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. 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. Reports of probable cases of CINCA in the current literature date from 1950, with formal description of the syndrome in 1981.

In 1835, Thomas Brayne, a surgeon from Bradbury in England, published a report of a young boy with enlargement of the epiphyses, 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 ankles, 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....
Travers and Allen: Thomas Brayne 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. 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.”

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REFERENCES