E-Poster

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Patient With Osteoporosis-Pseudoglioma Syndrome Caused by a New Variant, Under Treatment With Denosumab: A Case Report

Topic: Genetics

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BACKGROUND

Osteoporosis-pseudoglioma syndrome (OPPG) is a rare autosomal-recessive disorder, characterized by severe osteoporosis with spontaneous and low trauma fractures and early-onset blindness, caused by variants in the low density lipoprotein receptor-related protein-5 (LRP5) gene on chromosome 11. Our aim is to present a patient with osteogenesis imperfecta-like bone malformations and a personal history of multiple low energy fractures treated with denosumab, who underwent genetic sequencing and was diagnosed as OPPG, caused by a newly reported variant.

METHODS

A 69-year-old female, resident of the Hospice for neurodisability, presents with congenital blindness, short stature with long bone deformities, osteoporosis with fragility fractures, microcephaly, barrel chest, kyphoscoliosis, hypotonia and higher than average intelligence. She has a medical history of type II diabetes, chronic obstructive respiratory disease, Hashimoto's thyroiditis, idiopathic thrombocytosis and has undergone a total hysterectomy due to endometrium neoplasia. Her growth was normal until the age of two, had difficulty walking at four and wheelchair-only mobility from the age of seven. She had her first femoral fracture at eight and multiple long bone fractures since. She underwent brain computer tomography (CT), electromyography (EMG), muscle biopsy, electroencephalography (EEG) dual x-ray absorptiometry (DEXA) and, recently, diagnostic whole exome sequencing (WES), while receiving denosumab for the past six years and undergoing a personalized rehabilitation program.

RESULTS

Whole exome sequencing revealed the presence of variant c.1701delC in the chromosomal site 11q13.2 of the LRP5 gene, previously unreported in international data bases or published works, thus considered a new gene variant. It is estimated to have a 99% pathogenic score on the LRP5 protein, altering gene translation and causing early termination of protein synthesis. Brain CT and EEG were normal, EMG showed diffuse loss of muscle fibers and normal nerve conduction, muscle biopsy revealed diffuse muscle fiber change with mixed atrophy and edema. Osteoporosis was confirmed by DEXA with a T-score of -6.8 (left femoral) and -3.3 (spine).

CONCLUSION

Despite general practice of treating osteoporosis in OPPG with bisphosphonates, our patient has been clinically stable and has remained fracture-free in the six years of denosumab treatment, despite small scale trauma. She participates fully in her rehabilitation program and is content with her current treatment plan.

Statement of Disclosures

None

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