CASE REPORT

The Relationship between Osteogenesis Imperfecta and Spinal Muscular Atrophy

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Abstract

Objective

A 4-month-old female with osteogenesis imperfecta (OI) type II was admitted in PICU of our center due to severe respiratory distress and fever with a diagnosis of severe pneumonia, and mechanical ventilation was initiated. Due to severe hypotonia, NCV and EMG were performed, and spinal muscular atrophy (SMA) type I was diagnosed.

Keywords: Osteogenesis imperfecta; spinal muscular atrophy; hypotonia

Case report

The patient was a 4-month-old female with osteogenesis imperfecta type II (OI) due to fracture of both femurs at birth. She was put on biphosphonate therapy (pamidronate). The subject was born through repeat caesarean section and was the second child of the family. Her sister was a healthy 3-year-old girl with no history of osteoporosis or fracture. Her parents were first degree relatives. The patient was admitted to our center's PICU with severe respiratory distress due to pneumonia; thus, mechanical ventilation was initiated. She was alert with severe hypotonia in the frog-leg position with bluish sclera (Fig-1-3). There was a depressed occipital fracture, probably due to birth trauma. There was consolidation and collapse of the right middle and lower lung lobes. A pneumothorax developed 2 days after admission, which improved with a chest tube. The affected lung expanded with the appropriate antibiotics, chest physiotherapy, and suctioning of the secretions. Due to severe hypotonia and the NCV and EMG findings, SMA type I was diagnosed. The patient was ventilator-dependent and did not tolerate extubation.

Discussion

Osteogenesis imperfecta (OI), a secondary cause of osteoporosis, manifests principally as bone fragility that affects up to 1 per 10,000 (1,2). OI results from mutations in genes encoding for type I collagen (3). Type I collagen fibers are composed of a left-handed helix, formed by the intertwining of pro-alpha1 and pro-alpha2 chains. Mutations in the loci encoding these chains (COL1A1 on band 17q21 andCOL1A2 on band 7q22.1, respectively) cause OI. Mutant expression produces nonfunctional collagen (severe OI) or insufficient quantities of collagen (mild OI). There are 7 subtypes of OI, varying in severity, age of presentation, and clinical features (4-7). Biphosphonates have been shown to increase bone mass, decrease fracture rates, and relieve symptoms of OI patients (8).
SMA is the second most frequent autosomal recessive disease in Caucasians, with an incidence of 1 per 6000 to 10,000 live births and carrier rate between 1 in 34 to 50. SMA type I (Werdnig-Hoffmann disease), the most common and severe form, usually

presents within the first 6 months of life. Death, secondary to respiratory distress, occurs primarily within the first 18 months of life. Over 90% of all types of the disease are linked to the same region of chromosome 5q (9-11). This region contains the survival motor neuron gene, which may have areas of inversion, duplication, or deletion (12). SMA is classified into 4 major types by the international SMA consortium (13). In one study, 3 patients with multiple fractures and Werdnig-Hoffmann disease were presented. Two of the 3 were erroneously diagnosed as having OI. The etiology of these fractures appeared to be in utero osteoporosis, secondary to decreased movement that led to pathological fractures during birth. Immobilization led to uneventful healing in these cases, and no recurrent fractures were seen (14). The diagnosis of OI in our patient was made clinically; additional fractures did not occur, perhaps due to the prescription of pamidronate therapy. Because this patient has expired on behalf of his severe respiratory distress, we could not find the genetic mutation, on the other hand, we could not find any genetic associations between OI and SMA, but it is possible that there is an unknown genetic relationship between SMA and OI that is not defined for any of the 7 types of OI. SMA alone can affect fractures at birth due to osteoporosis that is caused by intrauterian immobilization. In fact, it is not clear whether she has OI with SMA or only SMA type I that is complicated by osteoporosis and bone fractures.

In conclusion, the diagnosis of osteogenesis imperfecta in our patient was made clinically, but additional fractures did not occur, which could have been due to the pamidronate. These observations need further studies.

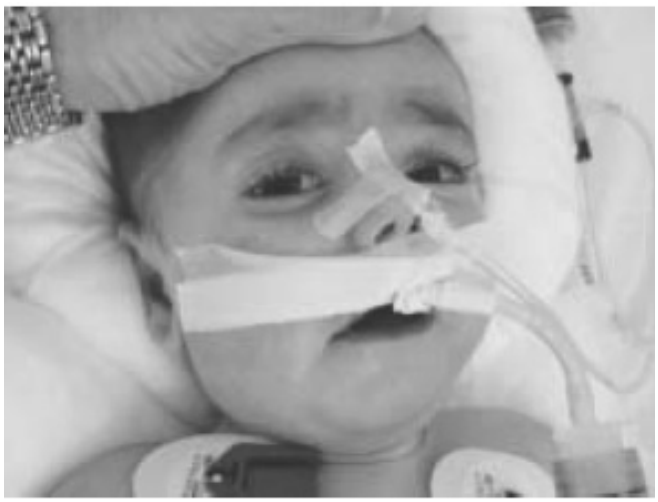

Fig 1: Bluish sclera

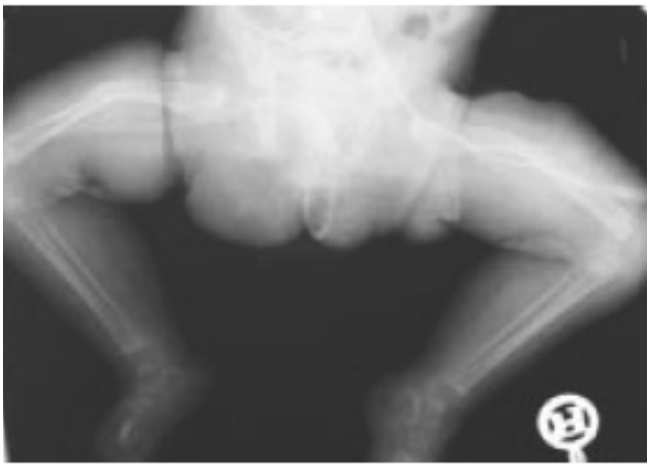

Fig 2: Radiographic signs at admission

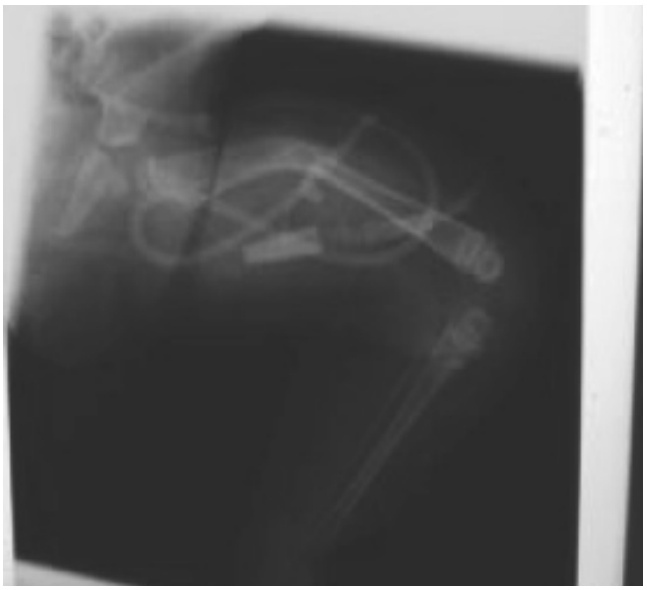

Fig 3. Radiographic signs after 2 months (no callus formation)

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