Tel Hashomer Camptodactyly Syndrome
A Case Report
K Shah¹, R Sreekanth², B Thomas², S Danda¹

ABSTRACT

Tel Hashomer camptodactyly syndrome (THCS) is a rare autosomal recessive camptodactyly with muscular involvement. The manifestations of THCS other than camptodactyly are clubbed feet, thenar and hypothenar hypoplasia, abnormal palmar creases and dermatoglyphic ridges, spina bifida and mitral valve prolapse. The syndrome was first described by Goodman et al in 1972 and thereafter two further cases with similar phenotype were seen. Herein, we present another case report and review of the literature of other syndromes associated with camptodactyly and mitral valve prolapse. Further cases with this syndrome need to be reported for mapping of the candidate loci. This will help in planning management and genetic counselling.

Keywords: Mitral valve prolapse, Tel Hashomer camptodactyly syndrome

INTRODUCTION

Tel Hashomer camptodactyly syndrome (THCS) or camptodactyly with muscular hypoplasia, skeletal dysplasia and abnormal palmar crease is a rare genetic disorder. A subset of patients also have mitral valve prolapse. The new connective tissue genetic disorder was proposed for the first time in 1972 by Goodman et al (1). A similar clinical phenotype was also seen by them in an Arabian consanguineous family and the name THCS was proposed (2). The most likely inheritance is autosomal recessive but the causative gene is still not identified. We further report an Indian patient with THCS.

CASE REPORT

We describe a 25-year old male who presented to the outpatient clinic for camptodactyly and symptomatic weakness. He
was born of a second degree consanguineous marriage and was fourth in birth order. Parents are unaffected. The elder male sibling had similar features but did not present to us for examination. Two female siblings are not affected. The index case was born of normal vaginal delivery at home. Developmental milestones were normal. He had a history of bilateral club feet and had surgery for these at five years of age. Examination of his face revealed prominent forehead, asymmetric face and hypertelorism with telecanthus (inner-canthal distance 4.2 cm). He had high arched palate and dental crowding. Thoracic scoliosis and bilateral focal hypoplasia were observed. On the right hand side, the proband had camptodactyly in all the fingers with thenar and hypothenar wasting, long slender fingers and adaptive shortening of long flexors (Figure). The left hand was less severely affected compared to the right but had all features.

X-rays of the hand revealed flexion deformity at the proximal interphalangeal joints. X-ray of the cervical spine showed spina bifida and there was mild scoliosis of the thoracic spine. Bilateral metatarsus varus was also visualized which is consistent with the physical findings. Echocardiography showed mitral valve prolapse and severe mitral regurgitation. Electromyography and nerve conduction studies suggested a myopathic process and a mild asymmetric sensory axonal neuropathy. Serum creatine phosphokinase was 236 U/L (normal range: 45–195 U/L). Muscle biopsy was planned but the patient did not attend. The hand surgeons did not think that camptodactyly surgery (contracture release and full thickness skin graft) would be successful in him. Correction of adaptive shortening of the long flexors can be beneficial for increasing the reach of the hand. This can be done first by physiotherapy (extensor out trigger traction) and followed by flexor-pronator slide surgery.

**DISCUSSION**

Tel Hashomer camptodactyly syndrome (OMIM-221960) has features of camptodactyly, mitral valve prolapse and musculoskeletal deformities. The index case had features consistent with the diagnosis of THCS. The likely mode of inheritance is autosomal recessive. Many of the earlier case reports mentioned occurrence in siblings of parental consanguinity as was the case with the index patient. Gollop et al (3) reported camptodactyly of the fifth finger in a father which might be a heterozygote manifestation. This is the only family reported so far where a parent had expression of the rare disease.

Patton et al carried out electromyography (EMG) and muscle biopsy, for the first time, which showed myopathy and muscle histology showed abnormal fibre size (4). Electromyography done in the present case showed myopathic features. Muscle biopsy represents an embryological failure in muscle development rather than progressive muscle disease (4). Pagnan et al had reported eleven patients. None of them had abnormalities of the heart (5). Our patient had mitral valve prolapse and mitral regurgitation. Toriello et al reported two siblings with THCS having mitral valve prolapse (6). Additional features described in the literature to date are summarized in the Table.

An OMIM search revealed 161 entries with camptodactyly. Five genetic disorders were identified when mitral valve prolapse and skeletal dysplasia were added. Tel Hashomer camptodactyly syndrome and Hunter McDonald syndrome are the syndromes whose gene loci are not mapped. For other genetic disorders such as congenital contractural arachnodactyly (CCA) and Shprintzen Goldberg syndrome, \( FBN1 \) and \( FBN2 \) genes are involved. Congenital contractural arachnodactyly shares skeletal features with Marfan syndrome (MFS) such as marfanoid habitus, arachnodactyly, camptodactyly and kyphoscoliosis. However, patients with CCA have the characteristic crumpled appearance of the ear helix and congenital contractures. Loeys Dietz syndrome (LDS) is characterized by the triad of arterial tortuosity and aneurysms, hypertelorism, and bifid uvula or cleft palate and is caused by heterozygous mutations in the genes encoding transforming growth factor \( \beta \) receptors 1 and 2 [\( TGFBR1 \) and \( TGFBR2 \)] (7). None of the salient features of LDS are present in our patient. Thereafter, when myopathy is included, the search refers only to this present syndrome (THCS).

The important differential diagnosis is MFS. Although the presence of contractures is specific for CCA, molecularly proven MFS patients with mild contractures have been re-

<table>
<thead>
<tr>
<th>Table: Additional features in patients reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toriello et al (1990)</td>
</tr>
<tr>
<td>Franceschini et al (1993)</td>
</tr>
<tr>
<td>Melegh et al (2005)</td>
</tr>
<tr>
<td>Smolkin et al (2011)</td>
</tr>
</tbody>
</table>
ported (8). Thus screening for FBN1 and FBN2 genes is required.

Classification from the other side, camptodactyly and myopathy, leaves fewer differentials. Nemaline myopathy can be considered but the clinical phenotype is quite different.

There are some features suggestive of connective tissue disorder such as mitral valve prolapse and high arched palate. The other features such as symptomatic weakness, electromyography findings and muscle hypoplasia point towards the myopathic process. Camptodactyly reveals a fibroblast proliferation defect.

Tel Hashomer camptodactyly syndrome has earlier been reported from Israel, India, Russia, Italy, Arabia and Brazil which suggests that the gene pool is present in all populations (3, 9–12). Tel Hashomer camptodactyly syndrome is a rare condition which is possibly under diagnosed. This case highlights the need for recognizing this rare entity so that more reporting of affected sporadic and familial cases would help in identifying the genetic basis of this syndrome. Family studies would help in mapping of genes. Modern molecular techniques including next generation sequencing would pave the way for delineating the molecular pathogenesis of this condition and confirming the exact mode of inheritance. It would also probably tell us if the combination of camptodactyly, myopathy and congenital heart disease (mitral valve prolapse) is a genetically heterogenous disorder or if it is allelic to one of the known single gene disorders. Understanding of the pathophysiology will help in planning management including the feasibility, outcome and rehabilitation of patients who undergo surgery for camptodactyly. Genetic counselling will be more meaningful once the gene is identified. The diagnosis of THCS should be taken into consideration when a patient presents with camptodactyly with symptomatic weakness. As mitral valve prolapse is a silent condition, a screening echocardiography is required in such patients. This will help to diagnose this very rare syndrome and delve into the pathophysiology and molecular analysis of the disorder.

ACKNOWLEDGEMENT
We thank the family for the photograph.

REFERENCES