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The anatomical distribution of radiological abnormalities
in Kashin-Beck disease in Tibet

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Abstract A radiological study of osteoarticular changes
in Kashin-Beck Disease (KBD) was undertaken on the
appendicular skeleton in 105 patients with KBD, in
31 healthy subjects living in an endemic area and in
30 healthy subjects living in a non-endemic area. The
bone age was delayed in all three populations with no
significant difference between the three studied Tibetan
populations. Radiological changes occur in 56% of pa-
tients with KBD, and are usually bilateral. An analysis of
the distribution of lesions shows a proximo-distal gra-
dient. The changes are more common in the distal aspect
of the limb and the lower limb is involved more com-
monly than the upper limb. The foot and ankle are in-
volved in 89.5% of cases. The radiological changes and
their distribution might be explained by the hypothesis
of inhibition of angiogenesis by mycotoxins, exacerbated
by chemical and physical environmental factors.

Introduction

In China, the diagnosis and severity of KBD is deter-
mined by radiological criteria [17, 19]. The classification
is based on changes seen on X-rays of the bones and
joints of the hand. In this study, we describe the changes
throughout the appendicular skeleton and propose a
grading system based on these changes and their relation
to clinical staging [9].

Materials and methods

The population which we studied included 166 children between 6
and 15 years of age who were divided into three groups: P1, 105
KBD patients; P2, 31 non-KBD patients living in an endemic area;
and P3, 30 non-KBD subjects living in a non-endemic area. The
endemic area includes Nyemo and Llundrup counties (Lhassa Prefec-
ture), Nuedong County (Lhoka Prefecture) and Shetome County
(Shigatse Prefecture). The non-endemic area includes Rinpung
County (Shigatse Prefecture) [6]). In each group, there was an
equal age distribution and boys represented two-thirds of cases.
Informed consent was obtained from the parents. AP X-rays of the
appendicular skeleton were taken, and lateral views of the knee
and ankle. A Lowenstein view of the hip and an oblique view of
the foot were also taken. X-rays were interpreted by two radiolo-
gists and one orthopaedic surgeon. The skeletal maturity was anal-
sed by linear regression. The following metaphyseal or epiphyseal changes were deemed to be diagnostic of KBD: irregularities of bony margins, sclerosis, a cone-shaped metaphysis, fusion or fragmentation.

The following grading system was applied:

Grade 0: no radiological changes.
Grade 1: radiological changes of the epiphysis or metaphysis.
Grade 2: radiological changes of the epiphysis or metaphysis without fusion.
Grade 3: local fusion of the metaphyseal growth plate.

The radiological scale for the whole patient consisted of the sum of the more severe radiological changes seen in the following areas: both hands and wrists; elbows, shoulders, ankles, knees and hips. This sum gives a scale from 0 to 36. This scale is divided into four stages: stage 0, I (1–10), II (11–20) and III (21–36). The bilateral presence of radiological signs was tested for each variable with the $\chi^2$-test. The relationship between the radiological changes and the clinical staging was studied by the $\chi^2$-test.

**Results**

Depending on the site, the reproducibility of the agreement of the interpretation of two X-rays by the two radiologists and the orthopaedic surgeon varied from good to excellent (0.60 $<$ $k$ $<$ 1). Bone maturity as determined from X-rays of the left hand was compared with actual age using the method of Greulich and Pyle [7]. The bone maturity of the Tibetan population in all three groups is significantly less than the western equivalent. Figure 1 shows the linear regression of actual age and bone maturity for the KBD population. In the present KBD population, the evolution of the bone maturity is 2.3 years delayed below the actual age ($P<0.001$). In the healthy population in endemic area (P2) and in non-endemic area (P3) the delay is respectively 3.4 ($P<0.001$) and 3.5 years ($P<0.001$) below the actual age. In between the three Tibetan populations (P1, P2 and P3) the differences are not significant.

The changes are bilateral in 96.6–100% of cases, depending on the site. The left side was used as a reference when comparing the frequency of lesions in different sites. In the KBD population at least one radiological lesion was seen in 56% of cases. In the P2 and P3 groups the percentage of lesions was respectively 13% and 7%. The details of the distribution and grading of the radiological signs are shown in Table 1. The lesions of the

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**Table 1** Radiographic features for the different osteoarticular locations in 105 KBD cases (Lhasa, Lhoca and Shigatse Prefecture, T.A.R.)

<table>
<thead>
<tr>
<th>Osteoarticular location (left)</th>
<th>Nb</th>
<th>Grade 0</th>
<th>Grade 1 (metaphysis)</th>
<th>Grade 1 (epiphysis)</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Total 1, 2, 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand phalanx</td>
<td>104</td>
<td>94</td>
<td>8</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Distal metacarp</td>
<td>104</td>
<td>91</td>
<td>11</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>Proximal metacarp</td>
<td>105</td>
<td>98</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Carpals bones</td>
<td>105</td>
<td>98</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Distal ulna</td>
<td>102</td>
<td>78</td>
<td>22</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>24</td>
</tr>
<tr>
<td>Distal radius</td>
<td>103</td>
<td>84</td>
<td>16</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>Proximal ulna</td>
<td>104</td>
<td>97</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Proximal radius</td>
<td>104</td>
<td>98</td>
<td>2</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Distal humerus</td>
<td>104</td>
<td>95</td>
<td>1</td>
<td>0</td>
<td>7</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Proximal humerus</td>
<td>104</td>
<td>92</td>
<td>4</td>
<td>1</td>
<td>6</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>Foot phalanx</td>
<td>103</td>
<td>79</td>
<td>17</td>
<td>0</td>
<td>5</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td>Distal metacarp</td>
<td>103</td>
<td>74</td>
<td>27</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>29</td>
</tr>
<tr>
<td>Proximal metatarsal</td>
<td>105</td>
<td>86</td>
<td>7</td>
<td>1</td>
<td>9</td>
<td>2</td>
<td>19</td>
</tr>
<tr>
<td>Tarsal bones</td>
<td>105</td>
<td>91</td>
<td>0</td>
<td>14</td>
<td>0</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Distal tibia</td>
<td>104</td>
<td>77</td>
<td>18</td>
<td>1</td>
<td>8</td>
<td>0</td>
<td>27</td>
</tr>
<tr>
<td>Distal fibula</td>
<td>104</td>
<td>84</td>
<td>17</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>Proximal tibia</td>
<td>105</td>
<td>94</td>
<td>6</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>Proximal fibula</td>
<td>105</td>
<td>99</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Distal femur</td>
<td>105</td>
<td>86</td>
<td>13</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>Proximal femur</td>
<td>102</td>
<td>96</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Cotyl</td>
<td>105</td>
<td>98</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>2185</td>
<td>1889</td>
<td>180</td>
<td>35</td>
<td>73</td>
<td>8</td>
<td>296</td>
</tr>
<tr>
<td>Percentage (%)</td>
<td>100</td>
<td>86.5</td>
<td>8.2</td>
<td>1.6</td>
<td>3.3</td>
<td>0.4</td>
<td></td>
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</tbody>
</table>
Fig. 2 A Carpal bone lesions in a 6-year-old boy. B Bilateral lesions of the talus in a 15-year-old girl

carpus and tarsus were classed as epiphyseal lesions and when present were often very advanced (Fig. 2). The frequency and sites of the lesions are shown in Fig. 3. An obvious proximo-distal gradient is seen, with more lesions seen distally than proximally. The lower limb is more frequently and more severely affected than the upper limb. A lesion of the foot and ankle is present in

89.5% of cases with positive radiological findings, and in 48.6% of the total KBD population. Figure 4 shows a typical lesion of the humerus and the clinical appearance of the same patient. Figure 5 shows the knee of a 6-year-old boy.

The relationship was analysed between the radiological features and the clinical staging as described by Mathieu et al. [9, 10]. There is a significant relationship between the radiological appearances of a particular anatomical site and the clinical stage, carpus (P=0.009), proximal ulna (P=0.028), proximal radius (P=0.042), distal humerus (P=0.012), tarsus (P=0.001), distal tibia (P=0.020), proximal fibula (P=0.039) and the hip (P=0.015). Table 2 shows the relationship between the severity of the radiological changes in the four clinical stages. A significant correlation exists between the two classifications (χ²: P<0.001). The sensitivity of the radiological examination is only 56% of the clinical diagnosis whereas the specificity reaches 90% for the X-ray examination.

**Table 2** Relation between the different clinical and radiographic stages in the population P1 and P2 in endemic area (nb=133)

<table>
<thead>
<tr>
<th>X-ray stage</th>
<th>Clinical stage</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>0 (0-10)</td>
<td></td>
<td>27</td>
<td>16</td>
<td>15</td>
<td>14</td>
<td>72</td>
</tr>
<tr>
<td>I (11-20)</td>
<td></td>
<td>4</td>
<td>10</td>
<td>25</td>
<td>15</td>
<td>54</td>
</tr>
<tr>
<td>II (21-36)</td>
<td></td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>31</td>
<td>26</td>
<td>41</td>
<td>35</td>
<td>133</td>
</tr>
</tbody>
</table>

**Discussion**

The present radiological study was undertaken under extremely difficult circumstances, and the plain X-rays were not always of a high quality. However, we have
Fig. 4 A Characteristic shortening of the humerus in a 16-year-old boy. B Clinical appearance of the patient

be able to describe for the first time in Tibet the characteristic radiological features of KBD in the appendicular skeleton. Bone maturity was delayed in all our KBD populations and controls in endemic and non-endemic areas. The delayed bone maturity appeared not to be specifically related to KBD and may be linked to iodine deficiency in these areas. A significant prevalence of goitre exists in Tibet. An appropriate dietary programme of iodine and selenium supplements should be encouraged [11, 12, 16].

The bilateral nature of the symptoms seen in 79% of the cases on a clinical basis [9, 10] is even more evident on radiological examination where 99.4% of the lesions are bilateral. According to the sensitivity and specificity calculation, the early diagnosis of KBD should be made clinically with the severity of the lesions being identified radiologically.

The proximo-distal gradient already described in clinical studies [9, 10] is confirmed by the radiological study. This gradient and also the fact that more frequent and severe lesions are present in the lower limb than the upper limb may be explained by the hypothesis of inhibition of angiogenesis by a mycotoxin produced by fungi present in barley grain [6, 8]. An absence of normal vascular development as observed by Pasteels et al. [13] may be exaggerated by environmental factors such as cold, hypoxia and microtrauma. The cartilage of the growth plate, for instance, and the epiphyseal cartilage seem particularly sensitive to cold, as seen after frostbite in childhood [1, 2, 3, 4, 5, 14, 15, 18]. The characteristics of the radiological lesions may be caused by ischaemia of the growing cartilage. In order further to understand the aetiology of KBD, it will be necessary to investigate the outcome of protecting the extremities from adverse environmental factors, before significant changes in the subchondral bone have occurred. The lesions of
the articular cartilage may appear late, and seem to be 
the result of deformity of joints caused by altered epiph-
ysial growth.

References

1. Bennett RB, Blount WP (1935) Destruction of epiphyses by 
freezing. JAMA 105:661–662
2. Bigelow DR, Ritchie GW (1963) The effects of frostbite in 
1087
changes in the hands following childhood frostbite in-
jury. Skeletal Radiol 6:33–37
6. Chasseur C, Suetsens C, Michel V, Mathieu F, Begaux F, 
Nolard N, Haubruge E (2001) Mycological approach of 
Kashin-Beck disease in Tibet: an overview of 4 years’ study, 
and future. Int Orthop DOI 10.1007/s002640000218
7. Greulich W, Pyle S (1989) Radiographic atlas of skeletal de-
velopment of hand and wrist. Stanford University Press, Stan-
ford
Orthop DOI 10.1007/s0026400100240
M (1997) Clinical manifestations of Kashin-Beck disease in 
Nyemo Valley, Tibet. Int Orthop 21:151–156
10. Mathieu F, Suetsens C, Begaux F, De Maertelaer V, Hinsen-
kamp M (2001) Effects of physical therapy for patients 
suffering from Kashin-Beck disease in Tibet. Int Orthop 
DOI 10.1007/s002640000206
11. Moreno-Reyes R et al. (1998) Kashin-Beck osteoarthropathy in 
rural Tibet in relation to selenium and iodine status. N Engl J 
Med 339:1112–1120
12. Moreno-Reyes R, Suetsens C, Mathieu F, Begaux F, Dun Zhu, 
Rivera T, Boelaert M, Nève J, Perlmutter N, Vanderpas J 
Orthop DOI 10.1007/s002640000016
13. Pasteels JL, Liu Fu-De, Hinsenkamp M, Rooze M, Mathieu F, 
Orthop DOI 10.1007/s002640000190
frostbite. Radiology 93:359–360
Pediatr 36:105–106
1158
ase: radiographic appearance in the hands and wrists. Radiol-
ogy 201:263–270
18. Wenzl JE, Burke EC, Bianco AJ (1967) Epiphyseal destruc-
tion from frostbite of the hands. Am J Dis Child 114:668–
670
pathology of Kashin-Beck disease. In: Chinese Academy of 
Preventive Medicine (CAPM): proceedings of the internation-
al workshop on Kashin-Beck disease and non-communicable 
diseases. WHO, Beijing, pp 56–62