The original family revisited after 37 years: odontoma-dysphagia syndrome is most likely caused by a microduplication of chromosome 11q13.3, including the FGF3 and FGF4 genes.

Fibroblast growth factors consist of receptor tyrosine kinase binding proteins involved in growth, differentiation, and regeneration of a variety of tissues of the head and neck. Their role in the development of teeth has been documented, and their presence in human odontogenic cysts and tumors has previously been investigated. Odontoma-dysphagia syndrome (OMIM 164330) is a very rare disorder characterized by clustering of teeth as compound odontoma, dysplasia and aplasia of teeth, slight craniofacial abnormalities, and dysphagia. We have followed the clinical course of the disease in a family over more than 30 years and have identified a genetic abnormality segregating with the disorder. We evaluated clinical data from nine different family members and obtained venous blood probes for genetic studies from three family members (two affected and one unaffected). The present family with five patients in two generations has remained one out of only two known cases with this very rare syndrome. All those affected showed teeth dysplasia, oligodontia, and dysplasia and odontoma of the upper and lower jaw. Additional signs included dysphagia and strictures of the oesophagus. Comorbidity in one patient included aortic stenosis and coronary artery disease, requiring coronary bypasses and aortic valve
replacement. Genome-wide SNP array analyses in three family members (two affected and one unaffected) revealed a microduplication of chromosome 11q13.3 spanning 355 kilobases (kb) and including two genes in full length, fibroblast growth factors 3 (FGF3) and 4 (FGF4). The microduplication identified in this family represents the most likely cause of the odontoma-dysphagia syndrome and implies that the syndrome is caused by a gain of function of the FGF3 and FGF4 genes. Mutations of FGF receptor genes can cause craniofacial syndromes such as odontoma-dysphagia syndrome. Following this train of thought, an evaluation of FGF gene family in sporadic odontoma could be worthwhile.