Fırat Tıp Dergisi 2012; 17(3): 167-169

Case Report

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Keutel Syndrome: A Case Report With Aortic Calcification

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ABSTRACT

Keutel Syndrome is a rare autosomal recessive syndrome. Laryngotracheobronchial calcification is a rare finding in young children and can occur in Keutel syndrome. Here we report 6 years old female patient with laryngotracheobronchial and aortic calcification and also review and discuss the clinical features of the syndrome. Concentric calcification of hepatic, renal, coronary and cerebral arteries were mentioned in Keutel Syndrome but to the best of our knowledge no previous aortic calcification was reported.

Key words: *Keutel Syndrome, Calcification*

ÖZET

Keutel Sendromu: Aort Kalsifikasyonu Olan Bir Vaka Sunumu

Keutel sendromu nadir görülen, otozomal resesif bir hastalıktır. Küçük çocuklarda nadir görülen laringotrakeobronşiyal kalsifikasyon nedenlerinden biridir. Bu vakada laringotrakeobronşiyal ve aort kalsifikasyonu olan 6 yaşında kız hastayı sunmayı ve beraberinde Keutel sendromunun klinik bulgularını gözden geçirmeyi amaçladık. Bilgilerimize göre literatürde Keutel sendromlu hastalarda hepatik, renal, koroner ve serebral arterlerde kalsifikasyonlar rapor edilmiştir ancak aort kalsifikasyonu daha önce rapor edilmemiştir.

Anahtar Sözcükler: *Keutel Sendromu, Kalsifikasyon*

Keutel Syndrome is a rare autosomal recessive syndrome manifested by midfacial hypoplasia, brachytelephalangism, abnormal diffuse cartilage calcification, peripheric pulmonary stenosis (PPS) and hearing loss (1, 2).

Investigations reported that mutations in the gene encoding the human extracellular matrix Gla protein cause Keutel syndrome. Matrix Gla protein gene (MGP) is a calcification inhibitor repressing bone morphogenetic protein 2 (BMP2). Loss of function mutations of MGP result in abnormal calcification of the soft tissues (3, 4). The reassessment of clinical features of Keutel Syndrome described tracheobronchial stenosis and calcification of pulmonary, hepatic, renal, coronary, meningeal and cerebral arteries (4).

Here we report a new case, review and discuss the clinical features of the syndrome.

CASE REPORT

Six years old female patient born to consanguineous parents was admitted with attention deficit. She was unable to concentrate and confused about colours and numbers. She had a history of two seizures at 9 th and 18 th months of age and was treated with phenobarbital for 2 years. The mother was healthy and the father had atrial septal defect. She had a healthy brother.

Her craniofacial appearance was characterized by midfacial hypoplasia with a broad and depressed nasal bridge. She had puffy eyelids, a sloping forehead, mild midface hypoplasia, depressed nasal bridge, hypoplasic alae nasi. The distal phalanges of the fingers and toes were thickened. She had mild conduction type hearing loss on left ear and moderate mixed type hearing loss on right ear. Height and weight were in normal ranges for her age. Cardiovascular examination revealed a

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grade 2-3/6 systolic ejection murmur on the left sternal border and parascapular areas.

Blood tests were unremarkable, serum calcium, phosphorus and alkaline phosphatase levels in serum were within normal ranges. The echocardiographic examination revealed a supravalvular and peripheric pulmonary stenosis. Her previous EEG at 9th months of age demonstrated bioelectrical abnormality and recent EEG revealed generalized epileptical activity. Denver test for the assesment of developmental delay yielded normal results yet Standford Binet Intelligence Scale revealed a mild delay in fine motor development. Chest radiography showed calcifications in the tracheobronchial tree (Figure 1). The hand x-ray showed short and broad distal phalanges of the first four fingers (Figure 2). The thoracoabdominal CT revealed circumferential wall calcification in descending aorta (Figure 3). The cranial magnetic resonance imaging was normal. Cytogenetic analysis from peripheral blood revealed a normal 46 XX karyotype and fluorescein in situ hybridization (FISH) test for chromosomes 22q11 and 7q11 showed normal signals.

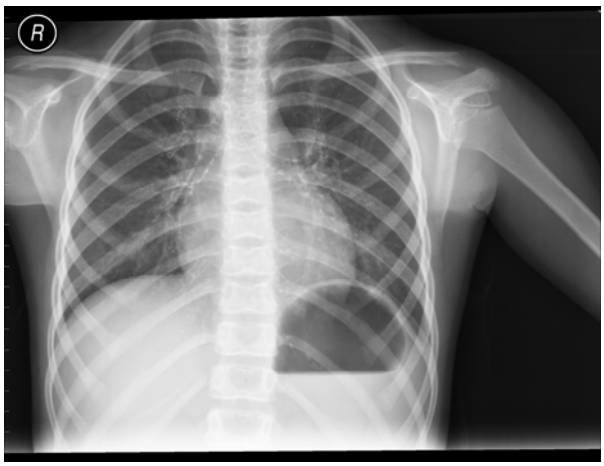

Figure 1. *Calcification of the tracheobronchial tree*.

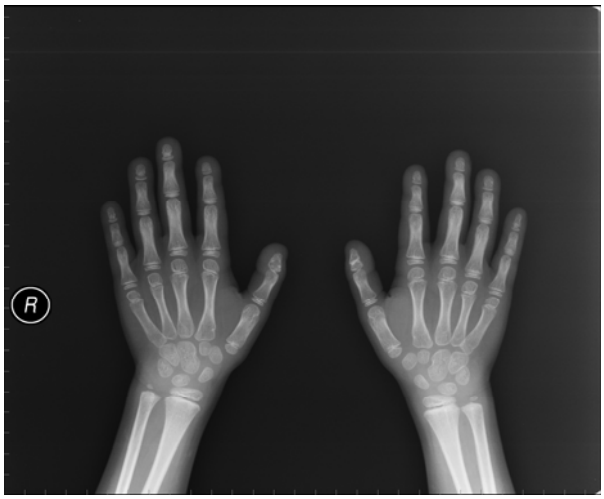

Figure 2. *Short and broad distal phalanges of the first four fingers, the fifth distal phalanx was relatively spared.*

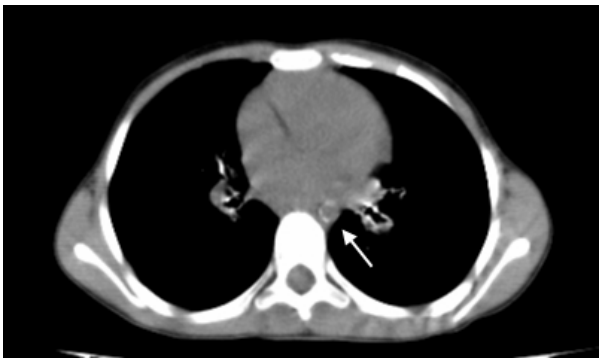

Figure 3. *The circumferential wall calcification in descending aorta and bronchial wall calcifications.*

DISCUSSION

Laryngotracheobronchial calcification is a rare finding in children under 13 years old (5, 6). It can develop due to cartilage degeneration in elderly and is accepted physiologic with increasing age (5). Tracheobronchial calcifications can occur in Keutel syndrome, congenital cardiac abnormalities, chondrodysplasia punctata syndrome, and warfarin sodium therapy or rarely it can be idiopathic (1, 2, 7-10).

Keutel syndrome is an extremely rare genetic disorder. To the best of our knowledge 24 effected individuals from 17 families with Keutel Syndrome have been reported until now. In the report by Meier et al., laryngotracheobronchial calcification in Keutel Syndrome was reported to cause dyspnea due to abnormal calcification and result in stenosis of the trachea and main bronchi in two young adult patients (4). Our patient did not suffer any respiratory problems yet she is under critical clinical follow-up, because tracheal stenosis could be a relatively late appearing symptom. Brachytelephalangy with sparing of the fifth distal phalanx is reported to be a characteristic even a diagnostic feature for Keutel Syndrome (1). This was one of our patient's features. The distal phalanges of the first four fingers were thickened, short and broad whereas the fifth distal phalanx was relatively spared.

It was reported that mice deficient in Mgp, are normal at birth but develop calcifications in all of the arteries within weeks (11). It was also hypothesized that in humans inhibition of some other proteins acting in similar fashion with Mgp might be needed for vascular calcification.

Our patients thoracoabdominal CT imaging revealed calcification in descending aorta. Concentric calcification of hepatic, renal, coronary, meningeal and cerebral arteries were mentioned in Keutel Syndrome but to the best of our knowledge no previous aortic calcification is reported (4).

Our patient showed normal cranial imaging, however it is possible that seizures were the indicator of undetectable microcalcifications.

With a sum up of 25 Keutel syndrome patients including the present case, it is by now quite apparent that laryngotracheobronchial and vascular calcifications in association with distinct facial characteristics should be suggestive of Keutel Syndrome and patients should be followed-up for respiratory symptoms as well as calcifications of vital vascular structures.

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Gönderilme Tarihi: 14.10.2011