Abstract
The authors present the changes in the mastication organ in the case of a 9-year old girl affected with von Recklinghausen’s disease. The symptoms included neurofibromatosis of her face, salivary gland and external ear in the form of an extensive tumour. The disease resulted also in acute right hemifacial hypertrophy. The computer-assisted tomography examination identified acute atrophy of zygomatic bone, maxilla, mandible alveolar ridge and right base of the skull. The clinical intraoral examination of the patient revealed right buccal occlusion and lingual occlusion on the opposite side.

KEY WORDS: neurofibromatosis, hypertrophy of the mandible, computer tomography.

Introduction
Medical literature defines von Recklinghausen’s disease, also known as neurofibromatosis type 1 (NF1), as an autosomal dominant disease characterized by abnormalities affecting tissues derived from the neural crest. Neurofibromatosis type 1 (OMIM 162200) occurs in the general population with frequency of approximately 1 in 3,500 livebirths [1]. It is caused by dominant loss of function mutations of the NF1 gene (OMIM 613113). NF1 gene is located on chromosome 17q11.2 and encodes neurofibromin – a cytoplasmic protein that is mostly expressed in neurons, Schwann cells, oligodendrocytes and leukocytes [2]. It is involved in various signaling cascades and one of the best characterized functions of NF1 protein is its action as a GTPaseactivating protein (Ras-GAP) [3]. NF1 gene shows one of the highest mutation rates among human genes, therefore about half of the NF1 cases result from new mutations [4]. Over 1,300 different mutations have been described so far in the human gene mutation database (HGMD®; http://www.hgmd.cf.ac.uk/ac/index.php). Majority of NF1 gene mutations (20-50%) are splicing mutations, that seriously alter the structure of the protein [5, 6, 7].

Due to extremely big size of the gene and enormous number of mutations, molecular diagnosis of NF1 is difficult and routinely limited to analysis of NF1 gene towards big deletions and duplications using MLPA analysis [5,6]. Von Recklinghausen’s disease is diagnosed when at least 2 out of the 7 following criteria are met: first degree relative afflicted with neurofibromatosis type 1, min. six café-au-lait spots with a diameter exceeding 5 mm (children) and 15 mm (adults), min. 2 neurofibromas of any type or one plexiform neurofibroma, freckles and/or discolouration found on covered parts of the body, optic nerve glioma, min. two Lisch nodules as well as characteristic bone lesion such as sphenoid wing dysplasia or thinning of long bone cortex [8]. According to the study carried out in 2007, the differential diagnosis of NF1 should focus on excluding such disorders as rare mosaic or segmental neurofibromatosis type 1, neurofibromatosis type 2, schwannomatosis, Noonan syndrome, Watson phenotype, café-au-lait spots inherited as an autosomal dominant condition, McCune-Albright syndrome, LEOPARD syndrome, Klippel-Trénaunay syndrome, Proteus syndrome, multiple lipomas, Bannayan-Riley-Ruvalcaba syndrome, fibromatosis, multiple endocrine neoplasia syndrome type 2B as well as homozygo-
sity for one of the genes responsible for causing hereditary non-polyposis cancer of the colon [9]. The aim of this study was to identify changes in the mastication organ and specify possibilities of orthodontic treatment of a patient suffering from von Recklinghausen’s disease.

**Case study**

We present a case of a 9-year-old girl of Polish origin suffering from von Recklinghausen’s disease with neurofibromatosis of face, salivary gland and external ear in the form of an extensive tumour. In consequence, acute right hemifacial hypertrophy was identified. The extraoral examination of facial features revealed that the central part of the chin moved towards the unaffected side of the face, while the angle of the mouth lowered significantly towards the affected side of the face. The clinical intraoral examination of the patient revealed right buccal occlusion and lingual occlusion on the opposite side. The computer-assisted tomography examination identified acute atrophy of maxilla, zygomatic bone, mandible alveolar ridge and right base of the skull. Despite a number of surgical procedures aimed at removing the tumour (first procedure when the patient was 6 years old), the tumour kept recurring.

**Discussion**

According to literature, neoplasia is an inherent characteristic of a phenotype seen in patients suffering from von Recklinghausen’s disease - therefore, it is the main factor influencing the selection of a therapy. Although there are certain single attempts of pharmacological treatment of ganglioneurofibromas at their early development stage, it is agreed that, in fact, no preventive actions are possible. Hence, in the case of neurofibromatosis type 1, reconstruction and aesthetic procedures are widely applied in treating the disease [10]. The orthodontic appliance used in the case of the analysed patient aimed, among others, at improving facial features by means of making a functional change in the position of the mandible. Von Recklinghausen’s disease in the oral cavity often manifests itself by gingival overgrowth, erosions, increased promenence to caries and to attachment loss due to problems with maintaining proper hygiene. Another phenomenon noticed in the case of the disease is the lack of teeth buds, teeth migration or intrusion. It is often underlined that until the skeletal development is complete, prosthetic restorations which could impact bone growth should not be used. The best solution seems to be the one offered by temporary restorations, the use of which should be consulted with an orthodontist. It was underlined that in many cases orthodontic treatment suffices, as restoration may be combined with the treatment of existing malocclusion with the use of orthodontic appliances. The appliances should be constructed with consideration to the missing teeth and they should restore them, prevent teeth migration, maintain space for erupting permanent teeth, restore correct articulation and occlusal conditions and stimulate maxilla’s and mandible’s bone development [11]. In the case of the described patient, orthodontic treatment with the use of removable appliance prevented further intensification of the malocclusion and it was not necessary to introduce any other elements to the Metzelder’s appliance.

Surgical treatment of a patient with a hemimandibular hyperplasia was conducted in the Maxillo-Facial Surgery Department in Poznań. The 18-year old patient with right hemimandibular hyperplasia underwent (based on pre-operative and operative measurements) a correction procedure - sagittal mandibular osteotomy at the side of the hyperplasia combined with dissection of inferior alveolar nerve and genioplasty. Additionally, sagittal split osteotomy of the mandible was conducted on the opposite side. The correction of the occlusion involved Le Fort I osteotomy [12]. In the analysed case, the hyperplasia was caused by a neoplastic tumour. The surgical action consisted in its enucleation, but despite the procedure relapses occurred requiring repeated surgical procedures. Studies conducted in 2007 suggested that in the case of children suffering from von Recklinghausen’s disease deciduous teeth erupt earlier. Researchers explained this phenomenon with the activity of osteoclasts, which are more prone to migrate and proliferate in comparison with the cells of healthy individuals. This leads to faster alveolar process bone resorption around deciduous teeth buds and thus earlier eruption of the teeth [9]. The applied orthodontic appliance, owing to its construction, could have been used by the patient during the entire process of the functional treatment, regardless of the presence of particular teeth during teeth replacement stage and did not inhibit the functioning of the mastication organ. During visits at the orthodontic surgery, special surfaces in the acrylic mass of the appliance were prepared to enable uninhibited eruption of permanent teeth. Finnish authors made a groundbreaking discovery of a sex-dependent characteristic in the case of patients suffering from neurofibromatosis type 1. Based on an analysis of pantomographic images of 55 patients (29 women and 26 men), the scientists proved that cement dysplasia around lower teeth root apexes affects only women. Additionally, they also pointed to the fact that 85% of cases showed enlargement of mandibular foramen and canal. Although the changes often accompany plexiform tumours located in this area, it is a characteristic of von Recklinghausen’s disease and may be taken into consideration in differential diagnostics also in cases in which neoplastic changes are not present in those anatomical areas [10]. Radiological testing of the patient showed no dystrophic cement changes around teeth roots, but it did show slightly enlarged mandibular foramen and canals. Neurofibromatosis type 1 is characterised by highly variable expression, even within the same family [4]. A recent study of monozygotic twins reported by Rieley et al. confirmed the opinion that different phenotype expression is observed not only in family members with the same mutation but also in individuals who have inherited the same NF1 germinal
mutations [13]. This variability is not well understood. Genotyp/phenotype correlation studies showed that the type of mutations in the NF1 gene does not have much influence on phenotype variability. Easton and Sabbagh et al. confirmed the impact of the modifier genes (including protein-coding genes, microRNA and long non-coding RNA) and environmental factors on the phenotypic variability [2, 14, 15]. Easton at al. concluded that the genotype at modifier loci determines the phenotypic expression [14]. A better understanding of the naturally occurring genetic modifiers, may contribute to improve the prediction and treatment (new therapeutics) of neurofibromatosis.

**Summary**

Considering the malocclusion they are suffering from, children diagnosed with von Recklinghausen’s syndrome should undergo orthodontic consultation and, if necessary, should be treated with the use of removable appliances, so that the malformation of the mastication organ does not intensify.

**Literature**


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