

## Slipped Capital Femoral Epiphysis in Two Indian Brothers – The Inheritance of Slipped Capital Femoral Epiphysis Reviewed

In the past, the inheritance pattern of slipped capital femoral epiphysis has been considered to be mainly autosomal dominant.<sup>1</sup> In certain communities, there appears to be a particularly higher incidence of familial slipped capital femoral epiphysis.<sup>1,2</sup> There is also increasing interest in the possible association of this disease with various human leukocyte antigen types.<sup>3-6</sup>

We report a pair of brothers who presented with slipped capital femoral epiphysis within a year. The first sibling was 11-year-old obese (body weight above 90<sup>th</sup> percentile for age), Indian boy who fell down, and sustained an acute, severe right slipped epiphysis. He did not have any endocrine disorders. He underwent traction, followed by gentle manipulation and pinning of the right slipped epiphysis. Unfortunately, his recovery was complicated by avascular necrosis of the right hip at 6 months of follow-up. His implants were removed. Last review at 52 months showed that he still had chronic right hip pain with limitation of range of motion (Fig. 1). Four months after the presentation of the younger sibling, his older 12-year-old brother (also obese with body weight above 90<sup>th</sup> percentile for weight) was admitted for left hip pain of 2 years' duration, which was aggravated by a recent fall. He was diagnosed to have an acute-on-chronic mild left slipped epiphysis. During the admission, he was found to have subclinical hypothyroidism, and was managed accordingly by the endocrinologist. He underwent in-situ pinning of the left slipped epiphysis. Thirteen months after the first slip, he developed a contralateral slip detected on follow-up, and was treated with in-situ pinning of the right slipped epiphysis. He recovered uneventfully, and implants were eventually removed at 23 months after first presentation. Review at 42 months showed that he was well.

The aetiology of slipped capital femoral epiphysis is multifactorial, with an interplay of genetic, environmental (in particular, mechanical) and hormonal factors.<sup>7</sup> In our 2 cases, the older brother, who was also obese, was also found to have subclinical hypothyroidism. We acknowledge that the presence of additional risk factors of obesity and hypothyroidism, with a predisposing positive family history, made this patient particularly at risk for bilateral hip involvement.<sup>7-9</sup>

In a multicentre study involving 1630 children by Loder,<sup>10</sup> a preponderance of males being affected is noted, and certain races are more predisposed to slipped capital femoral epiphysis (e.g., Black children compared to white children). Examining Loder's series, we also noted that the male-to-



Fig. 1. Radiograph showing avascular necrosis of the right hip in the first patient at 52 months after injury.

female ratio is different in different races.<sup>10</sup> These findings suggest a genetic component in this disease. However, environmental, social, and economic factors affecting the different races in different countries can contribute to this variation as well. After all, the susceptibility of an individual to slipped capital femoral epiphysis may be influenced by a genetically determined response to various environmental factors.<sup>11</sup>

Rennie<sup>1</sup> reported a 7% to 14.5% incidence of cases with a positive family history in the Grampian region of, while Loder et al<sup>2</sup> reported a much higher prevalence of 39% of a positive family history amongst the Amish people. These studies were done in stable populations where there may be inbreeding.<sup>2</sup> In his family studies, Rennie<sup>1</sup> suggested that autosomal dominant inheritance with variable penetrance was the likely mode of inheritance. However, he also noted a possibility of an autosomal recessive mode of inheritance in a smaller proportion of patients. There have been also other reports of multiple first degree family members being affected by slipped capital femoral epiphysis.<sup>11,12</sup>

Though the autosomal dominant mode of inheritance in slipped capital femoral epiphysis has been proposed, this has not yet been substantiated.<sup>7</sup> We feel that a multifactorial form of inheritance of slipped capital femoral epiphysis in most populations (which has also been proposed as a possibility by Crossan and Wynne-Davies,<sup>13</sup> may be the most probable form of genetic contribution to this disease for the following reasons:

1. The different incidence of slipped capital femoral epiphysis in different races,

2. A male preponderance is noted in all races,
3. The variation of male to female ratio is noted across populations, and
4. Inbreeding may lead to a concentration of genetic factors contributing to a higher incidence of disease within families in stable populations if a disease has a multifactorial mode of inheritance.

More recently, there has also been found to be a possible association between human leukocyte antigen typing (Human Leucocyte Antigen types A2, A11, B11, B12, B35, DR4, and DR52) and slipped epiphysis in studies of identical twins as well as unrelated patients.<sup>3-6</sup> However, the apparent association of many different human leukocyte antigen types with slipped epiphysis questions the practicality of using human leukocyte antigens as genetic markers for slipped capital femoral epiphysis routinely, and more studies in larger groups of patients need to be performed to study the significance of the association of various human leukocyte antigen types with this disease. However, if these antigens can be successfully used eventually, they can be used as markers for family screening. These laboratory studies were not done for these 2 brothers during the initial work-up because of the cost constraints.

In conclusion, while familial slipped capital femoral epiphysis appears to be associated with mainly autosomal dominant mode of inheritance with variable penetrance in certain populations, we believe that in most other populations across the globe, a multi-factorial form of inheritance is more likely, in this disease. More studies need to be done to understand the underlying genetics of this disease, with the recognition that local environmental conditions can affect the different incidence of slipped capital femoral epiphysis across populations. However, currently available studies suggest that first degree relatives of patients with slipped capital femoral epiphysis are at an increased risk for the disease, and the affected families should be educated accordingly, and screened when indicated.

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