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Legg-Calvé-Perthes disease in children with Down syndrome

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Objective: The aim of this study was to describe the features of Perthes disease in patients with Down syndrome.

Methods: The data of this retrospective case series were collected between 2000 and 2011. Patients were assessed according to demographic, clinical and radiographic classifications.

Results: The study included 7 hips of 6 patients (5 males, 1 female). Mean age at first visit was 6.1 (range: 3.5 to 12.7) years and mean follow-up period was 52.3 (range: 30.2 to 90.8) months. Initial complaints were pain and limping with limited range of motion at the first visit. Range of motion tended toward early improvement despite continuous radiographic changes. One patient had late onset Perthes disease and developed rapid femoral head collapse managed with total hip arthroplasty.

Conclusion: Perthes disease in children with Down syndrome must be followed despite clinical improvement. Radiographic characteristics of Perthes disease in patients with Down syndrome do not differ from those without it.

Key words: Down syndrome; hip; hypothyroidism; Perthes disease.

Legg-Calvé-Perthes disease (Perthes disease) results from avascular necrosis of the femoral head, and results in radiographic changes such as increased bone density, resorption and eventually femoral head deformity.[1] The etiology remains largely unknown and treatment is controversial given the unknown specific cause.[1] Perthes disease affects children, with an incidence four to five times higher in boys than girls.[1,2]

Down syndrome (Trisomy 21) is the most common chromosomal abnormality in children,[3] with incidence of 8.4 per every 10,000 of live births.[4] Down syndrome is associated with hip problems in 8 to 28% of cases.[5] A common finding is a pelvis with wide iliac wings and some children have low-acetabular index with unstable hips.[3] Down syndrome is related to ligamentous laxity and muscular hypotonia.[3,5]

A few reports of occurrence of Perthes disease in patients with Down syndrome have been reported in the literature. One previous study of 114 patients with Down syndrome described 11 with hip disorders; one with Perthes disease.[3]

The aim of this study was to describe the characteristics of Perthes disease in patients diagnosed with Down syndrome.

Patients and methods

After Institutional Review Board approval, 6 patients with Down syndrome who presented to our institution

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and were diagnosed with Perthes disease between 2000 and 2011 were identified. Perthes disease was diagnosed based on radiographic studies and clinical presentation. All medical records and radiographs were reviewed and data collected included patient height, weight, lower limb length, hips range of motion (ROM), severity of symptoms, and any associated medical problems. The first and the last clinical and radiographic assessments were reported for each patient. Radiographic evaluation included assessment of the stage of Perthes disease according to the Waldenström staging[6] and the classification of femoral head deformity based on the lateral pillar[7] and Catterall classifications.[8] Head to teardrop distance,[9] acetabular index,[10] center-edge angle,[11] migration percentage[12] and neck shaft angle were also measured. First visit radiographs were also assessed for head-at-risk factors.[13] Finally, clinical and radiographic findings between the first and the last visit were compared.

Samples were described using the mean for the continuous data, while frequency and percentage were used for categorical data.

Results

This study included 7 hips of 6 patients (5 males, 1 female) with Down syndrome who also had Perthes disease. Of these seven hips, five were the left side (Table 1). Mean age was 6.1 (range: 3.5 to 12.7) years, with 5 of the 6 patients under the age of 9 years. Mean follow-up period was 52.3 (range: 30.2 to 90.8) months.

According to the Waldenström staging, at the first visit, two hips were in Stage 1 (increasing density), four in Stage 2 (fragmentation) and one in Stage 3 (reossification). At the final visit, there were one hip in Stage 2, 3 hips in Stage 3 and 3 healed hips (Stage 4). According to lateral pillar classification, 5 hips were in Class C at the first visit and 2 at the final visit. Four hips were Catterall Class 4 at the first visit and 3 at the final visit (Table 2).

Gage's sign,[13] a V shaped lucency in the lateral part of the epiphysis, was observed in Patient number 3 on the left side. This patient had bilateral involvement and showed lateral calcification on the right hip (Fig. 1). Lateral calcification was also seen in Patient 6. Head to teardrop distance showed difference in patients with unilateral involvement (larger in the affected side). Migration percentage and center-edge angle were also used in order to assess lateral displacement of the femoral head. Three patients had leg length discrepancy of a mean of 1.2 cm.

At the final visit, 3 hips were in the healing stage (Waldenström Stage 4), 2 developed spherical femoral head and one did not. The left hip of Patient 3 had good sphericity of the femoral head (less than 2 mm difference from a circle) (Fig. 1). Patient 6 also had a healed femoral head with good sphericity on the left side although the height of the femoral head epiphysis was less than that of the contralateral normal hip. Patient 4 had a flattened femoral head congruous with the acetabulum.

At the first visit, all patients presented with pain and limping. Patient 2 presented at 12.7 years of age with a rapid progression (Table 3) and underwent total hip arthroplasty within 7 months (Fig. 2). All other patients demonstrated symptom relief (no pain and no limping) and were treated with physical therapy and mild analgesia. Patient 4 later presented to the clinic with severe pain that prevented him from walking. He had pelvic obliquity with stiff painful hip motion and acetabular and femoral osteotomies were suggested as treatment. Based on medical records, all patients demonstrated lim-

Table 1. Study characteristics.

Variables		n	%
Sex	Boys	5	83.3
	Girls	1	16.7
Age (years)	0–9	5	83.3
	>9	1	16.7
LLD	Yes	3	50
	No	3	50
Hip side*	Left	5	71.4
	Right	2	28.6
Treatment*	Physical therapy	6	85.7
	THA	1	14.3

*Frequencies and percentages are for 7 hips. LLD: leg-length discrepancy; THA: total hip arthroplasty

Table 2. Perthes disease staging and classifications.

		First visit		Last visit	
Variables		n	%	n	%
Waldenström	Stage 1	2	28.5	0	0
	Stage 2	4	57.1	1	14.2
	Stage 3	1	14.4	3	42.9
	Stage 4	0	0	3	42.9
Lateral pillar*	Class A	1	14.3	0	0
	Class B	1	14.3	2	28.6
	Class C	5	71.4	2	28.6
Catterall*	Class 1	1	14.3	0	0
	Class 2	1	14.3	0	0
	Class 3	1	14.3	1	14.3
	Class 4	4	57.1	3	42.9

*Two hips were normal at the last visit, and were considered in the percentage.

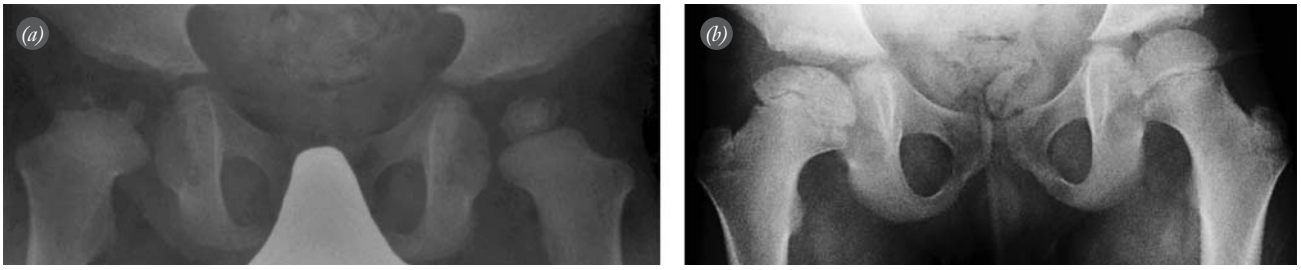

Fig. 1. Case 3; a 3-year-old male who presented with limping. Both hips were involved. **(a)** The patient had bilateral Waldenström Stage 2, lateral pillar and Catterall classifications were C and 4 for the right hip and A and 1 for the left hip, respectively, at the first visit. **(b)** After symptomatic treatment with analgesics, right hip was in Waldenström Stage 3 and left hip was healed at the 5th year follow-up.

ited abduction and internal rotation at the first visit although specific joint ranges could not be confirmed. However, they were asymptomatic (no limping, no pain and no decreased ROM) relatively early during the follow-up period.

One patient (Patient 2) was found to hav e hypothyroidism and 3 patients had normal thyroid function. There were no data on the thyroid status of the remaining 2 patients. Patient 2 developed symptoms of weight gain with increased tiredness and was later diagnosed with hypothyroidism. Table 3 demonstrates the data of our patient sample.

Discussion

The goal of this study was to characterize Perthes disease in patients with Down syndrome. Patients with Down syndrome have a higher incidence of several hip pathologies,[3] although there is no specific information published on Perthes disease in relation to Down syndrome.

Our sample of patients found that boys were more likely than girls to have Perthes disease. This observation has also been reported in otherwise normal children with Perthes disease.[2] The majority of our patients were younger than 9 years of age at the first visit (five patients, six hips) and showed mild to moderate progression of the disease. The late onset of Perthes disease in otherwise healthy children has been reported to have complicated outcomes including severe hip degeneration.[14,15] In our study, the oldest patient (12.7 years) developed the worst progression with rapid collapse and resorption of the femoral head which resembles the destructive pattern of Perthes' disease in the adolescents described by Joseph et al.[16] This patient required a total hip arthroplasty within 7 months of the first visit.

Pain and limping are generally the initial complaints in Perthes disease[1] and were the primary presenting symptoms in the patients in this study. However, these symptoms seemed to resolve relatively quickly with the exception of the older patient who developed severe resorption. Despite clinical improvement, patients showed radiographic signs of progression of the disease in the affected hips.

Catterall classified Perthes disease based on the extent of femoral head involvement[8] and described some radiographic signs as predictors of poor outcome

Table 3. Summary of Perthes staging, classifications, and radiographic measurements of patients in the sample.

					NSA		HTD		CEA		MP		AI		Wal		Lat P		Cat	
	Age	Sex	Side	LOF	First	Last	First	Last	First	Last	First	Last	First	Last	First	Last	First	Last	First	Last
Case 1	4.6	M	L	32.2	148	147	9.6	12.1	17	12	20	36	16	13	1	3	C	C	4	4
Case 2	12.7	F	L	6.9†	152	150	8.6	12.9	38	19	13	55	10	16	1	2	C	C	2	4
Case 3 R*	3.3	M	R	60	145	147	9	7.8	36	30	14	19	9	15	2	3	C	B	4	4
Case 3 L*	3.3	M	L	60	147	144	8	8.4	21	30	15	15	15	15	2	4	A	-	I	-
Case 4	8.5	M	L	21.5	150	152	12.2	15.6	8	10	47	46	16	13	3	4	C	-	4	-
Case 5	3.5	M	R	40.1	148	150	9.1	8	26	28	0	32	16	15	2	3	B	B	3	3
Case 6	4.2	M	L	65.3	147	144	8.6	9.1	30	34	0	0	15	13	2	4	C	-	4	-

*Case 3 is bilateral involvement (R: right, L: left). †Length of follow-up was calculated prior to THA. AI: acetabular index (angles); Cat: Catterall classification; CEA: center-edge angle (deg); F: female; HTD: head to teardrop distance (mm); Lat P: lateral pillar classification; LOF: length of follow-up (months), M: male; MP: migration percentage; NSA: neck-shaft angle (degrees); Wal: Waldenström classification.

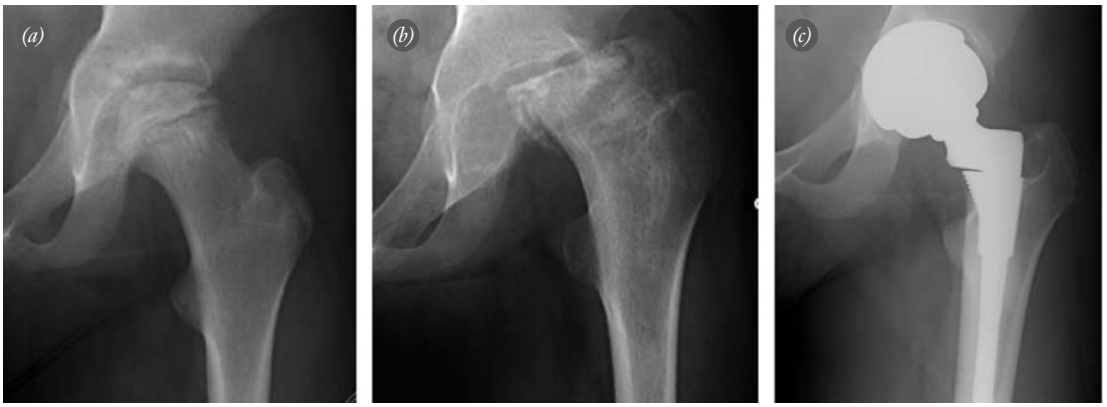

Fig. 2. Case 2; a 12.7-year-old female who presented with pain and limping from the left hip. **(a)** On her first visit, the hip was classified Waldenström Stage 1 **(b)** Seven months later, treated with anti-inflammatories and symptomatic activity restriction but with increased pain, her hip was classified as Waldenström Stage 2. **(c)** The deformity was then treated with total hip arthroplasty.

(head-at-risk factors).[13] Poor outcomes are more likely in patients with severe Perthes disease, classified Catterall 3 and 4.[1] Likewise, lateralization of the femoral head and lateral epiphyseal lucency (Gage's sign) are radiographic signs suggestive of poor prognosis,[14,17] although reliability is not strong.[18] The outcome of Perthes disease can be assessed radiographically based on the sphericity of the femoral head and severe Perthes disease may result in its flattening.[1] Assessment of the clinical outcomes of Perthes disease at skeletal maturity is more accurate.[1] No patient in our sample achieved skeletal maturity during the reported follow-up although the sphericity of the femoral head was used to describe the shape when healing was accomplished.

Treatment of Perthes disease aims to prevent the deformity of the femoral head and to keep it contained in the acetabulum. However, this becomes challenging with late presentation or late onset. Management of Perthes disease ranges from conservative (observation, traction, activity restriction) to surgical treatment (femoral osteotomy or acetabuloplasty). In our patients with Down syndrome, clinical presentation was subtle with few severe symptoms until end-stage disease when they developed pain and refused to walk. Cases of late onset of Perthes may require management with total hip replacement or hip fusion when there is a dramatic collapse of the femoral head inability to reconstruct the hip. Hip arthrodesis is less commonly used than hip arthroplasty despite the higher risk of complications after hip arthroplasty in young patients than older patients.[19] In the oldest patient in our sample, neither surgically feasible alternatives considered (hip fusion or arthroplasty) were ideal.

The presence of hypothyroidism in one patient may be due to hormonal dysfunction commonly seen in Down syndrome.[20] There are several medical conditions that cause changes in the femoral head that mimic Perthes disease, including hypothyroidism.[21] However, these changes need to be bilateral and symmetric.[1,21] The association of hypothyroidism with Down syndrome raises a question about the etiology of femoral head avascular necrosis. While hypothyroidism has been reported at a high frequency in normal children with Perthes disease,[22] this association was not found in other studies.[23]

Limitations of this study include the small study size, which limits the ability to generalize results. Additionally, there was lack of clinical measurement of hip joint ROM in the patient sample. Inference cannot be made based on a small number of cases; however, our observation in this case series is that hip joints tended to preserve good ROM compared to normal children. We also had the impression that pain in the affected hip tended to be less severe in children with Down syndrome.

In conclusion, patients with Down syndrome who present with Perthes disease can be managed and followed up in a manner radiographically similar to children without Down syndrome. Down patients who develop Perthes disease should remain under follow-up even with clinical improvement as radiographic changes continue similarly to unaffected children and may result in the permanent deformation of the femoral head. Hypothyroidism should also be considered in the clinical and laboratory assessment of patients with Down syndrome and Perthes disease.

Conflicts of Interest: No conflicts declared.

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