# Chronic Infantile Neurological Cutaneous and Articular Syndrome — An Early Description

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Chronic infantile neurological cutaneous and articular syndrome (CINCA), also known as neonatal onset multisystem inflammatory disease (NOMID), is characterized by arthropathy, central nervous system involvement, and rash[1]. The condition, which becomes evident in the first year of life, has recently been shown to be caused by missense mutations within CIAS1, a gene encoding cryopyrin[2]. Reports of probable cases of CINCA in the current literature date from 1950[3], with formal description of the syndrome in 1981[4].

In 1835, Thomas Brayne, a surgeon from Bradbury in England, published a report of a young boy with enlargement of the epiphyses[5], accompanied by a remarkable portrait Brayne himself had drawn (Figure 1). The clinical history of the 7-year-old boy, the sixth and only affected of 8 children, is given as follows:

"For the first fortnight after birth, nothing peculiar was observed about the child, except that he always cried on awaking from sleep, for which no adequate cause could then be assigned. In a week or two subsequent, he was affected with a diarrhoea, of which she only recollects that the discharges were very copious and very green. About the same time, slight appearances of stiffness and enlargement were observed in the right elbow. The diarrhoea continued unabated, in spite of various remedies; and at seven months he began to waste in his limbs and body, the knees then becoming enlarged, and lastly the wrists and ancles, though the growth of the knees seemed to proceed in a treble proportion to that of the other joints. His mother continued to suckle him until he was three-quarters of a year old. The emaciation and deficiency of the ordinary development in general growth, had become very marked by the time he was fifteen months old.... The diarrhoea continued with little variation; and, after the first year, the secretions often looked bloody and curdled, sometimes passed off insensibly, and were always very offensive.... A severe degree of prolapsus ani accompanied the diarrhoea for a long time; occasionally as much as four inches of the rectum descending, and remaining prolapsed for considerable periods. During the last year the purging has greatly decreased, and the stools have become more natural....

The general aspect of the poor child, is that attempted to be conveyed by the accompanying sketch, which I took as he sat in his mother's lap. The knees and elbows are anchylosed nearly at right angles, so that he is constantly compelled to this posture, whether sitting or lying. His countenance is sallow and rather vacant; but there is often a sparkling in the eyes, and a quickness of attention, when he is addressed, as well as a pertinence in his answers, which show at once that he possesses and has acquired much mental power; and which is in nothing more manifest than by the most perfect resignation, and often by the recommendation of it to his younger brothers, when they are peevish and discontented. His skin is dry and unhealthy, and there are many small spots of a scaly eruption, like the psoriasis guttata of Willan, scattered over his forehead, neck, and shoulders. His voice is squeaking and discordant, as though uttered through a reed, with a peculiar, dry, sibilous tone, which gives one the idea that there is something imperfect in the vocal cartilages or membrane. There is, however, no external hardness or enlargement about the throat, either of the laryngeal cartilages or of the thyroid gland. The shoulders are rather high; the ribs compressed laterally; the sternum prominent; and the extremity of the ensiform cartilage slightly everted. The anterior fontanelle is not yet quite closed; and the cranium measures, round the temples, one foot eight inches. The spine is weak, and curved backwards. The bones of the pelvis, and upper extremities of the thigh bones, present nothing unusual; the latter have the natural degree of curve in their bodies, but, in the view taken, the thighs are entirely concealed by the enlarged knees. The right knee measures one foot seven inches, in its greatest circumference. The elbow, wrist, and ancle joints, are also greatly enlarged, as the figure represents. The elbows are also so much anchylosed that all flexion and extension are destroyed, so much so, that he can only reach his lips with the ends of the fingers of the left hand, and this with the greatest difficulty. The hands are only the size of those of a child of two years old, and the fingers are clumsy and ill formed."

The title of his article indicates Brayne felt the case represented an unusual example of rickets. However, he

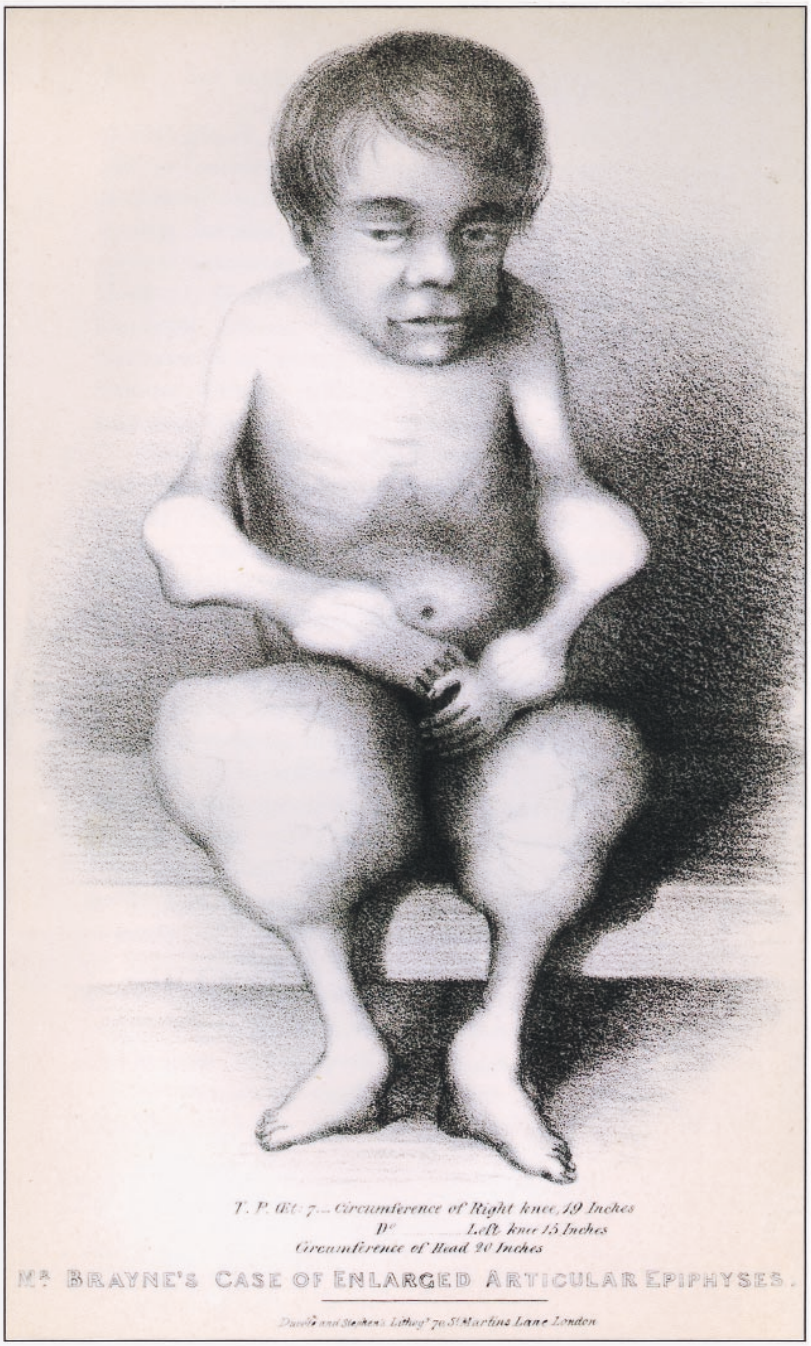


*Figure 1.* Thomas Brayne's 1835 drawing of the 7-year-old boy. Hutchinson J. Severe osteoarthritis in a boy — remarkable distortion of joints, & c. (with portrait). From Hutchinson J. Archives of Surgery 1893;17:82-5. With permission from *British Medical Journal.*

acknowledged that the joint symptoms, first noted in the right elbow in the neonatal period, occurred too early to be due to a dietary deficiency even though he still considered the abnormality in some way resulted from the child's diarrhea:

"...that the defective organization of the epiphyses was connected with some peculiar, but unknown, kind of derangement of the digestive and assimilative functions, is apparent from the reported state of the intestinal discharges. It is probable that, had they been minutely examined, they would have been found to contain, some at least, of the earthy constituents in which the bones were deficient."

He also commented that, for rickets, the predominant epiphyseal site of involvement was atypical in contrast to:

"...in ordinary cases of this defective state of the organization of bone in infancy, the middle of the long bone is found to bend, rather than the articular extremities to become large and spongy. In the subject of the present history, there seems either to have been no disposition to softening in the bodies of the bones of the extremities, or, from his crippled state, weight sufficient to bend them...."

The illustration was republished in black and white by Jonathan Hutchinson in 1893 (better known for his description of abnormal dentition in congenital syphilis), who thought that the condition represented osteoarthritis secondary to chronic rheumatism[6]. The pattern of marked epiphyseal overgrowth, the nonclosure of the anterior fontanelle, and the rash suggest this is a case of CINCA. Thomas Brayne can perhaps be commended for his insightful conclusion as to the possible etiology given the now recognized genetic defect: "...the diseased actions being almost coeval with respiratory life, it is impossible to say whether there may not have been some inherent defect in the foetal organization itself, from the very first actions of the nisus formativus."

## ACKNOWLEDGMENT

We thank the Department of Medical Illustration at the Royal Melbourne Hospital, Melbourne, for reproducing the illustration; and Dr. Jane Smith, Deputy Editor, *British Medical Journal*, for permission to do so.

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