

## REGIONAL ODONTODYSPLASIA: AN OVERVIEW

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## ABSTRACT

*Regional odontodysplasia is a rare developmental anomaly involving dental tissues. The precise etiology is not yet known. The affected teeth are usually small with atypical morphology with yellow or brown discoloration. One hundred and seventy six cases of regional odontodysplasia have been published to-date. Analysis of the published cases shows that the age at the time of diagnosis ranges from 1-23 years. Maxilla is more commonly affected with predilection for anterior teeth. Radiographic images of the involved teeth show a ghost-like appearance. Histologically, almost all dental tissues are altered. Enamel and dentin appear as hypoplastic and hypocalcified and the pulp is larger than normal. Treatment of regional odontodysplasia needs to be individualized and requires a multidisciplinary approach. Although regional odontodysplasia is known for more than six decades, the literature is almost limited to case reports only. Further epidemiological, experimental and genetic studies are needed.*

**Key Words:** *Odontodysplasia, Regional, overview.*

## INTRODUCTION

Regional odontodysplasia (RO) is defined as a localized developmental anomaly involving both deciduous and permanent dentitions with adverse effects on the formation of enamel, dentin, and pulp.<sup>1,2</sup> It was first described by Hitchin in 1934.<sup>3</sup> It has been designated by various terms, such as "arrested tooth development"<sup>4</sup>, "shell teeth"<sup>5</sup>, "unilateral dental malformation"<sup>6</sup>, and "ghost teeth"<sup>7</sup>. Zegarelli et al. (1963)<sup>10</sup> coined the most widely used term "odontodysplasia". Later in 1970, Pindborg<sup>8</sup> added the term, "regional" emphasizing the localized nature of this disease. It is usually found isolated, however, it can be associated with some developmental anomalies such as ectodermal dysplasia, hypophosphatasia, unilateral facial hypoplasia, neurofibromatosis, and vascular and epidermal nevi.<sup>9</sup>

The purpose of the present article was to review the English-language literature and to provide an overview of various aspects of RO. The etiology, pathogenesis, epidemiology, clinical presentation, radiographic, macroscopic, ultrastructural, light microscopic, immunohistochemical features, and treatment of RO are discussed.

## ETIOLOGY &amp; PATHOGENESIS

The exact etiology of odontodysplasia is not clear, although several theories have been suggested. Some authors suggest a correlation with trauma and infection;<sup>6,10</sup> however, this correlation was not proved, since

the correlation was based on patient history alone. The distribution of affected teeth in all four quadrants makes some authors suggest that somatic mutation may be the causative factor.<sup>11</sup> Witkop also suggested that a somatic mutation in early development could cause alterations in the ontogenesis.<sup>12</sup> Nagai et al.<sup>13</sup> had transplanted tooth germs in mice and found alterations in the tooth formation after inducing polyoma virus. Thus, viral infection of odontogenic epithelium was also suggested as a possible cause.<sup>7</sup> Nevertheless, no evidence of virus is present in any of the reported cases in the literature. Dahllöf et al. presented a case of a patient with concomitant regional odontodysplasia and hydrocephalus, and suggested a neural origin.<sup>14</sup> Sibley and Zimmermann<sup>15</sup> reported a patient with a history of hypocalcaemia and correlated this with RO. Moreover, it has been suggested that an imbalance of important proteins, such as metalloproteinases, might lead to the structural disorganization seen in this anomaly.<sup>16</sup>

The most prevalent theory relates RO to vascular etiology. Numerous reported cases are associated with a disturbance in the local circulation overlying the affected area. Walton et al.<sup>17</sup> reported three cases of regional odontodysplasia with a birthmark occurring on the skin, overlying the affected teeth. This vascular disturbance seems to be a consistent finding amongst patients with odontodysplasia, as reported by several authors.<sup>2,18-22</sup> This theory is further supported by animal experimental studies, as resection or ligation of different head and neck arteries resulted in similar disturbances of the dental hard tissues.<sup>23,24</sup> All the reports agree that this is a non-inherited condition, because no cases were reported in other family members.<sup>16,25-27</sup> Fujiwara et al.<sup>28</sup> suggested that the developmental anomaly in the case they reported may not be genetically determined, but rather environmentally induced. Conclusive evidence

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of the aforementioned theories is still lacking, since the studies were based on the case reports. The newer reports revolve around idiopathic etiology, as most of them failed to identify any local or systemic etiological factors.<sup>29,25,30,31</sup> However, whatever is the etiology, the causative factor must be active in both primary and secondary dentitions of the affected area.

## EPIDEMIOLOGY & CLINICAL PRESENTATION

Many authors have considered RO to be an uncommon condition.<sup>9,32,33</sup> Tervonen et al<sup>34</sup> reviewed 138 cases of RO published in the international literature during 1934-2002, and assembled the epidemiological data. In the present review, all well-documented case reports of RO from 2002 and until the reporting of the present study, were retrieved from PubMed database search, and the epidemiological data were evaluated. Since 2002, 38 cases<sup>16,25-61</sup> of RO have been reported in the literature, making a total of 176 cases. The present review showed a 1.2:1 ratio of females to males, a somewhat similar finding to that of Tervonen et al. (1.7:1). The age at the time of diagnosis ranges from 1-23 years and shows bimodal peaks at 4 and 10 years of age.

The maxilla was more commonly affected with predilection for the anterior teeth, which is in accordance with Tervonen et al. The most common clinical symptom is failure of tooth eruption, which was also found by Tervonen et al.<sup>34</sup> Other symptoms include hyperplastic tissue overlying the unerupted or partially erupted teeth, inflammation of the gingiva, periapical infection, fistulas, and localized pain. RO was also associated with facial asymmetry in 5% of patients, and with facial hemangioma in 7.4% of the cases.<sup>34</sup> The affected teeth generally show yellow or brown discoloration.<sup>34,62</sup> The teeth are usually small with atypical morphology. The teeth surface show a varying appearance, such as an irregular contour, shallow furrows and pitting, and grooves predominate.<sup>9</sup> The enamel has been reported to be soft on probing and tends to be hypoplastic and hypocalcified.<sup>31,32</sup> The condition usually affects one quadrant.<sup>34</sup> However, some cases cross the midline.<sup>43,45,62</sup> Three cases reported in the literature showed generalized involvement.<sup>17,63,64</sup> It has been shown that this condition is not limited to any specific ethnic group.<sup>9</sup>

## RADIOGRAPHIC FEATURES

Previous case reports of RO have stated distinctive and characteristic radiographic findings.<sup>36,62,65,66</sup> Radiographic images of the involved teeth show a ghost-like appearance, due to reduced radio-density of the thin enamel and dentin, and enlarged radiolucent pulp. The teeth appear with an abnormal morphology, a hypoplastic crown, and a faint outline of hard tissue. There is absence of contrast between enamel and dentin. In some cases, the affected teeth show features of arrested development, such as short roots with open apices and abnormally large pulp chambers. Additionally, the teeth are usually associated with enlarged follicles. Pulp stones may occasionally be visible.<sup>9,34</sup> The unerupted teeth are sometimes surrounded by large radiolucency

with distinct borders, which resemble cysts or neoplasms. The adjacent alveolar bone sometimes appears thin, with a decrease in trabeculae.<sup>67,68</sup> Few reports have described computed tomography (CT) findings of RO.<sup>26,69</sup> These findings indicated that hypocalcification is more severe in enamel than in dentin. The reports also suggested that dense fibrous connective tissue or hard tissue-like structures were present in the dental follicles of the affected teeth.<sup>26,69</sup>

## MACROSCOPIC/ULTRASTRUCTURAL/LIGHT MICROSCOPIC/IMMUNO-HISTOCHEMICAL FEATURES

Macroscopically, the altered teeth shows an irregular morphology, rough surfaces, and yellowish to brownish discoloration.<sup>30</sup> Scanning electronic microscopic (SEM) and transmission electron microscopic (TEM) studies showed wide-ranging defects of the involved teeth.<sup>30,70</sup> The enamel is generally thin, and the enamel prisms are irregular. The enamel appears laminated due to alterations in the hydroxyapatite crystals and inter-prismatic regions.<sup>30,71</sup> The coronal dentin is usually more affected than the radicular dentin. Dentin appears thin and globular in structure. Interglobular spaces and cellular and amorphous areas are prominent. Dentinal tubules show changes of orientation, density, size, distribution and shape.<sup>30,72,73</sup>

Histologically, all dental tissues are usually altered.<sup>36,65,72</sup> In most of the reports, enamel was not evaluated histologically, because of the decalcification processes.<sup>36,50</sup> However, in ground sectional studies, the enamel appears as hypoplastic and hypocalcified, with variable thickness and irregular surfaces.<sup>9,45</sup> The dentin is also hypoplastic and reduced in thickness. Clefts of various sizes, interglobular dentin, focally-widened pre-dentin zones, and decreased number of dentinal tubules are prominent features of the affected dentin.<sup>44,65</sup> Cellular dentin and amorphous areas are remarkable features of dentin in some cases.<sup>1</sup> The pulp chamber is usually larger than normal showing various forms of fibrosis and calcifications.<sup>30</sup> The odontoblasts appear flattened, rimming the margin of the pre-dentin.<sup>36</sup> Pulpal extensions sometimes extend to the cuspal or incisal enamel.<sup>19</sup> The follicular tissues surrounding un-erupted teeth may be enlarged and exhibit scattered odontogenic rests, whorled fibrous tissue, and focal basophilic calcifications.<sup>30</sup> In some cases, the cementum appears normal;<sup>65</sup> however, when it is affected, it is altered at a lower grade. It may be thinner than normal with no structural changes<sup>30</sup>, or with globular structures.<sup>70</sup>

The gingival and alveolar mucosa surrounding the affected teeth may show foci of calcification and islands of odontogenic epithelium.<sup>30,74,75</sup> It was found that the soft tissue calcification were associated with mesenchymal vimentin-positive cells and with odontogenic cytokeratin-positive epithelial remnants, as shown by the immunohistochemical investigations.<sup>30</sup> Courson et al.<sup>16</sup> examined the gingival tissues surrounding the affected teeth and found a decreased collagenic network and extremely fragmented collagen fibers.

Additionally, quantitative measurements showed an imbalance between MMP-1 and MMP-2 and their inhibitors TIMP-1 and TIMP-2, which suggested that the increase in enzymatic activity could explain the disorganization of the connective tissue.<sup>16</sup>

## MANAGEMENT

The management of RO is often challenging, requiring cooperation among multiple disciplines. The objective of the management is to maintain a good oral function, improve the esthetics, and facilitate normal jaw growth.<sup>25,36</sup> There has been a considerable controversy about whether to remove the affected teeth. Many of the reports recommended removal of the affected teeth, as these teeth are considered to be potential source of infection,<sup>39,62,68</sup> while others suggested a conservative approach of preserving the involved teeth for as long as possible.<sup>25,76</sup> The conservative approach would maintain the alveolar bone and enhance normal jaw development.<sup>9,25,76</sup> There is no general agreement on the management of this disease. However, several factors should be considered, including the patient's age, relevant medical history, previous dental experience, degree of involvement, and attitudes of both child and parent regarding dental treatment.<sup>25,77</sup>

## SUMMARY

Regional odontodysplasia is a rare non-hereditary condition causing severe dental disturbances. The etiology of this disease remains unknown. Treatment of RO needs to be individualized and requires multidisciplinary approach. Although RO is known for more than six decades, the literature on RO is mostly limited to case reports only. Further epidemiological, experimental and genetic studies are needed.

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