

## CASE REPORT

# Pierpont syndrome-Report of a new patient

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## Abstract

We report on a 6-year-old girl with Pierpont Syndrome who was diagnosed using the whole-exome sequencing technique. In addition to commonly recognized traits, our patient had scoliosis, a feature reported only in one other occasion.

## KEYWORDS

female, Pierpont Syndrome, scoliosis

## 1 | INTRODUCTION

Only few cases with Pierpont Syndrome have been published worldwide. We report on a 6-year-old Albanian girl with distinct clinical features, who was diagnosed using the whole-exome sequencing technique. In addition to commonly recognized traits, our patient had scoliosis, a feature reported only in one other occasion.

Pierpont syndrome is a rare multiple congenital anomaly syndrome with unknown etiology. Up till now, only few cases with Pierpont Syndrome have been reported worldwide. Highly suggestive characteristics of the syndrome constitute a distinct facial phenotype and growth and developmental delay. The facial phenotype includes a number of characteristics such as mild midfacial hypoplasia, high forehead, narrow and upward slanted palpebral fissures, high anterior hairline, broad philtrum, broad nasal ridge and tip, flat occiput, full cheeks, together with bowed upper lip and "pouting" lower lip. The confirmation of the diagnosis for the Pierpont syndrome is detection of a specific TBL1XR1 mutation on whole-exome sequencing.<sup>1-4</sup>

We report on a 6-year-old Albanian girl with moderate developmental delay, fat pads at the anteromedial aspect of the heels, difficulty in speaking, reduced hearing, deep palmar and plantar grooves, and a distinct facial phenotype.

## 2 | CASE REPORT

The patient was the first child of healthy and nonconsanguineous Albanian parents and was born after an uneventful pregnancy in the 40th gestational week. She was slightly hypotrophic at birth, having a birth weight of 2950, length of 44 cm (<P3;  $z = -3.62$ ), and occipital frontal circumference (OFC) of 32 cm. At birth, she was diagnosed of having multiple dysplasia of the epiphysis, congenital cataract and pes equinoarus.

Conventional chromosome analysis and array comparative genomic hybridization were normal (46XX).

After six months of breastfeeding, she started supplementary feeding and afterward regular feeding without difficulties. Until age five<sup>5</sup> she was not able to walk.

At the admission, she has hypotrophy and short stature (weight 12 kg, length 85 cm). The global development was delayed. She had no speech development and showed stereotypic behaviors. Facial features included frontal bossing with high forehead, deep-set eyes, flat philtrum, depressed nasal bridge, and everted lower lip. The teeth were widely spaced, and the palate was high arched. She had curly blond hair and low-set ears.

Fat pads were located on the medial border of both feet just anterior to the calcaneus. The toes were overlapping with

the second toe over the third on both sides. Fetal finger and toe fat pads were present as well.

She had a short neck and a discreet pectus excavatum. There was excess skin over arms and legs, causing them to appear puffy (Figure 1A-D). She also had a scoliosis and pes equinovarus (Figure 2A and B).

Brain MRI showed relatively cortical and central hypoplasia of the brain, small frontal lobes as well as minor dilatation of the third and lateral ventricles.

### 3 | METHODS AND RESULTS

A total of 50 ng of genomic DNA was extracted from circulating leukocytes of the patient. The coding exons of 4813 genes, that are associated with known clinical phenotypes, was enriched by his parents. Enrichment was carried out by means of TruSight-One kit (Illumina) following the instructions

from the manufacturer's protocol. Subsequent 150 nucleotide paired-end sequencing was performed on an Illumina MiSeq via v3 chemistry (Illumina). Variant calling and mapping to hg19 was carried out through standard parameters with CLC Biomedical Genomics Workbench (Qiagen).

We identified the heterozygous de novo mutation in TBL1XR1: NM\_024665.4: c.1337A > G, p. (Tyr446Cys) in the patient. The mutation was confirmed via Sanger sequencing. We did not find any other pathogenic variants.

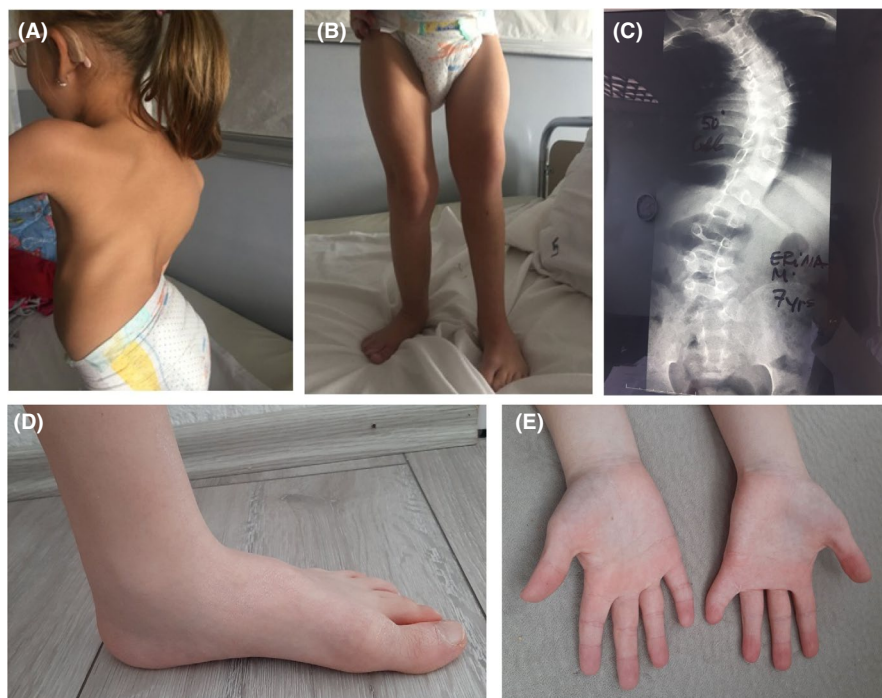
### 4 | DISCUSSION

There are still ambiguities on whether Pierpont syndrome can be categorized as a distinct entity. To the hypoplastic midface, high forehead, a short, broad nose and small, persistent fetal digital pads, widely spaced teeth, fat pads or fullness anteromedial to their heels, together with a significant



**FIGURE 1** A-D, Facial features of the patient: Frontal bossing with high forehead, deep-set eyes, depressed nasal bridge, flat philtrum, and everted lower lip. Widely spaced and the palate was high arched. She had curly blond hair and low-set ears. Short neck and a discreet pectus excavatum

**FIGURE 2** A-E, Fat pads were on the medial border of both feet just anterior to the calcaneus. Fetal finger and toe fat pads were present as well. There was excess skin over arms and legs, causing them to appear puffy. Patient also has a scoliosis (X-ray)



developmental delay originally described as typical for the syndrome,<sup>1,5-7</sup> we added multiple dysplasia of the epiphysis, congenital cataract and pes equinovarus, and confirmed scoliosis<sup>1</sup> as a feature that has been reported in one previous case only and pes equinovarus. Therefore, not all features of the syndrome are clear as well.

Similarly, it is not clear which are the risk factors of the syndrome. For instance, one potential explanation is the advanced age of the parents which makes a new dominant mutational mechanism, resultant in a point mutation in an as yet unidentified gene. Although originally described in male patients, Burkitt and associates reported syndrome in female patient so did we. So, it is not likely that the syndrome is linked to the gender. The role of environmental factors and their modifying influence remains unclear as well. To add up to the ambiguities, there is no reported instance of a child with Pierpont syndrome being born to consanguineous parents, nor of any affected nontwin sibling pairs.

## 5 | CONCLUSION

Beside all uncertainty related to etiology, risk factors and even clinical features, the number of reports of patient with distinctive phenotypic characteristics and delay in development is growing. Therefore, it is very important to stay aware of the possibility of Pierpont syndrome every time we face patient with distinctive craniofacial features, fat pads anteromedial and fetal digital pads to the heels, significant delay in neurological development and growth.

Genetic testing, that should follow the suspicion is reliable to confirm the diagnosis.

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## CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

## AUTHOR CONTRIBUTIONS

All authors are major contributors to the article. VIJ: primary author of the manuscript and together with SHSK did the medical workout of the patient, AJ coauthored the manuscript and reviewed the literature.

## ETHICAL APPROVAL

The article was approved by the Ethical Committee of the Chamber of Doctors of Kosovo and the Ethical Committee of the University Clinical Center of Kosovo.

## DATA AVAILABILITY STATEMENT

I confirm that my article contains a Data Availability Statement even if no data is available (list of sample statements) unless my article type does not require one (eg, Editorials, Corrections, Book Reviews, etc). I confirm that I have included a citation for available data in my references section, unless my article type is exempt.

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