Kashin-Beck disease should fall under scope of Bone and Joint Decade

Progress in treating the disease is inching forward, but the pervasiveness of KBD in some regions demands our attention.

by Maurice Hinsenkamp, MD, PhD

At the dawn of the third millennium, it is surprising to discover how little we know about the origin of an endemic osteoarthropathy known as Kashin-Beck disease (KBD). The disease was described for the first time in 1849 and bears the name of two military surgeons of the Cossack troupes based in Siberia who first studied the disease at the end of the 19th century.

It is a daunting challenge to treat and perhaps eradicate a disease affecting nearly 3 million people in a crescent-shaped region starting in the southeast region of Siberia, crossing the main part of Manchuria in China and North Korea, and ending in central Tibet. KBD is a disabling osteoarticular disease involving growth and joint cartilage. The first symptoms start to appear in patients around age 5. Usually one or two joints become painful and progressively enlarged, and by the time the patient turns 25 years old, more and more joints may be affected.

The thickening of the metaphysal area serves as the inspiration for the Chinese name for KBD, "Taguijiping" or "Big Joint disease." In patients with the disease, the growth of some diaphyses may be impaired, resulting in shorter bone in adults and in some cases a dwarf appearance. The mean size of the adult KBD
Many patients present with a shortened humerus. Above, a 16-year-old boy with KBD exhibits characteristic knee enlargement and bilateral shortening of the humerus.

Pictured is a radiograph of the humerus of the same 16-year-old boy.

population in central Tibet is slightly smaller (males = 157 cm +/- 7; females = 146 cm +/- 9) than the normal Tibetan population. In patients older than 20 years, the evolution of the disease is aspecific; the deformed joints undergo an irreversible osteoarthritic degeneration. Advanced cases may result in severe varus or valgus knee deformities.

Getting involved on the front lines

Our involvement began in 1992 when physical therapist Françoise Mathieu, working for Médecins Sans Frontières (Doctors Without Borders)—Belgium (MSF-B), came to us after performing a survey of KBD incidence in central Tibet. She observed that the disease sometimes affects up to 80% of a village in an

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endemic area, whereas in the same valley other villages present only a few cases. For those districts plagued by widespread KBD, the resulting orthopaedic problems represent a major public health concern.

Despite the heavy human and social economical consequences associated with the disease, there are many reasons why the KBD issue remains unresolved. The endemic areas are typically limited to poor, isolated and rural communities. There is no evidence of a genetic transmission, nor is it contagious. The incidence drops significantly in more civilized regions.

Scientific research on the subject essentially evolved from three groups—the Russians (1850-1950), the Japanese (1905-1945) and the Chinese (1950-present) — but those groups were separated by time and different languages. Even today, very few exchanges exist among the research centers involved in the study of KBD.

KBD requires an international and multidisciplinary treatment approach, since the disease appears to be the manifestation of a multifactorial etiology. Started in 1992 in central Tibet at the initiative of MSF-B, our program was able to gain the commitment and cooperation of the different specialized teams needed for this complex approach. The teams’ enthusiasm was essential to overcoming the practical difficulties they met on the “field”: difficult access to the endemic areas/villages, the problems of working at altitudes over 4000 meters, and no local medical equipment. We presented the first results of our findings and progress in 1999 in Beijing at an international symposium organized by Médecins Sans Frontières under the auspices of the Société Internationale de Chirurgie Orthopédique et de Traumatologie (SICOT). A selection of the most relevant papers will be published soon in International Orthopaedics, the official journal of SICOT.

These results present a description of the disease based on the epidemiological survey and the anthropometry of KBD, the clinical features associated with the disease, and the results of frequent but just as characteristic is the shortening of the humerus.

Tracking the etiology

In the second phase of our program, we investigated the validity behind our most probable etiological hypothesis, which was the presence of a selenium deficiency among the residents of endemic areas, the contamination of the local grain by mycotoxines, and the hemic acids in the drinking water. Selenium is believed to have a protective effect on the chondrocyte membranes against free radicals generated by the mycotoxines or the hemic acids. The population in the endemic area has a mean selenium concentration of 9 ng/ml in the serum, compared to a normal level over 53 ng/ml. However, the same low concentration was also observed in healthy subjects living in the endemic KBD area. Also, the selenium deficiency we suspected did not precisely match that of residents in the endemic area, and as such we were not able to explain the disease based on that criterion alone.

Moreno et al at the Erasme Hospital at the Université Libre de Bruxelles underlined the possible interaction of the combined deficiency in iodine and selenium. In a few cases, goiters and cretinism have been associated with KBD.

An interesting study by Chasseur et al at the Scientific Institute of Public Health in Brussels revealed a positive correlation between the presence of four fungi types in the barley grains and the incidence of KBD. The barley is produced locally and constitutes the main component of these residents’ food. The basic meal is tsampa, which is made with roasted barley flour mixed with tea and yak butter, and the common alcoholic beverage is tsang, made from fermented barley grain. Due to the Tibetans’ local tradition and to the climate, the barley grains are cultivated, harvested and stocked
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in humid conditions, which are an ideal culture medium for the fungi.

An inhibitory effect of mycotoxins

Haubruge et al at the Faculty of Agricultural Sciences in Gembloux, Belgium, identified and analyzed the mycotoxins produced by the involved fungi. These studies, when combined with the histological observation of Pasteels et al, may suggest an inhibitory effect of the mycotoxin on the angiogenesis at the growth plate level. The combination of a deficient vascularization of the metaphysisal area; hypoxia, anemia and hypothyroidism associated with chronic exposure to the cold (involving the extremities of the limbs); and microtraumatism generated by primitive rural working conditions could represent the multifactorial origin of KBD.

Lagrange et al with the MSF-B is currently studying humic acids and especially fulvic acid, an organic acid deriving from the decomposition of plants. Their presence in the spring water continues to be scrutinized, as well as the consequences of the different types of containers used to store the water inside the houses.

Grading prevention efforts

The third approach that is being applied involves investigating the success of ongoing efforts to supplement selenium and iodine levels, decontaminate grains to eliminate the fungi, and institute a sanitation program to improve the quality of the water. Mathieu and colleagues at the MSF-B and the Université Libre de Bruxelles are studying the effect of a physical therapy program involving local Tibetan health assistants who received specific training in working with KBD patients. So far, the results these professionals have had on the mobility of patients’ affected joints have been encouraging. The effects these and other efforts have had on the long-term evolution of the disease, however, are still under investigation. Experimental animal models are also being studied and are part of the ongoing research effort to address longer-term results of the prevention campaigns.

It is clear that given the scope of the KBD problem throughout central Asia there is still work to be done, but progress is being made. On behalf of the various scientific multidisciplinary teams, I acknowledge the hard work of the permanent mission at Médecins Sans Frontières in Lhasa, Tibet, which, given the difficult working conditions, has provided indispensable support for our program. Without them, hope for the children with KBD would not exist.

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