Lobodontia: Genetic entity with specific pattern of dental dysmorphology

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ABSTRACT

A characteristic pattern of dental anomalies including cone-shaped premolars, multitubercular molar crowns, pyramidal molar roots with single root canals, shovel-shaped incisors with palatal invaginations and hypodontia usually described as lobodontia was recognised as a separate entity. Only a few family reports on this condition have been published until now. The prevalence of the condition is estimated to be less than 1:1000.000. In the present paper we tried to delineate and clarify some additional aspects of this rare genetic entity in three families with 17 affected members. This represents the largest number of cases recorded since now. The analyses of dental morphology, crown-size profile patterns, pedigree analyses, and analyses of digitopalmar dermatoglyphics were performed in 7 examined patients. Crown-size profile pattern was calculated for seven patients and compared with standards for the Croatian population. The most striking features of the condition are conical premolars, triturubercular canines, single pyramidal molar roots, multitubercular molar crowns and invaginated upper incisors. A considerable reduction of crown-size was observed for all premolars, particularly in mandible. The alveolar process in the premolar region was hypoplastic and thin in all patients studied. Gender ratio of affected individuals was approximately M1:F1. Our data suggest that the prevalence of this condition is less than 1:300,000 in the Croatian population, which is considerably higher than previously reported in the literature. The analysis of the anomaly in all the families showed a slight variability in the clinical picture and autosomal dominant (AD) mode of inheritance. It could be concluded that this rare condition described as lobodontia represents a true genetic entity which follows AD mode of inheritance and displays variability in its expression.

1. Introduction

The condition with a specific pattern of multiple dental anomalies was first described by Robbins and Keene (1964). They described the condition in a 19-year-old boy which followed the autosomal mode of inheritance. Their description of multiple dental anomalies comprised dens invaginatus, single conical unifurcated posterior root forms, multitubercular molar crowns, carnivorous structure of canine and premolar crowns, and generalised reduction in tooth size. Later, the term “lobodontia” was coined by Keene and Dahlberg (1973) to denote multiple dental anomalies including teeth crowns of canines and premolars resembling those of carnivores or wolves. Brook and Winder (1979) gave a detailed description of a family with autosomal dominant mode of inheritance of this condition. Previous reports show that all teeth classes are affected. Both the maxillary and mandibular molars show a multitubercular pattern with numerous pointed cusps. All molar teeth displayed single pyramidal roots with a single root canal. The morphology of premolars shows characteristic tapering, large pointed buccal cusps and small lingual cusps. The upper incisors display palatal invaginations with pronounced cingulum or are shovel-shaped (Robbins and Keene, 1964; Brook and Winder, 1979). A few cases were described of patients with unusual or bizarre combination of dental anomalies (Nguyen et al., 1996; Metgud et al., 2009).

Only a few additional cases were described and published later (Ather et al., 2013; Kiyano et al., 2013). Since very few cases have been described until now, we will attempt to delineate and clarify some additional aspects of this rare genetic entity in the largest sample so far. The aim of this study has been to describe three families with seventeen affected members and to analyse dentitions of seven affected patients and their digitopalmar dermatoglyphic traits. Our intention was also to further delineate this condition and to discuss possible aetiology of lobodontia.

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2. Material and methods

Three families with 17 affected members (10 males and 7 females) were evaluated in this study. Seven patients from three families were available for examination. Clinical, radiographic and bloodline analyses were made in seven patients affected with lobodontia. All subjects were examined and evaluated for the clinical signs of lobodontia and other abnormalities. The bloodlines were drawn up for the analysed families based on the detailed family history. The mode of inheritance was established for each family. Panoramic and periapical radiographs were evaluated for characteristic features of lobodontia. These included cone-shaped canines and premolars, hypodontia of premolars, single-rooted molars, and invaginations on upper incisors. Invaginations affecting maxillary incisors were classified according to Oehlers (1957). Other morphological changes and alterations in tooth shape were recorded and analysed.

Mesiodistal (MD) dimensions of all teeth were measured by the same author under clear light on study models using an electronic digital calliper (BGS Germany Vernier Calliper) with an accuracy of 0.01 mm. Only undamaged teeth were measured. The MD distance was measured as the greatest distance between the contact points on the approximal surfaces of the tooth crown, using a common procedure described and suggested by Moorrees and Reed (1964).

Crown-size profile patterns (CSPP) of all teeth for patients with lobodontia were plotted against Croatian population standard (Lovric, 1985). Z-scores for mesiodistal (MD) dimensions were calculated for all teeth to plot crown-size profile pattern as a deviation from means of healthy controls. Z-scores as a measure of the divergence of an individual result from the population mean were calculated. If a z-score is 1.96 or higher, $P = 0.05$ or less, the observed difference between the examined sample and the population mean is probably significant (Langley, 1979). Seven of the affected individuals have had tooth size analyses. Crown-size profile pattern (CSPP) analysis was performed according to the method used by Garn et al. (1968) and Cohen et al. (1970), and modified according to principles applied by Ward (1989). Z-scores were calculated for seven patients (3 males, and 4 females) and compared with gender–matched Croatian controls (Lovric, 1985).

The digitopalmar dermatoglyphics of 6 patients were taken according to the instructions of Cummins and Midlo (1961). The analysis of quantitative characteristics was performed according to the usual methods (Cummins and Midlo, 1961; Holt, 1968; Penrose, 1968), whereas the fingertip pattern analysis was made according to the traditional classification (Holt, 1968; Penrose, 1968). Palmar patterns were analysed according to the topological classification proposed by Penrose and Loesch (1970). Dermatoglyphic findings obtained from phenotypically healthy subjects (167 males and 178 females) from Zagreb population were used as control data for the analysis of digitopalmar traits (Skrinjaric and Rudan, 1979).

3. Results

3.1. Family reports

3.1.1. Family 1

The analysis of family history revealed six affected members (three males and three females). The condition was transmitted through three generations as an autosomal dominant trait (Fig. 1). The proband (1.III-6), a 12-year-old boy displayed lobodontia with numerous dental anomalies (Table 1). Intraoral examination revealed cone-shaped premolars with reduced crown-size and multiple pointed cusps on all molars (Fig 2A and B). The panoramic radiograph (Fig. 3) showed multiple dental abnormalities including single rooted molars, cone-shaped canines and premolars, palatal invaginations on all upper incisors, and missing second permanent maxillary molars. All upper incisors displayed type I invagination classified according to Oehlers (1957). Primary maxillary second molars were persistent and displayed single conical roots.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Abnormal findings in patients with lobodontia.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observed characteristics</td>
<td>Patient</td>
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<tr>
<td>1. Conical premolars</td>
<td>1.III-6</td>
</tr>
<tr>
<td>2. Pyramidal molar root</td>
<td>1.III-6</td>
</tr>
<tr>
<td>3. Invaginated incisors</td>
<td>1.III-6</td>
</tr>
<tr>
<td>4. Shovel-shaped incisors</td>
<td>1.III-6</td>
</tr>
<tr>
<td>5. Multitubercular molars</td>
<td>1.III-6</td>
</tr>
<tr>
<td>6. Tritubercular premolars</td>
<td>1.III-6</td>
</tr>
<tr>
<td>7. Missing teeth/number</td>
<td>1.III-6</td>
</tr>
<tr>
<td>(a) Maxillary</td>
<td>1.III-6</td>
</tr>
<tr>
<td>(b) Mandibular</td>
<td>1.III-6</td>
</tr>
<tr>
<td>8. Hypoplastic alveolar ridge</td>
<td>1.III-6</td>
</tr>
<tr>
<td>9. Distorted dermatoglyphics</td>
<td>1.III-6</td>
</tr>
</tbody>
</table>

Legend: Patient 1.III-6: Family 1, generation III, number 6 (in row), etc.; n—the number of observed characteristics in total sample of analysed patients (7).
as permanent molars. The same root morphology was observed for a deciduous mandibular first left molar.

The parents and the sister of the proband were personally examined. The proband’s father (1.II-9) had a partial loss of teeth but the remaining teeth displayed all characteristic morphological features of lobodontia; tritubercular lower premolars with larger pointed buccal cusps (Table 1). All molars on the panoramic radiograph showed single conical roots with single root canals. The mother and sister of the proband had normal teeth.

3.1.2. Family 2

In Family 2, lobodontia was transmitted through three generations as an autosomal dominant trait (Fig. 4). A relatively small pedigree showed only three affected females. The proband was a 15-year-old girl displaying tritubercular premolars with pointed cusps and multitubercular molars (Fig. 5A). Maxillary teeth were characterised by tritubercular canines and first premolars, missing second premolars, and shovel-shaped incisors (Fig. 5B; Table 1). Canines and first premolars had a characteristic appearance with large pointed buccal cusps and small lingual cusps (Fig. 5C). The panoramic radiograph of the proband from Family 2 showed pyramidal molar roots, missing second maxillary premolars, and tritubercular canines and premolars with pointed buccal cusps (Fig. 6). The proband’s mother (2.II-2) was only clinically examined and had characteristic features of lobodontia.

3.1.3. Family 3

On the basis of the family history, a pedigree was drawn for Family 3 (Fig. 7). It was established that eight family members were affected (four females and four males). The condition was transmitted through four generations as an autosomal dominant trait with complete penetrance. Four family members were personally examined and analysed in this study (3.III-1; 3.III-5; 3.IV-1, and 3.IV-2). The proband (3.IV-1), a 33-year-old woman, had characteristic findings of lobodontia including pointed crowns of maxillary premolars, multitubercular molars, and missing maxillary and mandibular premolars (Fig. 8A). Her younger sister aged 26 (3.IV-2) had premolars with pointed cusps and reduced crown size of all premolars (Fig. 8B). Maxillary left second premolar was displaced in buccal direction and orthodontic treatment was carried out. Analysis of panoramic radiographs revealed multiple dental anomalies including all molars with single pyramidal roots, tritubercular or pointed crowns of all premolars, invaginations on all upper incisors, and some missing premolars (Fig. 9A and B). Panoramic radiographs of patients (3.IV-2) show presence of all maxillary premolars (Fig. 9B). The invaginated incisors displayed type I anomaly according to Oehler’s classification. All examined members showed the most characteristic features of lobodontia clinically and radiographically (Table 1). Apart from other traits, patient 3.III-5 displayed severe hypodontia with nine missing teeth (7 in the maxilla: 15, 14, 12, 22, 23, 24, 25; and 2 in the mandible: 31, 41).

3.2. Tooth-size analysis

The results of dental measurements in patients showed significant deviations from the normal controls matched for gender (Tables 3 and 4). Control data for tooth measurements were taken from the results obtained from 200 adults (100 males and 100 females) from the Croatian population (Lovric, 1985). The crown-size profile patterns (CSPP) showed significant size reduction in all premolars and maxillary canines (Figs. 10 and 11). Negative
z-scores of M-D dimensions of premolars were observed in all patients. Total size reduction was most pronounced in maxillary canines and premolars. Tooth-size reduction was slightly more pronounced in males than in females. The most severely affected teeth were the first and second permanent premolars showing abnormal shape, reduced dimensions or hypodontia. Second maxillary premolars were the most frequently missing teeth. Maxillary teeth were more frequently affected by hypodontia than the mandibular teeth (Table 1).

Fig. 5. Dental anomalies in the proband girl (2.III-1) at 15 years of age: (A) Lateral view of permanent teeth showing tritubercular premolars and multitubercular molars with pointed cusps in both jaws; (B) Occlusal view of maxillary teeth in the proband (2.III-1) shows tritubercular canines and first premolars, missing second premolars, and shovel-shaped incisors. Note the preventive filled invaginations on lateral incisors and trepanation of maxillary first left molar; (C) tritubercular maxillary canine and first premolar showing a large pointed buccal cusp and small lingual cusps.

Fig. 6. Panoramic radiograph in proband 2.III-1 showing pyramidal molar roots, tritubercular canines and premolars with pointed cusps, missing second maxillary premolars, and invaginations on maxillary lateral incisors. The tooth 37 was extracted.

Fig. 7. Pedigree of Family 3 shows eight affected members (four females and four males) and autosomal dominant transmission of lobodontia. The proband (3.IV-1) is marked by an arrow.

Fig. 8. Dental findings in patients from Family 3: (A) Lateral view in a girl aged 33 (3.IV-1) showing pointed crowns of maxillary premolars and missing lower second premolar; (B) Frontal view of teeth in the proband’s sister (3.IV-2), aged 28, showing premolars with pointed cusps and reduced crown size. Maxillary left second premolar was displaced in buccal direction and orthodontic treatment was done.
3.3. Dermatoglyphic findings

The findings of palmar and finger-tip patterns are presented in the form of formulas in Table 2, along with the frequencies of the same formulas in general Croatian population (Skrinjaric and Rudan, 1979). The palmar and finger-tip patterns were analysed in 6 patients with lobodontia. The patients exhibited a presence of relatively rare palmar formulas in general population (Table 2). The frequent presence of more distal axial triradial (r') in 5 cases, significantly distal (r'') in two cases, and border triradius (p') in one case, which are quite rare in general population, indicates distortion in palmar dermal patterns. A tendency of distal and border position of the axial triradii could be considered generally present.

4. Discussion

The cases of lobodontia described so far show certain variability in clinical pictures. All types of dental dysmorphology are not seen in all cases but the analysis of our cases and those previously published showed certain stability of some features. The complexity of tooth morphology in this condition is consistent with previous descriptions of canines and premolars in the literature as multiple conical teeth, tritubercular teeth, wolf teeth, carnivore-like teeth, torch shaped teeth, odd shaped teeth (Robbins and Keene, 1964; Shuff, 1972; Keene and Dahlberg, 1973; Brook and Winder, 1979; Dahlberg and Keene, 1990).

The most constant clinical findings are single pyramidal molar roots and tritubercular crowns with pointed buccal cusps of maxillary canines and premolars (Fig. 5C). Tritubercular shape of canines and premolars resembles the dentition of Canis lupus familiaris or domestic dog. The shape of triconodont class is characteristic for early mammalian stage of teeth development and is common in dogs and other carnivores (Nelson and Ash, 2010).

Lobodontia is a very rare condition. Its prevalence is estimated to be less than 1:1000,000 (Brook and Winder, 1979). The review of the literature reveals a very limited number of cases described so far (Robbins and Keene, 1964; Shuff, 1972; Brook and Winder, 1979; Nguyen et al., 1996; Metgud et al., 2009; Ather et al., 2013; Kiyon et al., 2013). In this paper we present three families with 17 affected members, suggesting that the prevalence of lobodontia in Croatian population is less than 1:300,000. This is considerably higher than it was previously reported in the literature.

Although Ather et al. (2013) reported a case with generalised microdontia; our cases do not support this finding. Rather, canines and premolars display significant crown-size reduction while the size of other teeth varies within normal limits (±1 s.d. from population mean). The analysis of tooth size in seven cases presented here in the form of crown-size profile patterns (CSPP) shows that significant deviations from population standards can be observed only for all maxillary premolars and canines (Figs. 10 and 11). Tooth size analysis presented in the form of CSPP gives a very characteristic pattern which is specific for this condition. The CSPP is primarily characterised by negative z-values deviating from the

![Fig. 5](image-url)
Table 3
Means and $z$-scores for mesio-distal dimensions of maxillary teeth in patients with lobodontia and controls.

<table>
<thead>
<tr>
<th>Group</th>
<th>Right side</th>
<th>Left side</th>
<th>Tooth</th>
<th>Group</th>
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<th>Left side</th>
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<tr>
<td></td>
<td>$M^1$</td>
<td>$M^2$</td>
<td>$p^1$</td>
<td>$p^2$</td>
<td>$C$</td>
<td>$l_1$</td>
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<td>8.60</td>
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<td>5.09</td>
<td>6.65</td>
<td>5.95</td>
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<td>–</td>
<td>1</td>
<td>2</td>
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</tr>
<tr>
<td>Controls M</td>
<td>9.70</td>
<td>9.99</td>
<td>–</td>
<td>6.55</td>
<td>7.65</td>
<td>6.30</td>
</tr>
<tr>
<td>$n$</td>
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<td>77</td>
<td>–</td>
<td>89</td>
<td>97</td>
<td>92</td>
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<td>–2.50</td>
<td>–0.56</td>
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<td>Lobodontia</td>
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<td>9.13</td>
<td>5.65</td>
<td>6.00</td>
<td>6.50</td>
</tr>
<tr>
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<td>4</td>
<td>–</td>
<td>3</td>
<td>4</td>
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<tr>
<td>Controls M</td>
<td>9.16</td>
<td>9.49</td>
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<td>7.38</td>
<td>6.13</td>
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<td>83</td>
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<td>$Z$</td>
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<td>–0.82</td>
<td>–1.05</td>
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<td>0.64</td>
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</table>

$X$—values for patients, $M$—means for controls, s.d.—standard deviation, $n$—number of teeth, $Z$—$z$-scores.

Table 4
Means and $z$-scores for mesio-distal dimensions of mandibular teeth in patients with lobodontia and controls.

<table>
<thead>
<tr>
<th>Group</th>
<th>Right side</th>
<th>Left side</th>
<th>Tooth</th>
<th>Group</th>
<th>Right side</th>
<th>Left side</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>$M_1$</td>
<td>$M_2$</td>
<td>$P_1$</td>
<td>$P_2$</td>
<td>$C$</td>
<td>$l_1$</td>
</tr>
<tr>
<td>Lobodontia X</td>
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<td>10.70</td>
<td>5.90</td>
<td>5.90</td>
<td>7.10</td>
<td>5.90</td>
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<td>3</td>
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<tr>
<td>Controls M</td>
<td>10.41</td>
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<td>10.27</td>
<td>6.70</td>
<td>6.55</td>
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<td>1.61</td>
<td>–1.48</td>
<td>–0.38</td>
<td>1.21</td>
<td>0.97</td>
</tr>
</tbody>
</table>

$X$—values for patients, $M$—means for controls, s.d.—standard deviation, $n$—number of teeth, $Z$—$z$-scores.

Fig. 10. Crown-size profile pattern of maxillary teeth in patients with lobodontia: canines and premolars show the smallest mesiodistal dimensions.
standard for more than one or two standard deviations for all premolars. Deviations in crown-size of maxillary teeth are somewhat more pronounced than those in the mandible. Canine morphology is characterised by reduced crown size and very pointed cusps with three lobes. The middle labial lobe is cone-shaped (Fig. 5C). The most striking clinical findings are tritubercular crowns with pointed buccal cusps of maxillary canines and premolars (Figs. 10 and 11). The maxillary incisors display shovel-shaped form with palatal enamel invaginations from the cingulum area. When classified according to Oehlers (1957), the invaginations display type I degree of the anomaly.

Different genetic mechanisms can be responsible for morphological changes affecting the dentition in lobodontia. It is known that some genes such as Pax9, Bmp4, Msx1, Left1 and their overlapping expression play a key role during tooth development. Several homeobox genes (Msx1/2, Dlx1-6, and Barx1) and combination of their expression lead to different types of teeth: multicuspids teeth and monocuspids teeth (Miletich and Sharpe, 2003). It was suggested that overlapping domains of homeobox genes such as Msx1, Dlx1 and Dlx2 might be responsible for the development of canines or premolars (McCollum and Sharpe, 2001).

Recent studies provide new data about candidate genes that might be responsible for teeth abnormalities observed in lobodontia. Moustakas et al. (2011) recently described gene expression patterns of Fgf10, Fgf4, Shh, Spry2, and Spry4 in cap stage germs of different tooth classes. They hypothesise that the expression of Fgf10 in the epithelium of canine germs and in the primary enamel knots of premolar and molar tooth germs leads to differences in tooth cusp height and sharpness. Teeth with exceptionally sharp and tall cusps, specifically canines, premolars, and molars, also have epithelial expression in the primary knots of Fgf10. They concluded that epithelial expression of Fgf10 led to increased epithelial proliferation and increased cusps height of those teeth.

Nakatomi et al. (2013) showed that mutation of Evc gene leads to reduced molar size, malformed cusps, and single-rooted molars. Mutation or inactivation of Evc, Evc2, or both, cause defective response of Ihh, a homologue of Shh, and formation of single-rooted molars. It is suggested that mutations in Evc or Ihh could be responsible for the formation of molars with single roots and abnormal cusps.

Genes that regulate molar morphogenesis such as Dlx1 and Dlx2 also regulate proximal jaw skeletal development and genes that regulate incisor morphogenesis also regulate distal jaw development. This observation shows that jaw morphogenesis and tooth patterning are controlled by the same genes (McCollum and Sharpe, 2001). It could explain the association of reduced crown size of premolars and canines with hypoplastic alveolar ridge in cases of lobodontia.

Hypoplastic alveolar ridge bone was observed in maxillary and mandibular jaws. The alveolar ridge bone might also be affected by the same gene mutation (McCollum and Sharpe, 2001). Hypodontia was observed in almost all patients and teeth affected were predominantly maxillary second premolars, and rarely mandibular second premolars (Table 1).

Radiographic findings of pyramidal-shaped molar roots seem to be the most constant finding and of key importance for the diagnosis apart from the characteristic crown morphology of canines and premolars. Single rooted molars with pyramidal roots are characteristic of Ackerman’s syndrome (Ackerman et al., 1973; Gorlin et al., 2001). This tooth abnormality is a common finding in some other syndromes such as Down syndrome, Turner syndrome, oto-dental syndrome, and hypohidrotic ectodermal dysplasia (Witkop et al., 1988; Skrinjarić et al., 1992; Gorlin, 1998; Gorlin et al., 2001). Witkop et al. (1988) consider this anomaly to be the result of disrupted developmental homeostasis. Pyramidal-shaped single rooted molars, taurodontism, and fused molar roots are considered to be a phenotypic variant of the common genetic causation (Ackerman et al., 1973; Bixler, 1976).

Since the pattern type and ridge count of dermatoglyphics reflect the status of the palmar mesodermal structures in an early period of embryonic development, they can point to possible disharmonies and distortions in the early hand development (Cummins and Midlo, 1961; Holt, 1968). Various palmar abnormalities are known to be accompanied by marked changes in the dermatoglyphic findings. Thus, for instance, in patients with hypoplasia of distal phalanges the frequency of arches on fingertips and toes is very high. In such cases the arches can quite frequently be found in all 10 fingers. Contrary to this finding, in patients with Turner’s syndrome a higher frequency of large patterns and a high number of the fingertip ridges are present (Cummins and Midlo,
1961; Robinow and Johnson, 1972; Schaumann and Alter, 1976; Loesch, 1983).

Our finding of rare palmar patterns formulas and frequent presence of distal axial triaids (‘or ‘) and a borderline triadrix (‘), should be taken as features of distorted dermatoglyphics. Dermatoglyphics as highly genetically controlled features reflect the status of the phylogenetic palmar pads and the obtained results suggest disarray in the development of the mesodermal structures of the hands (Penrose and Loesch, 1970; Skrinjaric and Rudan, 1979).

In conclusion, lobodontia is a specific genetic condition with a characteristic pattern of dental anomalies. The condition is inherited as an AD trait with complete penetrance. Prevalence of the condition is much higher in general population and its frequency is less than 1:300,000. The most frequent dental anomalies which characterise this condition are cone shaped premolars, pyramidal molar roots, triturubercular premolars and canines, and invaginated incisors. Triturubercular canines and premolars along with pyramidal molar roots are the most constant findings of this condition and could be considered as key features for the diagnosis of lobodontia.

References


