Int. J. Oral Maxillofac. Surg. 2014; 43: 7–12
http://dx.doi.org/10.1016/j.ijom.2013.06.017, available online at http://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Clinical paper
Head and neck oncology

Incidence and grading of cranio-facial osteosarcomas

H. van den Berg, J. H. M. Merks
Department of Paediatric Oncology, Emma Children's Hospital, Academic Medical Centre, University of Amsterdam, The Netherlands

H. van den Berg, J. H. M. Merks: Incidence and grading of cranio-facial osteosarcomas. Int. J. Oral Maxillofac. Surg. 2014; 43: 7–12.

Abstract. Osteosarcoma of the cranio-facial structures and skull is rare. In children, only 5.6% of cases are localized in these areas. It is claimed that the mean age at presentation is at least 10–15 years higher than for osteosarcomas in other parts of the body. However these reports are based on data from single institutions or compiled from several registries. It is further claimed that tumours in the mandible and maxilla are less malignant, as based on observations of a better prognosis and lower incidence of metastatic spread as compared with osteosarcomas arising elsewhere. We report all histologically proven cranio-facial osteosarcomas in The Netherlands occurring over a 20-year period, based on the national registration covering all Dutch pathology laboratories (PALGA). The age-corrected incidence of primary osteosarcoma ranged from 0.33 to 0.41 per million across the age ranges. The mandible was the most frequent site of involvement. Only 61% had a high malignant histological grading. Our data indicate that the age-corrected incidence of primary osteosarcomas is similar across all age ranges. In respect to histology, a lower grade of malignancy is more frequent. Maxillary lesions significantly more often have a lower histological grade of malignancy.

Key words: osteosarcoma; jaw; primary tumour; secondary tumour; malignancy grading; incidence; age.

Accepted for publication 3 June 2013
Available online 12 September 2013

Osteosarcoma is the most common malignancy of bone, with an age-related incidence of up to 16 per million at the age of 16 years. Osteosarcoma of the cranio-facial structures and skull is rare and represents only 5.6% of cases in the paediatric age group.[1] It is claimed that the mean age at presentation is at least 10–15 years higher than for osteosarcomas in other parts of the body. However these reports are based on data from single institutions or compiled from several registries.[2–9] It is further claimed that tumours at the most frequent sites, i.e. mandible and maxilla, are less malignant based on a better prognosis and lower incidence of metastatic spread as compared with osteosarcomas arising elsewhere.[8,10,11] We report all histologically proven cranio-facial osteosarcomas occurring over a 20-year period in The Netherlands, based on the national registration covering all Dutch pathology laboratories (PALGA).

Methods

A population-based study was carried out examining all osteosarcomas seen in the Dutch pathology laboratories between 1 January 1991 and 31 December 2011, based on the Pathologisch Anatomisch Landelijk Geautomatiseerd Archief (PALGA; http://www.palga.nl) registry. The PALGA registration system has 100% coverage of all histology specimens in The Netherlands. The search for osteosarcoma specimens was restricted to certain topographical sites using the following terms: skull, mouth, dental elements, mandible, maxilla, jaw, nasal sinuses, head, face, cheek, pterygoid area, neck, and intracranial site. Items collected were specimen number, date of investigation, gender, age at the time of specimen collection, and description of the pathological findings. Sequential specimens taken from the same patient were linked to the individual person based on the date of birth and the first four characters of the family name. In cases where more than one sample was available, the topography and diagnosis were ascribed to the first sample. Primary osteosarcomas were

0901-5027/0107 + 06 $36.00/0

defined as non-metastatic lesions and malignancies not preceded by an anomaly of bone, local irradiation, or an underlying syndrome. Osteosarcoma lesions not meeting these criteria were termed secondary.

Thirty-one reports were retrieved from the literature for comparison purposes.[2–5,7–10,12–34] With regard to the grading of pathology, the data were expressed based on Broders' grading, adjusted as follows: all grade III and IV tumours were defined as high-grade, in line with the World Health Organization (WHO) grading system.

IBM SPSS Statistics, version 19.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Calculations of incidence were done on the basis of population data, obtained from the Statline Database of Statistics Netherlands. Statistics Netherlands is the governmental organization responsible for collecting and processing data in order to publish statistics for use in practice by policymakers and for scientific research (http://www.cbs.nl).

Results

Four hundred and ninety-four samples were collected from the database. Some of the samples were excluded, for the following reasons: five were from non-cranio-facial sites, 10 originated from patients not living in The Netherlands, 24 had a diagnosis other than osteosarcoma, four were metastatic lesions, 17 osteosarcomas originated from irradiated areas, three specimens proved to be specimens taken at relapse, and one patient had been suffering from Paget's disease. The age of the remaining patients ranged from 0 to 96 years (median age 42 years, mean age 42 years). The age of patients with secondary non-metastatic osteosarcoma lesions ranged from 13 to 77 years (median 56 years, mean 50 years; two-sided *t*-test $P = 0.19$). The total population of The Netherlands increased from 15.0 to 16.6 million inhabitants during the study period. Accordingly the incidence rate of primary cranio-facial osteosarcomas was 0.39 per million. On relating the incidence rates to specific age cohorts, it was found that the incidence of primary tumours was similar across age ranges, whereas the incidence of secondary non-metastatic osteosarcoma lesions increased with age (Table 1). Further analysis was done only on the data of the 121 patients suffering from primary osteosarcomas. The distribution by age was indeed found to be similar to the population pyramid (Fig. 1). The distribution of the sites of primary osteosarcoma is given in Fig. 2.

Table 1. Age-corrected incidences of primary and secondary tumours per million.

Age range, years	Primary tumours	Secondary tumours
0–20	0.3274	0.0393
21–40	0.4096	0.0482
41–60	0.3682	0.0409
61–80	0.3436	0.0654
81–100	0.3555	0

With respect to the histological subtypes, a juxtacortical osteosarcoma was diagnosed in one patient and a periosteal osteosarcoma was found in another patient; the remaining tumours were classical osteosarcomas. Forty-eight percent of the patients were male. With respect to the grading of malignancy, 61% were graded as high malignant, 7% as intermediate malignant, and 28% as low malignant. No conclusion on the grade of malignancy could be drawn from the pathology report in 4% of cases. The statistical analysis revealed that tumours located in the maxilla were more often of low malignancy grade (12 out of 35; $P = 0.033$, χ^2 analysis).

Thirty-one reports were retrieved from the literature for comparison purposes.[2–5,7–10,12–34] A summary is given in Table 2. Only six reports were based on primary tumours alone; a comparison of these data with the data from all reports found in the literature and our data is given in Table 3.[7,10,14,16,18,29]

Discussion

Osteosarcomas are mostly noted in the long bones and are presumed to have the highest incidence in the second decade of life. International studies on osteosarcomas have excluded cranio-facial osteosarcomas based on the presumed lower malignancy grade of these tumours at higher ages. Several problems were encountered when comparing our data from the comprehensive national registry with the literature data. First of all, many reports originate from single institutions or from voluntary registries, possibly leading to various types of bias. The cited studies reporting on cranio-facial osteosarcoma considered 1382 cases in total. The number of patients per report ranges from 7 to 496, with a mean of 45 cases per report. Secondly, a considerable number of patients had developed osteosarcomas related to a primary bone disease (mainly Paget's disease or fibrous dysplasia), or had developed osteosarcoma after previous irradiation. Thirdly, some reports

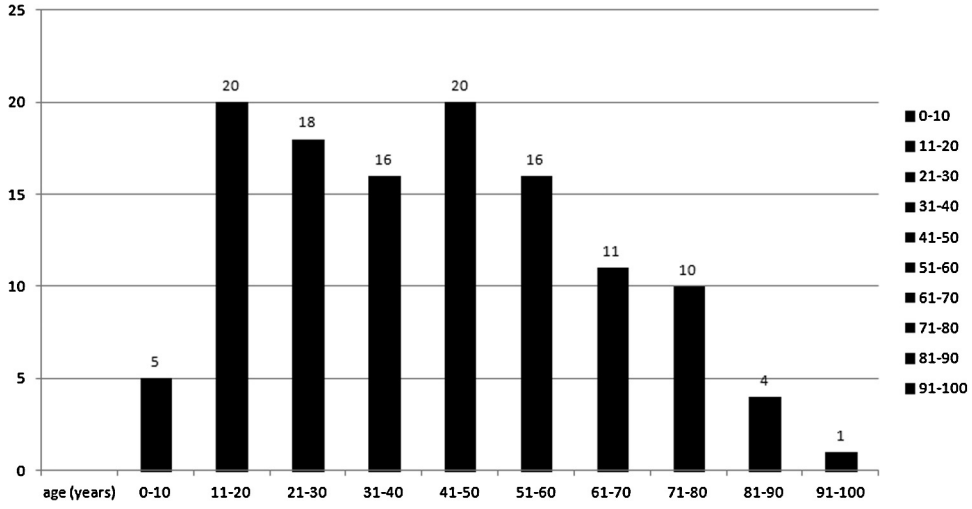

Fig. 1. Distribution according to age.