Abstract In 1919, the first report on Kashin-Beck disease (KBD) made by a Japanese doctor described an endemic occurrence in the northern district of Korea. In the 1930s, Dr. Takamori and his colleagues at Manchuria Medical College produced a series of reports on its endemiology, clinical and roentgenological findings observed in the north-eastern district of China. In 1940s, a Tokyo University group led by Dr. Ogata found that the salivary glands of KBD patients were markedly degenerated. Administration of the condensed water taken from the endemic area into experimental rats produced degeneration of the salivary glands and changes in bones and joints similar to those of KBD. Thus, they proposed parotin deficiency theory as the etiology of KBD, and they recommended parotin therapy for KBD in its early stage. In the 1950s, Dr. Takizawa and his colleagues at Chiba University demonstrated that ferulic acid and p-hydroxy-cinnamic acid, found in the drinking water in the endemic area, caused degeneration of the salivary gland in rats. They recommended boiling the drinking water or using activated charcoal for the prevention of KBD. In the 1970s, the Japanese Ministry of Health and Welfare made a nationwide survey for the incidence of KBD in Japan. They concluded that there was no case of KBD in Japan with the exception of a few patients who had been brought up in the northeastern district of China and later had moved to Japan.

Résumé En 1919, la première observation faite par un médecin japonais sur la maladie de Kashin-Beck (KBD) décrit la présence endémique de la maladie dans une région du nord de la Corée. Au cours des années 30, le Dr. Takamori et ses collègues de la Faculté de Médecine de Manchurie présentèrent une série de communications sur l’épidémiologie, la clinique et la radiologie du KBD étudiée au nord de la Chine. Dans les années 40, un équipe de l’Université de Tokyo dirigée par le Dr Ogata découvrent une dégénérescence des glandes salivaires chez les patients atteints de KBD et montre que l’administration de l’eau recueillie dans les régions endémiques produit chez le rat une dégénérescence des glandes salivaires et une modification des os et des articulations semblables au KBD. Ils proposent comme étiologie du KBD une insuffisance parotidienne et recommandent un traitement de “parotine” pour les stades précoces du KBD. Dans les années 50, le Dr Takizawa et ses collègues de l’Université de Chiba démontrent que l’acide ferulique et l’acide p-hydroxy-cinnamic présent dans l’eau des régions endémiques provoque la dégénérescence des glandes salivaires du rat et recommandent soit de faire bouillir l’eau potable ou soit d’utiliser du charbon de bois activé pour prévenir du KBD. Dans les années 70, le Ministère Japonais de la santé a réalisé une enquête nationale sur l’incidence du KBD au Japon qui a conclu son absence au Japon à l’exception de quelques cas qui ont séjourné dans la région du nord-est de la Chine et sont retournés ultérieurement au Japon.

Introduction

This paper presents a historical overview of studies on Kashin-Beck disease (KBD) carried out by Japanese researchers. In 1919 a Japanese army doctor, T. Okano [29], first reported on an endemic condition of progressive polyarthritis found in the northern district of the Korean Peninsula where the altitude above sea level is 1000 m.

Professor Tokio Takamori and his colleagues from Manchuria Medical College made the first discovery of the endemic occurrence of KBD in the northeastern China in the early 1930s. They reported on its clinical features, endemiology, radiology and pathological anatomy at the General Congress of the Japanese Society of Internal Medicine in 1934 [33]. From that time, Takamori and his colleagues kept reporting on various aspects of KBD basing on their own surveys and pathological analyses until the end of World War II [32, 34, 35, 36, 37, 38, 39]. Takamori called the condition dysostosis enchondralis.
endemic area based on its pathological and endemiological findings. Figure 1 illustrates a map drawn by Takamori indicating the endemic area of KBD and goiter in 1940. Takamori classified KBD into three stages based on roentgenological analyses of 116 KBD patients and comparing them with 500 healthy people living in the nonendemic areas in China. He described that, in addition to various grade of deformity and swelling of joints and retarded growth, roentgenological findings of the hand in the first stage of KBD include uneven epiphyseal cartilage, particularly of the proximal phalanx. In the second-stage, ossification in the epiphyseal cartilage, a funnel-shaped defect in the metaphysis and flattened and deformed head of the phalangeal bones was seen. In the third stage, abnormally widened metaphysis, narrowed joint space, advanced osteoporosis of phalangeal bones, and no epiphyseal line were seen on the roentgenogram. Kubo, Aiso, Kako and Hiyeda were among those at Manchuria Medical College who worked with Professor Takamori in studying KBD very intensively in north-eastern China in the 1930s. Kubo et al. [14, 15, 16, 17, 18, 19, 20], Aiso et al. [1,2] and Kako [10, 11, 12] all produced a series of reports on KBD. Hiyeda et al. [4, 5, 6, 7] found that the concentration of iron ions in the blood of KBD patients was higher than that of the normal control subjects, and they proposed the iron intoxication theory as etiology of KBD in 1936 and 1937.

In the 1940s, a Tokyo University group began studying the etiology of KBD. Noguchi et al. [21, 22] reported in 1943 and 1944 that the KMnO₄ concentration in drinking water in the endemic area was much higher than that in the nonendemic area. Ide et al. [8] reported in 1951 that administration of the condensed water taken from the endemic area into rats produced degeneration of the salivary gland and changes in bones and joints similar to those of KBD. Professor Tomosaburo Ogata and his colleagues [23] from Tokyo University reported in 1942 that the salivary glands of KBD patients histologically show marked degeneration and that, therefore, their endocrine function must be impaired. Ogata and Takizawa [23, 24, 25, 26, 27, 28] produced experimental aptalistic rats by excising the salivary glands, and they demonstrated degeneration of the articular cartilage and atrophy of the subchondral bone in these animals. From these facts, Ogata and Takizawa considered that parotin deficiency caused by some exogenous factors might be the cause for KBD. Thus, Ogata and Takizawa proposed parotin deficiency theory as the etiology for KBD. They stated that organic substances contained in the drinking water in the endemic area caused the degeneration of the salivary gland and the gland’s endocrine dysfunction induced osteochondroplasia. They recommended “parotin treatment” for KBD in its early stage. A series of their studies on experimental aptalism in rats and its influences on the