Bone and Mineral Metabolism
BONE AND MINERAL CASE REPORT

Osteogenesis Imperfecta With Cerebral Atherosclerosis: A Family Report

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Background: Osteogenesis imperfecta (OI) is a rare hereditary connective tissue disease. It is mainly associated with pathogenic variants in COL1A1 or COL1A2. Patients with OI usually have repeated history of bone fractures. Besides, osteogenesis imperfecta is associated with some cardiovascular complications, such as aortic and mitral valve dysfunction, aneurysm and aortic dissection. But the relationship between these diseases has not been well studied.
Case Presentation: A 55-year-old man was admitted to our hospital mainly due to "dizziness for 2 hours". He had a 4-month history of hypertension and a history of smoking for more than 20 years. He had no history of drinking alcohol. He had hunchback and O-type legs. Besides, the patient and some of his relatives had a history of repeated brittle fractures,which was considered as "osteogenesis imperfecta". The clinical manifestation of OI in this family varies to a certain extent, from simple tooth disintegration to severe fracture deformity. The most serious patient of his family was unable to walk. CT and MRI revealed multiple systemic arteriosclerosis, including vertebral artery, posterior inferior cerebellar artery, cervical artery, and bilateral cerebellar multiple lacunar cerebral infarction. The blood sample of the patient was tested by whole exome sequencing, and the saliva samples of the patient's family members were tested by Sanger sequencing. A mutation c.3159 + 2T > A was detected in COL1A2 gene associated with OI, also found in the other affected family members, which had not been reported before. It was a segregating mutation in the family. The clinical severity of the family members was heterogeneous.
Discussion: This case is worth learning from the following aspects: 1. A pathogenic heterozygous mutation, c.3159 + 2T > A was detected in COL1A2 gene in the patient with OI, which is not reported in previous cases of OI. 2. The clinical manifestation of OI in this family varies to a certain extent, from simple tooth disintegration to severe fracture deformity. The most serious patient of his family was unable to walk. It presented the clinical heterogeneity of OI. Further basic researh on the mutation site of related gene of OI are needed. 3. We found the possibility of developing cerebral atherosclerosis in patients with OI. Therefore, patients with OI should give up smooking, exercise properly and keep on a low fat diet. They should pay attention to control blood pressure and blood lipid so as to reduce the risk of atherosclerosis.
Conclusion: A c.3159 + 2T>A mutation in COL1A2 gene detected by whole exome sequencing was the causing reason of OI, the discovery enriched the gene mutation spectrum of OI. We also found that OI may have relationship with premature atherosclerosis, and the abnormal bones of the cervical spine may lead to vertebrobasilar ischemia.

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Osteopetrosis - A Case Series Exploring Complications and Multidisciplinary Management

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Background: Osteopetrosis is a group of rare inherited skeletal dysplasias, with each variant sharing the hallmark of increased bone mineral density (BMD). Abnormal osteoclast activity produces overly dense bone predisposing to fracture and skeletal deformities. Whilst no cure for these disorders exists, endocrinologists play an important role in surveillance and management of complications.
Clinical Cases: A 43-year-old female had findings suggestive of increased BMD on radiographic imaging performed to investigate shoulder and back pain. X-ray of lumbar spine demonstrated a 'rugger jersey' spine appearance, while shoulder X-ray revealed mixed lucency and sclerosis of the humeral head. DXA scan showed T-scores of +11 at the hip and +12.5 at the lumbar spine. MRI of head displayed bilateral narrowing and elongation of the internal acoustic meatus and narrowing of the orbital foramina. Genetic assessment confirmed autosomal dominant osteopetrosis with a *CLCN7* variant. Oral colecalciferol supplementation was commenced and multi-disciplinary management instigated with referral to ophthalmology and ENT teams. A 25-year-old male presented with a seven-year history of low back pain and prominent bony swelling around the tibial tuberosities and nape of neck. Past medical history included repeated left scaphoid fracture in 2008 and 2018. Recovery from his scaphoid fracture was complicated by non-union requiring bone grafting with open reduction and fixation. Plain X-rays of the spine again demonstrated 'rugger jersey' spine. DXA scan was notable for elevated T scores; +2.9 at hip and +5.8 lumbar spine. MRI spine showed vertebral endplate cortical thickening and sclerosis at multiple levels. The patient declined genetic testing and is under clinical review. A 62-year-old male was referred to the bone metabolism service following a DXA scan showing T scores of +11. 7 at the hip and +13 at the lumbar spine. His primary complaint was of neck pain and on MRI there was multi-level nerve root impingement secondary to facet joint hypertrophy. Past medical history was significant for a long history of widespread joint pains; previous X-ray reports described generalized bony sclerosis up to 11 years previously. Clinical and radiological monitoring continues.
Conclusion: Individuals with osteopetrosis require a multidisciplinary approach to management. There is no curative treatment and mainstay of therapy is supportive with active surveillance for complications.

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Paget 's Disease: Not So Typical for Atypical Femur Fracture

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