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Biomechanics of walking in adolescents with progressive pseudorheumatoid arthropathy of childhood leads to physical activity recommendations as therapeutic focus

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ABSTRACT

Background: Progressive pseudorheumatoid arthropathy of childhood is a rare disease with an estimated prevalence of approximately 1/1,000,000. The disease manifests around the age of three to eight years and progresses with symptoms of early fatigue, muscle weakness, joint swelling and stiffness. The resulting functional limitations are often described as having a waddling gait. Walking is difficult and can be managed with multilevel compensation movements only. Aims of this study were to determine typical malpositions that arise during walking and to identify preventive strategies to reduce excessive joint damage.
Methods: This study presents data of three-dimensional gait analysis of nine patients with progressive pseudorheumatoid arthropathy of childhood (♀ = 2; ♂ = 7; 13.3 y; 47.0 kg; 1.39 m; BMI: 24.2 kg/m^2) performed with eight infrared cameras and the Plug-in-Gait Model. For comparison of spatiotemporal and kinematic parameters with age-matched healthy controls (♀ = 6; ♂ = 3; 13.4 y; 49.0 kg; 1.61 m; BMI: 18.9 kg/m^2), the Mann–Whitney *U*-test was applied with a significance level of $P < 0.05$.
Findings: The patients had a significantly lower height, but higher BMI. Walking speed was reduced with wide, but short steps and significant motion anomalies in the pelvis, hips, knees and ankles. Small ranges of motion in propulsion-supporting movements were typical, especially in the sagittal plane. The gait analysis revealed dominant compensatory movements in pelvic obliquity and rotation.
Interpretation: The deficits can be attributed to pronounced muscle weakness plus functional joint impairment and pain. Therapeutic preventive strategies therefore should consider continuous muscle power exercises, stretching programmes and restrictive weight control.

1. Introduction

Progressive pseudorheumatoid arthropathy of childhood (PPAC), also called progressive pseudorheumatoid dysplasia (PPD), is a bone dysplasia following an autosomal recessive inheritance (Spranger et al., 1983a, 1983b). Several mutations in the WISP3 gene on chromosome 6q22 have been identified in patients with PPAC (el-Shanti et al., 1997; Fischer et al., 1998; Temiz et al., 2011). The disease is rare in Europe, with an estimated prevalence of one per million in Great Britain (Wynne-Davies et al., 1982), but occurs more frequently in the Middle East (Teebi and Al Awadi, 1986).

Children suffering from PPAC appear to be quite well within the first years of life. The first symptoms usually occur between the age of three and eight years (Ekbote et al., 2013; Wynne-Davies et al., 1982). Early fatigue, muscular weakness, gait abnormalities, joint swelling and sometimes joint deformities as well as pain and stiffness are primary manifestations (Garcia Segarra et al., 2012; Kozlowski et al., 1986; Shivanand et al., 2007). Joint palpation reveals hard bony overgrowth, which is in contrast to inflammatory effusions and synovial hypertrophy in juvenile idiopathic arthritis (JIA). Rapidly progressive joint contractures are typical in PPAC (Shivanand et al., 2007). The pattern of involved joints is usually symmetric, including large and small joints. Radiographic signs are seen early on during the course of disease in the spine (Ekbote et al., 2013). Our observations show that spine involvement generates the typical clinical appearance with a short trunk at the age of approximately 8 to 9 years. el-Shanti et al. (1997) described a male patient with universal platyspondyly and additional kyphoscoliosis deformity that became obvious at the age of six years.

Diagnosis of PPAC can be verified by typical radiologic features. The joint-forming bones are large and prominent with a metaphyseal enlargement mimicking joint swelling (Garcia Segarra et al., 2012), and the trabecular pattern is coarse (el-Shanti et al., 1997). A characteristic

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radiographic feature of PPAC is the widening of the ends of the phalanges, mainly the ground phalanges. There is no known cure or preventive strategy for PPAC patients to date. Non-steroidal anti-inflammatory drugs (NSAIDs) may relieve pain, but they do not prevent joint destruction. Disease-modifying antirheumatic drugs (DMARDs) and biologic agents have no substantial effect on PPAC (Ye et al., 2012). Consequently, joint replacements may become necessary as soon as the second decade of life to reduce pain and maintain mobility (Garcia Segarra et al., 2012). Regular physiotherapy is very important to decelerate the progress of immobility, and it is mandatory for a functional benefit after successful joint replacement. Measures to sustain mobility including stretching and activation/motivation are important components of therapy in our clinic.

Progressive joint restrictions, muscle weakness, early fatigue and pain cause difficulties in everyday functions. In several case reports, walking abnormalities are presented (el-Shanti et al., 1997; Kaya et al., 2005; Kozlowski et al., 1986) but not specified yet. Most PPAC patients have major walking difficulties. Multilevel compensation movements with other parts of the body are necessary for PPAC patients to walk.

In this article, nine patients with PPAC are presented and compared to a healthy control group (CG) focusing on the results of 3D gait analysis.

The aim of this work is to find typical gait deviations of PPAC and to determine predictors of these functional limitations. The results will help to develop recommendations for efficient preventive strategies.

2. Methods

2.1. Study design and subjects

This study summarises analyses of clinical 3D gait diagnostics in nine PPAC patients who were seen in our clinic between 2006 and 2010.

The median age of the patients (female = 2, male = 7) was 13.3 y (range 7.4–18.8 y). Median height was 1.39 m (range 1.30–1.49 m) and body weight 47.0 kg (range 37.0–62.3 kg) resulting in a median Body-Mass-Index (BMI = body weight/body height^2 (kg/m^2)) of 24.2 kg/m^2 (range 19.7–29.6 kg/m^2). We compared the data of PPAC patients to an age-matched healthy CG of nine young persons (female = 6, male = 3; median age: 13.4 y (range 9.5–19.6 y); height: 1.61 m (range 1.43–1.66 m); weight: 49.0 kg (range 37.0–63.8 kg); BMI: 18.9 kg/m^2 (range 14.6–24.3 kg/m^2)). Age-matching was performed by an election throughout a normal data pool. Gender was assumed to be irrelevant as only minor differences in BMI between female and male were observed in the relating age group (Kurth and Schaffrath Rosario, 2007). Ethical approval has been given by an external medical research ethics committee (Reference 351/14).

2.2. Clinical manifestation

Disease onset in all children was within the first 4 years of life, with the youngest, a girl, presenting the first symptoms around the age of 10 months. The diagnosis of PPAC, however, was delayed in all children until they were between 6 and 12 years old. In five of the nine patients (two brothers), the diagnosis was verified additionally by determining the mutation in the WISP 3 gene. The other four patients (one sibling pair) were diagnosed due to typical clinical and radiologic findings.

All but one of the children showed an abnormal gait as a first symptom. It is usually described as waddling with an enlarged step width (Ye et al., 2012). Another early symptom was swelling of the interphalangeal finger joints. In three patients, muscular weakness was a leading early symptom, and in two of them, this resulted in a muscular biopsy, which was normal. Joint pain at onset was only described in three patients.

Pain and functional impairment was progressive in all patients. At the time of this investigation, the measurement of joint mobility with the neutral-zero-method (Cave and Roberts, 1936; Hepp and Debrunner, 2004) showed severe contractures in sagittal plane in hip, knee and ankle joint. In detail, the hip joint motion was limited in six of nine patients in extension direction and nine patients had contractures in the flexion. Seven patients had restrictions in the knee joint in maximum extension and flexion. The ankle dorsal extension was limited in five patients and all nine had strong deficits in plantarflexion. All limitations occur symmetrically. The gait was severely reduced in four patients, aged 14, 15, 17 and 19 years old. Their free walking distance was less than 100 m. The others were able to walk for at least 10 min. All patients, however, relied on walking aids for everyday life. One patient was measured after consecutive joint replacement of the right knee with a distant of 15 months.

2.3. Instruments and data collection

The clinical gait analysis was performed on a 9 m long walkway with a 3D motion analysis system that contained eight infrared cameras (200 Hz) (Vicon MX F40, Vicon Motion System Ltd., Oxford, England). The participants were marked in accordance to the Plug-in-Gait Model for the lower extremities with 16 reflecting markers (∅ = 14 mm) at defined places from the pelvis downwards (Fig. 1) (Davis et al., 1991).

The participants were asked to select a walking speed that was comfortable for them. To gain confidence with the measuring situation, the participants started with walking along the gangway without being monitored. An experienced investigator decided individually the duration of this phase. While the CG needed at least four test trails, the PPAC patients were measured with only one, or even without test trial due to pain and early fatigue so as being accustomed to demonstrate their physical abilities during medical examinations. This difference was not expected to influence the results because the investigator decided about the validity of every walking trail in dependency on nativeness and regularity.

The gait was scaled and normalised in gait cycles starting with the initial contact and ending with the next initial contact of the same leg (Perry, 2003). The final evaluation considered five left and five right gait cycles for each subject. Both legs were included to get further information about the symmetry between the left and right side.

The analysis focused on the spatiotemporal parameters walking speed, step length and step width. Additional considerations include the duration of the stance phases, loading response, midstance, terminal stance, pre-swing phase and the moment of toe off during one gait cycle as well as the relation between the duration of single support and double support phase.For kinematics, the angle courses of pelvic tilt, obliquity and rotation, hip flexion/extension, knee flexion/extension, ankle dorsal-/plantarflexion, plantar angle in order to describe the roll-off behaviour of the foot and the foot progression angle were considered. We used the range of motion (RoM) between special gait sections as well as the maximum hip extension and the initial ankle (plant/dorsal) position during a gait cycle.

2.4. Statistical analysis

Due to the lack of normal distribution, as determined by the Kolmogorov–Smirnov test, and the small patient group, statistical analyses between the PPAC patients and the CG were performed using the Mann–Whitney *U*-test. Comparisons were made for the left and right sides. For descriptive indices, the median plus quartile 25 and 75 were used. The analyses were bilateral, and statistical significance was determined at the level of $P < 0.05$ (Bortz, 2005). SPSS® 22.0 (IBM, Armonk, USA) was used for the statistical analyses.

3. Results

PPAC patients were compared to an age-matched CG of healthy volunteers with no statistically significant differences in age or weight ($P > 0.05$). The CG however was found to be significantly taller ($P < 0.001$) and consequently had a lower BMI ($P < 0.001$) than the PPAC patients.