Osteochondroma: Review of 431 patients from one medical institution in South China

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ABSTRACT

Background: The geographic distribution of osteochondroma (OC) varies greatly around the world. There has been no recent report on OC in a large Chinese population. The aim of this study was to characterize OC by an epidemiological analysis of the clinical data from one medical institution in South China.

Methods: We searched medical electronic records from January 2001 to January 2016 in one large hospital in South China to identify patients with a definite diagnosis of OC. Their epidemiological data were collected and analyzed statistically, including gender, tumor site, age at first diagnosis and symptoms, local recurrence and malignant transformation. Differences between genders and between solitary osteochondroma (SO) and multiple osteochondroma (MO) were particularly analyzed.

Results: A total of 431 OC patients (291 males and 140 females; 329 SOs and 102 MOs) were identified. The gender ratio was 2.08 with a male predominance. OCs were mostly located around the knee (250 cases). 280 patients were in their 0s to 20s upon first diagnosis. The average age at the time of first diagnosis was 20.63 years for all, 18.47 years for males and 25.11 years for females (P=0.000). OC recurred locally in 35 patients (15 SOs and 20 MOs), with a significant difference between SO/MO (P=0.000) but not between genders (P=0.100). The average interval from the primary surgery to local or malignant recurrence was 37.41 months. Malignant transformation was found in 5 patients (4 males and 1 female), showing no gender difference (P=0.549).

Conclusions: OC may have a male predominance in Chinese population. It mostly occurred at 0–20 years of age and around the knee. Upon the first diagnosis of OC, the males tended to be younger than the females, and so did the MO patients than the SO ones. In addition, MO had a higher incidence of local recurrence. Intervals from primary surgery to local recurrence or malignant transformation in MO patients were longer than in SO patients.

1. Introduction

Osteochondroma (OC), also known as osteocartilaginous exostosis or cartilage-capped exostosis, is a broad (sessile) or narrow (pedunculated) skeletal protrusion comprised of marrow and cortical bone [1–4]. The cartilaginous cap is the site of growth, which normally diminishes after skeletal maturity. The tumor is presented as a locally benign neoplasm, which favors the meta-epiphyseal region of long bones like the distal femur, as well as the proximal tibia or humerus in the extremity [5,6,8]. Of all benign bone tumors, OC accounts for more than one-third, the most common benign bone tumor around the world [4,7–11,15]. Although it is benign, its biological behavior still has a malignant potential. Chondrosarcoma arising in osteochondroma has been recognized for many years [12–14]. It is generally believed that malignant transformation of osteochondroma towards secondary peripheral chondrosarcoma is estimated to occur in 0.5–5% [14].

The epidemiological characteristics of OC from different countries or regions appear to be quite variable. The incidences of OC for Asian populations in India, Thailand and Iran were respectively 18.5% [15], 21.4% [16] and 31.9% [7]. When it comes to Europeans, it had an incidence of 17.2% [17] in the Black Sea region and 21.3% [18] in Croatia. The incidence was about 9.9% for American population [9], and 31.3% [8] in Mexico. In the Africans in Nigeria, it even ranged from 15.2% to 27.7% [19–22].

In China, He et al. [5] and Feng et al. [23] reported only primary bone tumor above 20 years. To date, however, the epidemiological survey on a large series of Chinese OC patients has not been found. Therefore, it is necessary to conduct surveys for knowledge of the...
current epidemiological characteristics of OC in Chinese population. The present study investigated the current epidemiological characteristics and clinical symptoms of solitary osteochondroma (SO) and multiple osteochondromas (MO) treated at our institution, Nanfang Hospital, Southern Medical University, Guangzhou, China.

2. Patients and methods

2.1. Study design and data sources

This retrospective analysis collected the data (including images) from the medical electronic records at our institution where in the period from January 2001 to January 2016, 431 patients with a definite diagnosis of OC, including SO and MO, were treated. We conducted eligible assessment when the initial records of the patients had been retrieved (Fig. 1).

2.2. Inclusion and exclusion criteria

Eligible patients were those with a confirmed diagnosis of body OC involving extremity bones and non-extremity bones (e.g. clavicle, scapula, rib, spine, etc.) and with complete medical records regarding gender, tumor localization, age at the first diagnosis, age upon symptom presentation or when the tumor was found, local recurrence and malignant transformation of osteochondroma, family history, and symptoms before surgery. All lesions acquired by biopsy or resection were analyzed at the Department of Clinical Pathology. The final histological diagnosis was correlated with clinical presentations and imaging findings by two authors.

We excluded from this present study those who: (1) had been diagnosed with OC in the head bones (e.g. skull, jaw, etc.); (2) had been suspected as patients with OC but without a final pathological diagnosis; (3) lacked sufficient medical information.

2.3. Analysis of data collected

We analyzed overall epidemiological data of OC to find the gender ratio, the most likely site, the peak age range and, in particular, the effects of gender on tumor site, age at the first diagnosis, local recurrence and malignant transformation of osteochondroma and clinical symptoms. We further compared our findings with those reported in other parts of China [23–26].

2.4. Statistical analysis

Continuous variables were expressed as the mean and standard deviation. Descriptive statistics were performed to calculate the frequency and percentages of the aforementioned variables. Age distribution was stratified into various groups at 10-year intervals. T-test was carried out to evaluate the differences of continuous variables between two genders. Chi-square test was applied to assess the differences of dichotomous variables. Statistically significant difference was defined as P value of < 0.05. The statistical analysis was done using the SPSS 17.0 software (Chicago, Illinois).

3. Results

3.1. Eligible patients for analysis

Patient identification: A total of 626 patients were identified initially. After the records were reviewed, we finally included 431 eligible patients for the present study. Of them, 426 (98.8%) were treated by at least one surgery at our institution and the remaining 5 only followed. The average follow-up was 7.21 years (range, from 1 to 16 years). The follow-up was done by a periodical clinical examination and radiography. The identification and inclusion process was illustrated in Fig. 1.

3.2. Findings of analysis

3.2.1. Primary tumor site and family history

In the present study, 313 tumors were located in the upper limb, 691 in the lower limb and 45 at other sites. 541 osteochondromas were on the left hemi-body, 499 on the right and 9 on other sites. However, significant differences were observed regarding SO and MO distribution
between the left and the right hemi-body, but no significant differences between males and females.

The top three tumor locations were the proximal part of tibia (215 cases), the distal part of femur (173 cases) and the proximal part of fibula (92 cases). Besides, a sum of 480 tumors were around the knee (Table 1), accounting for 45.76% of the whole OC. Being a little different from the third top tumor location in the proximal fibula for MO, male and female, SO was given the proximal humerus (Tables 1, 2). The top three tumor locations for SO and MO and Gender were listed in Tables 1 and 2.

Of all the 102 MO cases, 15 (14.7%) were reported to have had a family history, but none of the SO cases had a family history. Likewise, of 15 MO patients, 9 males and 6 females were found to have a family history without a difference (Table 1).

### Table 1
Clinical data of 431 OC patients.

| Items                                      | Male     | Female   | P value |
|--------------------------------------------|----------|----------|---------|
| Patients                                   | 291      | 140      | –       |
| Total tumors                               | 757      | 292      | –       |
| SO/MO ratio                                | 2.83 (215/76) | 4.38 (114/26) | 0.084 |
| Left/right/others                          | 400/349/8| 141/150/1| 0.189  |
| Lower limb/upper limb/others               | 493/233/31| 198/80/14| 0.528  |
| Tumors located around the knee (%)         | 334(44.1%)| 146(50.0%)| 0.087  |
| Top three tumor locations                  |          |          |         |
| Proximal part of tibia (%)                 | 137(18.1%)| 78(26.7%) | –       |
| Distal part of femur (%)                   | 130(17.2%)| 43(14.7%) | –       |
| Proximal part of fibula (%)                | 67(8.9%)  | 25(8.6%)  | –       |
| Age at 1st diagnosis (year) Mean (SD)      | 18.47(12.52) | 25.11(17.30) | 0.000 |
| Symptoms or discovery age (year) Mean (SD) | 15.34(12.29) | 22.46(17.31) | 0.000 |
| Local recurrence (%)                        | 28(6.6%)  | 7(5.0%)   | 0.100  |
| Chondrosarcoma arising in osteochondroma (%)| 4(1.37%)  | 10(7.2%)  | 0.549  |
| Interval from 1st surgery to local recurrence or malignant transformation (month) mean (SD) | 38.97(48.95) | 31.30(35.73) | 0.000 |
| Family history (%)                         | 9(3.1%)  | 6(4.3%)  | 0.527  |

### Table 2
Comparison of SO and MO in 431 OC patients.

| Items                                      | SO       | MO       | P value |
|--------------------------------------------|----------|----------|---------|
| Patients                                   | 329      | 102      | –       |
| Sex ratio (male/female)                    | 1.89(215/114) | 2.92(76/26) | 0.084 |
| Left/right/others                          | 158/163/8| 383/336/1| 0.000  |
| Lower limb/upper limb/others               | 230/88/11| 461/225/34| 0.156 |
| Tumors located around the knee (%)         | 164(49.85%)| 316(43.89%)| 0.072 |
| Top three tumor locations                  |          |          |         |
| Proximal part of tibia (%)                 | 90(27.4%)| 125(17.4%)| –       |
| Distal part of femur (%)                   | 59(17.9%)| 114(15.8%)| –       |
| Proximal part of humerus (%)               | 26(7.9%) | –        | –       |
| Proximal part of fibula (%)                | –        | 77(10.7%)| –       |
| Age at the first diagnosis (year) Mean (SD)| 21.80(15.22) | 16.85(11.49) | 0.003 |
| Symptoms or discovery age (year) Mean(SD)  | 19.73(14.91) | 10.95(10.62) | 0.000 |
| Local recurrence (%)                       | 15(4.6%) | 20(19.6%)| 0.000  |
| Second surgery on the other location (%)   | –        | 11(10.8%)| –       |
| Chondrosarcoma arising in osteochondroma (%)| 2(0.6%)  | 3(2.9%)  | 0.055  |
| Interval from 1st surgery to local recurrence or malignant transformation (month) mean (SD) | 27.94(26.67) | 42.00(53.09) | 0.000 |
| Family history (%)                         | 0(0%)    | 15(14.7%)| –       |

#### 3.2.2. Average age at first diagnosis and symptoms age

As revealed by Figs. 3 and 4 of age distribution, the overall average age at the first diagnosis was 20.63 years (range, 0–71 years), and the average age when the symptoms or tumors were found was 17.65 years (range, 0–70 years). 280 patients (64.97%) first diagnosed with OC and 308 patients (71.46%) with symptomatic or tumors found age were in their 0s to 20s.

Significant differences were identified regarding the average ages at the first diagnosis and when the symptoms or tumors were found not only between males and females but also between SO and MO (Tables 1 and 2).
3.2.3. OC local recurrence and malignant transformation

In our series, altogether 45 patients (10.44%) were treated by at least two surgeries at a local hospital or our institution. Of them, 35 (15 SOs and 20 MOs) had tumor local recurrence (Fig. 5). Tumors around the knee accounted for the largest part (40.54%). A statistical difference regarding local recurrence was observed between SO and MO, but not between genders (Tables 1 and 2). The mean interval from the first surgery to local recurrence or malignant transformation of osteochondroma was 27.94 months for SO and 42.00 months for MO respectively, showing a significant difference. Likewise, it was not a significant difference between genders.
difference between males and females (Table 1).

Malignant transformation of osteochondroma was observed in 5 patients (4 males & 1 female; 2 SOs & 3 MOs), showing no significant differences regarding gender or tumor site. The 5 primary tumor locations were the proximal tibia and spine for SO and the proximal fibula and the iliac bone and clavicle for MO.

3.2.4. Symptoms before surgery and treatment of 431 osteochondromas

The most common symptoms before surgery for both SO and MO were cosmetic problems inadvertently found and pain. However, the malformation of forearms and calves was not uncommon for MO. Of all the 102 MOs in our study, only 15 (14.7%) had a positive family history, SO/MO ratio also approximate to those reported in other countries which occurred in an age range of 0–30 years in Chinese population, which is similar to other reports in China [23–26] (Table 4).

3.3. Comparison with similar studies in China

Similarities between our findings and those reported in other regions in China [23–26] were identified in gender ratio, SO/MO ratio, OC’s rank in benign bone tumors, top two tumor locations, and the age group most commonly affected (Table 4).

Table 3
Clinical symptoms and treatment of 431 OC patients.

| Items | SO | MO |
|-------|----|----|
| Symptoms before surgery | | |
| Asymptomatic (Cosmetic problems or inadvertently found) | 198 | 34 |
| Pain | 106 | 37 |
| Gradually grow up | 20 | 10 |
| Swelling | 13 | 7 |
| Decreased range of movement | 13 | 16 |
| Compression of peripheral nerves | 10 | 6 |
| Malformation | 7 | 26 |
| Limb weakness or vessel compression | 3 | 1 |
| Ligament injury | 2 | 1 |
| Post trauma | 2 | 0 |
| Dislocation | 1 | 5 |
| Leg-length discrepancy | 1 | 0 |
| Joint effusion | 1 | 0 |
| Paraplegic | 1 | 0 |
| Pathological fracture | 0 | 2 |
| Surgical treatment | | |
| Resection or extensive curettage | 328 | 98 |
| Correlative osteotomy | 2 | 8 |
| Open reduction with fixation | 0 | 6 |
| Ligament repair | 2 | 1 |
| Neurolysis | 1 | 2 |
| Bone grafting | 0 | 2 |
| Joint replacement | 0 | 1 |

4. Discussion

This paper presents a large record of OC from a single institution that caters to South China. OC might have a male predominance in Chinese patients and frequently occurred in an age of the first 2 decades. In fact, most lesions were found during the period of rapid skeletal growth. According to our findings, local recurrence might occur after a mean time of 37.41 months following the first surgery.

With regard to gender ratio, our finding (2.08) is in accordance with previous reports that body OC in Chinese population showed a predominance in men (from 1.35 to 2.65) [5,23–26]. Besides, our gender ratio also approximate to those reported in other countries which had a slightly greater proportion of females (56%) in those with multiple hereditary exostoses who responded. In addition, our SO/MO ratio (3.23) is approximate to 3.60 reported by Altay's study [29], but much lower than that (7.86) reported by Ahmed [12].

Although, in our study, osteochondromas might occur on any bone (Fig. 2) preformed in cartilage, they were especially seen on the long bones of the extremities, predominantly around the knee. In fact, the lower limb seemed to be at a higher risk of the tumor than the upper limb (Table 2). With regard to the most frequent locations in the total OC patients, our findings agree with other reports in China (Table 4) and Mexico [8] on the top two locations: distal part of the femur and proximal part of theibia. It is interesting that in the current study the top three OC locations respectively for males, females and total OC patients were the same (the distal femur, the proximalibia and the proximal fibula). According to the literature [34,35], however, the proximal humerus ranked the third place for SO while the proximal fibula for MO (Tables 1 and 2). About half of the OCs were located around the knee in the current study, but other studies reported different percentages of OC around the knee, ranging from 37.6% to 40% [27,32,43].

Of all the 102 MOs in our study, only 15 (14.7%) had a positive family history, but approximately 62% of the MO patients did according to Legeni-Mallet [33]. Some researchers think Multiple Hereditary Exostoses (MHE) is caused by mutations in two genes, EXT1 and EXT2 [14,34,35]. OC patients may have a male predominance because their mode of transmission is autosomally dominant and females tend to have a milder phenotype [14,33].

Regarding the age distribution, we found that OC frequently occurred in an age range of 0–30 years in Chinese population, which is similar to other reports in China [23–26] (Table 4). Moreover, similarities were also identified between the current study and other studies in the average ages at first diagnosis for total, male and female patients respectively. Age at first diagnosis (average 20.63) and symptoms age (average 17.65) are shown in Figs. 3 and 4. The age range most
commonly affected by OC was 11–20 years (42.9%; 185 cases), followed by 21–30 years (22.0%; 95 cases) and 1–10 years (15.8%; 68 cases). In our study, the youngest patient was a 5-month-old boy, with tumor at the left distal part of the radius while the oldest patient was a 71-year-old male, with SO in the fourth and fifth lumbar vertebrae.

In current study, the local recurrence rate of OC was 8.12%. The local recurrence rate of MO (19.6%) was significantly higher than that of SO (4.6%), but showing no significantly difference between males and females (Tables 1 and 2). However, Bottner et al. [32] reported that the local recurrence rate was 5.8% (1.2% for SO and 13.3% for MO). Indeed, surgical procedures (curettage, extensive curettage and resection) might have affected the outcomes, especially the recurrence rate. There is also a great difference in the local recurrence rates of OC reported, ranging from 1.8% to 5.8% [27,32,36,37]. As is shown in Fig. 5, the top three sites of local recurrence were the proximal tibia, distal femur and proximal humerus. Besides, no significant difference was observed in the average interval from the first surgery to local recurrence or malignant transformation between genders, but a significantly longer interval was observed in MO patients than in SO ones, with a median of 37 months (range, 1–240 months) for the total patients. Some authors [38,39] indicated that the local recurrence was seen in cases of incomplete removal of the cartilage cap but young age at the time of surgery might have been an additional prognostic factor.

Osteochondromas are benign lesions that do not affect life expectancy. However, the risk of malignant transformation (to secondary chondrosarcoma) should be taken onto consideration, especially in cases of multiple exostoses. MO Patients seemed to have a much higher rate of malignant transformation than SO ones (2.9% versus 0.6%), but no statistical difference was found (P = 0.055) (Table 2). Therefore, a much larger sample size is needed to elucidate whether there is a SO/MO difference in this point. There was no significant difference in chondrosarcoma arising in osteochondroma between genders. Similar to our study (1.16% for total), the incidence of malignant transformation for total reported previously ranged from 1% to 5% (from 1% to 3.57% for SO and from less than 1–25% for MO) [6,13,26,27,32,40,41]. In this current study, histological evaluation showed a well-differentiated low-grade chondrosarcoma (with a better prognosis) in five patients (1.16%) who were 19, 34, 49, 28 and 62 years old, respectively. The first three had MO and the latter two SO. All the five lesions were located in the proximal tibia and thoracic vertebra (SO) and in the pelvis, proximal fibula and clavicle (MO) respectively. Moreover, the patients with malignant transformation (with a mean age of 38.4 years) were older than those without malignant transformation (with a mean age of 20.4 years).

Osteochondroma is generally asymptomatic or discovered accidentally, but it can cause pain, local swelling, bony deformities, fracture, bursa formation, arthritis and impingement on adjacent tendons, vascular or neurologic compromise, and dislocation [14,32,42–44]. In our study, most SOs caused no symptoms and were discovered incidentally, but pain was the most common symptom in MO patients (Table 3). Interestingly, two subungual osteochondromas were found with a definite trauma history in our study, as reported by DaCambrã [45]. The tumor might have been a reactive metaplasia resulting from micro-trauma. As pointed out by Goud [41], MO is a chronic, often painful disease that has a more profound impact on quality of life. Surgery should be indicated when the lesion is large enough to be unsightly or produce symptoms from pressure on surrounding structures, or when roentgenographic features suggest malignancy. In most situations in which excision of osteochondroma was chosen, surgery was usually curative. In addition, surgeries varied with different situations (Table 3).

This study has several limitations. First, it is a retrospective review of the data prospectively gathered and we noted some lost data because of incomplete medical records. Secondly, as our study was based on the medical records from one institution, the sample size was very limited. Further investigations, especially multi-centered ones with a much large sample size, should be conducted to overcome the limitations of our study.

5. Conclusions

Our epidemiological survey provides medical professionals with useful information about gender ratio, peak occurrence age, frequent locations and average intervals between the first surgery and local recurrence and malignant transformation in Chinese OC patients, which may help the OC therapy in some way. Importantly, males were younger when the tumor was diagnosed or found than females, and so were MO patients than SO ones. Moreover, MO had a higher local recurrence. Intervals from the first surgery to local recurrence or malignant transformation in MO patients were longer than in SO ones. Follow-ups for MO patients should be longer than for SO ones. Patients with the diagnosis of SO should be monitored regularly.

Conflict of interest statement

The authors certify that they, or any members of their immediate families, have no funding or commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

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