;22:1–5.
40. Charpurlat RD, Meunier PJ. Fibrous dysplasia of bone. Baillière’s. Clin Rheumatol. 1994;10(3):285–98.
41. Lustig LR, Holliday MJ, McCarthy EF, Nager GT. Fibrous Dysplasia Involving the Skull Base and Temporal Bone. Arch Otolaryngol Head Neck Surg . 2001;127(10):1239–47.
42. Sorensen PH, Lynch JC, Qualman SJ. PAX3-FKHR and PAX7-FKHR gene fusions are prognostic indicators in alveolar rhabdomyosarcoma: a report from the children’s oncology group. J Clin Oncol. 2002;20(11):2672–79.
43. Cristante MF, Eliana MM, Maria TS, Adriana DB, Niltza NF. Rhabdomyosarcoma of the Oral Tissues - Two new cases and literature review. Med Oral Patol Oral Cir Bucal. 2006;11:136–40.
44. Chen JS, Liaw CC, Wang HM, Tsa MH. Osteosarcoma of the Head and Neck in Pediatric Patients. A
Clinicopathologic Study of 22 Cases with a Review of the Literature. Cancer. 2001;91(3):598–605.

48. Shao Z, He Y, Wang L, Hu H, Shi H. Computed tomography findings in radiation-induced osteosarcoma of the jaws. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;109:88–94.

49. Mendenhall WM, Fernandes R, Werning JY, Vaysberg M, Malaya RS, Mendenhall NP, et al. Head and neck osteosarcoma. Am J Otolaryngol. 2011;32(6):597–600.

50. Ogundewo MO, Ajayi OF, Adeyemo WL, Ladeinde AL, James O. Osteogenic sarcoma of the jaw bones: A single institution experience over a 21-year period. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:76–81.

51. Es RJV, Keus RB, Waal JVD, Koole R, Vermylen A. Osteosarcoma of the ts. Long-term follow up of 48 cases. Int J Oral Maxillofac Surg. 1997;26:191–7.

52. Batsakis JG, Solomon AR, Rice DH. The pathology of head and neck tumors: neoplasms of cartilage. Head Neck Surg. 1980;3(7):43–57.

53. Clark JL, Unni KK, Dahlin DC, Devine KD. Osteosarcoma of the jaw. Cancer. 1983;51(12):2311–6.

54. Garrington GE, Scofield HH, Cornyn J, Hooker SP. Osteosarcoma of the jaws. Analysis of 56 cases. Cancer. 1967;20(3):377–91.

55. Ha PK, Eisele DW, Frassica FJ, Zahrakur ML, McCarthy EF. Osteosarcoma of the head and neck: A review of the Johns Hopkins experience. Laryngoscope. 1999;109(6):964–9.

56. Cavalcanti MGP, Ruprecht A, Yang J. Radiological findings in an unusual osteosarcoma in the maxilla. Dentomaxillofac Radiol. 2000;29(3):180–4.

57. Hayden JB, Hoang BH. Osteosarcoma: Basic Science and Clinical Implications. Orthopedic Clinics of North America. 2006;37(1):1–7. Available from: https://doi.org/10.1016/j.orth.2005.06.004.

58. Saito Y, Asakage T. Neck Dissection of the Head and Neck Sarcoma. Neck Dissection -Clinical Application and Recent Advances. Available from: http://www.intechopen.com/books/neck-dissection-clinical-application-and-recentadvances/neck-dissection-of-the-head-and-neck-sarcoma.

59. Forteza G, Colmerero B, López-Barea F. Osteogenic sarcoma of the maxilla and mandible. Oral Surg Oral Med Oral Pathol. 1986;62(2):179–84.

60. Ruus JH, Jesse RH. Management of osteosarcoma of the maxilla and mandible. Am J Surg. 1980;140(4):1572–6.

61. Disher MJ, Shulkin BL, Kuppersmith RB, Deveikis JP, Clevens RA, Frey K, et al. Management of an Osteogenic Sarcoma of the Maxilla. Ann Otol Rhinol Laryngol. 1994;103(5):408–12.

62. Smeelde LE, van der Wal JE, van Diest PJ, van der Waal I, Snow GB. Radical surgical treatment in craniofacial osteosarcoma gives excellent survival. A retrospective cohort study of 14 patients. Oral Oncol Eur J Cancer. 1994;30(6):374–6.

63. Altuwairigi O, Papageorge MB, Karp DD. Maxillary chordoblastic sarcoma: Presentation of two cases and a literature review. J Oral Maxillofac Surg. 1996;54(11):1357–64.

64. LeComer MG, Chuang SK, Kaban LB, August M. Osteosarcoma of the Jaws: Factors Influencing Prognosis. Journal of Oral and Maxillofacial Surgery. 2011;69(9):2368–2375. Available from: https://doi.org/10.1016/j.joms.2010.10.023.

65. Delattre O, Zucman J, Melot T, Garau XS, Zucker JM, Lenoir GM, et al. The Ewing Family of Tumors - A Subgroup of Small-Round-Cell Tumors Defined by Specific Chimeric Transcripts. N Engl J Med. 1994;331(5):294–9.

66. Rossi S, Nascimento AG, Canal F, Tos APD. Small round-cell neoplasms of soft tissues: An integrated diagnostic approach. Curr Diagn Pathol. 2007;13(2):150–63.

67. Lawlor ER, Mathers JA, Bainbridge T, Horsman DE, Kawai A. Ewing JH, et al. Peripheral primitive neuroectodermal tumors in adults: documentation by molecular analysis. J Clin Oncol. 1998;16(3):1150–7.

68. Siegal G, Wilcox WR, Reinsus WR, Gilula LA, Foulkes MA, Kissane JM, et al. Primary Ewing’s sarcoma involving the bones of the head and neck. Cancer. 1987;60(1):2829–40. 

69. Horowitz ME, Malawer MM, Woo S. Ewing’s sarcoma family of tumours: Ewing’s sarcoma of bone and soft tissue and the peripheral primitive neuroectodermal tumours. Pediatr Oncol. 1997.p 831–63.

70. Batsakis JG, MacKay B, El-Naggar AK. Ewing’s Sarcoma and Peripheral Primitive Neuroectodermal Tumor: An Interim Report. Ann Otol, Rhinol Laryngol. 1996;105(10):838–43.

71. Prinzhall G, Willert HG, Notter G. Local therapy of rhabdomyosarcoma, osteosarcoma and Ewing’s sarcoma of children and adolescents. Euro J Pediatr. 1985;144(2):120–4.

72. Windfuhr JP. Primitive Neuroectodermal Tumor of the Head and Neck: Incidence, Diagnosis, and Management. Ann Otol, Rhinol Laryngol. 2004;113(7):533–43.

73. Allam A, El-Husseiny G, Khafaga Y, Kandili A, Gray A, Ezzat A, et al. Ewing’s Sarcoma of the Head and Neck: A Retrospective Analysis of 24 Cases. Sarcoma. 1999;3(1):11–5.

74. Vaccani JP, Forte V, de Jong AL, Taylor G. Ewing’s sarcoma of the head and neck in children. Int J Pediatr Otorhinolaryngol. 1999;48(3):209–16.

75. Abdelrahman H, El-Baradie T, El-Baradie M, Bahaa S, Shalan M. Management Head and Neck Ewing’s Sarcoma Family of Tumors: Experience of the National Cancer Institute, Cairo University. J Egypt Nat Canc Inst. 2010;22(1):41–48.

76. de Alava E. Diagnosis of small round cell tumours of bone. Curr Diagn Pathol. 2001;7(4):251–61.

77. Wunder J, Paulian G, Huvos A, Heller G, Meyers P, Healey J, et al. The Histological Response to Chemotherapy as a Predictor of the Oncological Outcome of Operative Treatment of Ewing Sarcoma*. J Bone Joint Surg Am. 1998;80(7):1020–33.

78. Peter M, Couturier J, Pacquement H, Michon J, Thomas G, Magdeleinat H, et al. A new member of the ETS family fused to EWS in Ewing’s sarcoma. Oncogenesis. 1997;14(10):1159–64.

79. Sorensen P, Lessnick SL, Lopes-Terrada D, Liu XF, Triche TJ, Denny CT, et al. A second Ewing’s sarcoma translocation, t(21;22), fuses the EWS gene to another ETS–family transcription factor, ERG. Nat Genet. 1994;6(2):146–51.

80. Lawlor ER, Mathers JA, Bainbridge T, Kawai A, LeCornu MG, Chuang SK, Kaban LB, August M. Osteosarcoma of the jaws: A subgroup of small-round-cell tumours defined by specific chimeric transcripts. N Engl J Med. 1994;331(5):294–9.

81. Folpe AL, Hill CE, Parham DM. Immunohistochemical detection of FLI-1 protein expression: a study of 132 round cell tumors with transcripts. Am J Surg Pathol. 2000;24:1657–62.
85. Rossi S, Orvieto E, Furlanetto A, Laurino L, Ninfa V, Tos APD, et al. Utility of the immunohistochemical detection of FLI-1 expression in round cell and vascular neoplasm using a monoclonal antibody. *Mod Pathol*. 2004;17(5):547–52. doi:10.1038/modpathol.3800193

86. Daw NC, Mahmoud HH, Meyer WH, Jenkins JJ, Kaste SC, Poquette CA, et al. Bone sarcomas of the head and neck in children. *Cancer*. 2000;88(9):2172–80. doi:10.1002/(sici)1097-0142(20000501)88:9<2172::aid-cncr25>3.0.co;2-
7

87. Grier HE, Krailo MD, Tarbell NJ, Link MP. Addition of ifosfamide and etoposide to standard chemotherapy for Ewing’s sarcoma and primitive neuroectodermal tumor of bone. *N Engl J Med*. 2003;348:694–701.

88. Sneige N, Batsakis JG. Ewing’s Sarcoma of Bone and Soft Tissues. *Ann Otol, Rhinol Laryngol*. 1989;98(5):400–2.

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