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Case Report
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Ehlers-Danlos Syndrome – An Underdiagnosed Condition

*Rubini C[1], Mohd Sharil IMH[2] and Mohammad CM[3]**

[1]Medical and Health Officer, Klinik Kesihatan Miri, Sarawak Malaysia

[2]Medical and Health Officer, Klinik Kesihatan Merchang, Terengganu, Malaysia

[3]Lecturer/ Family Medicine Specialist, Kulliyyah of Medicine, IIUM Kuantan, Pahang, Malaysia

Abstract

Failure to thrive is a common clinical presentation discovered during continuity of child care at primary care clinic1. The causes of failure to thrive are multifactorial which a challenge becomes in diagnostic process. Hence, the pitfall arises when there are overlapping causes whereby nutritional and psychosocial issues mask the suspicion of medical cause [1]. A well-looking child with failure to thrive is probably considered as normal variants of growth or having nutritional deficiency [2]. We highlighted a case report of a 4 years 9 month-old girl with red flag of failure to thrive who was recently diagnosed to have Ehlers-Danlos Syndrome Hypermobility type based on manifestation of classical signs with a positive Beighton score of eight [3]. She had unresolved failure to thrive after birth despite intervention, with all anthropometric criteria below expected for age and gender. Otherwise, she was asymptomatic and developmentally-age-appropriate. These provide a clue to evaluate for a pathological condition which leads to discovery of this undiagnosed syndrome. Even though there is no cure for Ehlers-Danlos Syndrome, a correct diagnosis helps for appropriate treatment plan to monitor potential complications and provide genetic counselling for the family [3].

Keywords: Failure to thrive; Ehlers-Danlos syndrome hypermobility type

Introduction

Ehlers-Danlos Syndrome (EDS) is a clinically and genetically heterogeneous group of Hereditary Connective Tissue Disorders (HCTD) that involves a genetic defect in collagen and connective tissue synthesis and structure [4]. It is generally characterized by joint hypermobility, skin hyperextensibility and tissue fragility [5]. Despite being a genetic disorder either by autosomal dominant or recessive, the established diagnosis is usually delayed during adolescent or adulthood [4]. Based on Villefranche criteria in 1997, there are six different major types of EDS with varying degrees of tissue involvement, has been widely used as the standard for clinical diagnosis [3]. Recently, the International EDS Consortium 2017 proposed a revised EDS classification, which recognized 13 subtypes with distinct set of clinical criteria serve as a new standard for the diagnosis [4]. The hypermobility type-EDS are the most common subtype with unexpected disability potential [3]. Clinical recognition of the various types of EDS is important, particularly for vascular type (Type IV) as it potentially lethal result from arterial rupture [4].

Case Presentation

We highlighted a case report of 4 years 9 month-old girl with red flag of failure to thrive. She was under paediatric clinic follow-up for failure to thrive but defaulted since two years mainly due to social issues as the access to tertiary hospital is within 1 hour and both her parents are breadwinner of the family. Antenatally, she was small for gestational age but her mother had no obstetric problem. She was born at 37 weeks of gestation with small gestational age of 2.26 kg *via* emergency caesarean for acute fetal distress. Her cord thyroid stimulating hormone, TORCHES screening and ultrasound cranium were unremarkable.

She was developmentally-age-appropriate as assessed by Denver II Chart. She had difficulty in chewing food because of her dental caries and missing deciduous teeth. She taking three main meals with snacks in between and being a "bucket programme" recipient under the Programme for the Rehabilitation of Malnourished Children (PPKZM) since 2 years old till date. Despite adequate nutritional intake, she was still unable to achieve catch-up growth.

The family history revealed that the patient's father had highly flexible joints which were

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*Correspondence:
Muhammad bin Che-Man, Clinical Lecturer and Family Medicine Specialist, Department of Family Medicine, International Islamic University Malaysia (IIUM), Kuantan, Pahang, Malaysia.
E-mail: mohdcheman@iium.edu.my

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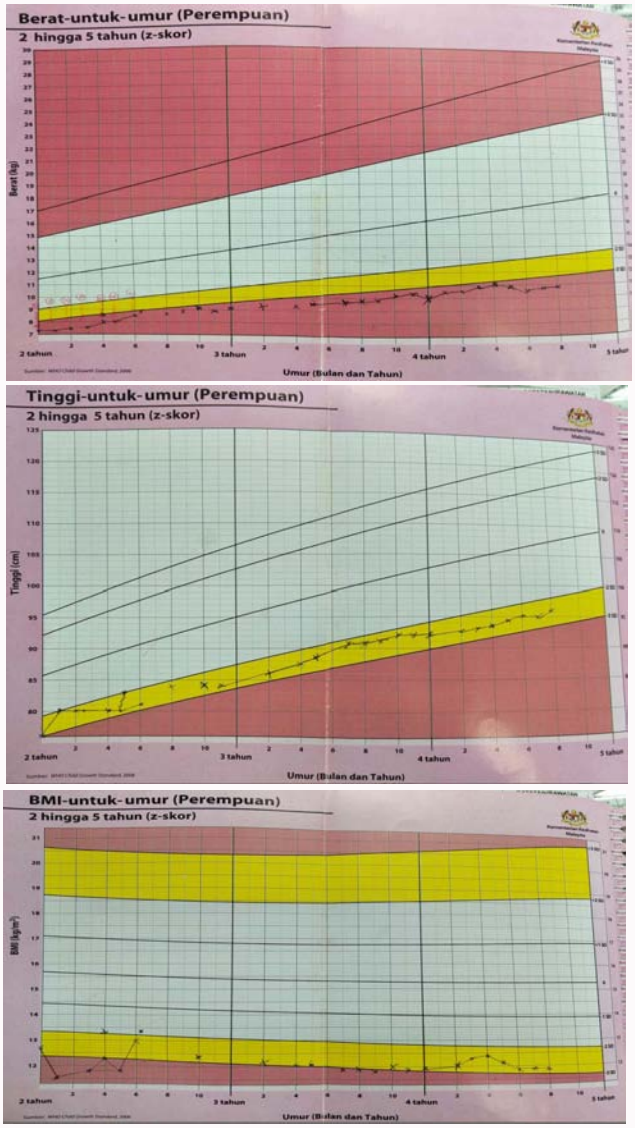

Figure:

undiagnosed. She is the eldest of two siblings with the younger sister thriving well and there is no parental consanguinity. She was taken care by her grandmother while both of her parents are working with low monthly income. Generally, she is an active girl, attending pre-school and had no restriction with her daily life activities. She had mild blue scleras with obvious dental caries. Her growth chart for age and gender shows consistent trend of poor growth evidenced by weight of 10.6 kg (below -3SD), height of 96 cm (below -2SD) and weight-for-height is below -3SD. She also had microcephaly with the head circumference of 42 cm (below -3SD). Parental anthropometric measurement shows that father has microcephaly with head circumference 51 cm and short stature with a height of 150 cm (Figure).

Overall, she had unresolved failure to thrive after birth with all anthropometric criteria below expected for age and gender. The musculoskeletal examination showed joint hypermobility of fingers of both hands, bilateral elbow and knee obtain positive Beighton score of 8/9. The stretching did not cause any pain or ecchymosis. Otherwise, she had normal gait, no bony deformities or joint dislocations and no scoliosis. These leads to discovery of Ehlers-Danlos syndrome

Table 1: Patient had positive Beighton score of 8/9.

No	Characteristic	Score
1	Passive dorsiflexion of each little finger beyond 90^0	2
2	Passive apposition of each thumb to the flexor aspect forearm	2
3	Hyperextension of each elbow beyond 10^0	2
4	Hyperextension of each knee beyond 10^0	2
5	Forward flexion of the trunk, with knee straight, so that the palms of the hands rested easily on the floor	0

hypermobility type based on manifestation of classical features. There was no evidence of non-accidental injury and no neurological deficit noted. The M-CHAT assessment and routine blood investigations are unremarkable.

Discussion

Routine practice of anthropometric monitoring by plotting the growth chart helps us to identify child with failure to thrive easily [2]. In this case, failure to thrive has been the eye opener in the diagnosis. Further focused assessment with detailed history taking and physical examination which lead to the diagnosis of Ehlers-Danlos syndrome.

In this case, she had nutritional and psychosocial issues that can be commonly associated with failure to thrive which can deviate us from getting to the precise diagnosis [1].

The nutritional issue contributed by dental caries and missing deciduous teeth interferes with her food intake [5]. The psychosocial aspects such as non-parental caregiver and low socioeconomic background hinder her eating habit and contribute to failure to thrive [1].

The past history of small for gestational age and paternal side with similar musculoskeletal findings creates a high index of suspicion towards genetic disorder [3]. Another concern was she is a well-looking girl with a normal developmental milestone despite her failure to thrive. Her unresolved failure to thrive over time despite adequate nutritional intake via the "bucket programme" for more than 24 months was alarming.

In this patient, the connective tissue hyperplasia which was manifested in the gingiva, must have prevented the eruption of the permanent teeth and resulted in the difficulty in chewing in this patient [5]. Blue sclerae among EDS patients are likely caused by more visible uveal blood vessels through thinner sclera [3]. The patient's score was eight on the Beighton scale (scores which are ≥ than 5 describe hypermobility) [3] (Table 1).

The classic clinical findings, along with the exclusion of other failure to thrive causes, confirmed the diagnosis [3]. She fulfilled International EDS Classification 2017 with presence of Criteria 1, Criteria 2 (feature A and B) and Criteria 3 [4]. She was referred to the Paediatrics Orthopaedic Clinic and diagnosed with hypermobility type Ehlers-Danlos syndrome. Besides the cutaneous and articular anomalies; the patients may show cardiovascular complications (such as aneurysms and mitral valve prolapse) and ocular defects [3]. She had been referred to particular departments to screen for anticipating complications.

Conclusion

Failure to thrive is a clue that requires careful attention to find the key to the primary cause. A systematic approach with focused history and clinical assessment remain the mainstay tool to which solves

majority of failure to thrive cases. We intend to draw attention for primary care provider to recognize different subtype of Ehlers-Danlos syndrome that have pathognomonic signs of joint hypermobility, skin hyperextensibility and tissue fragility.

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