Neuroendocrinology Letters Volume 37 No. 4 2016
ISSN: 0172-780X; ISSN-L: 0172-780X; Electronic/Online ISSN: 2354-4716
Web of Knowledge / Web of Science: Neuroendocrinol Lett
Pub Med / Medline: Neuro Endocrinol Lett

Odontogenic keratocysts in the Basal Cell Nevus (Gorlin-Goltz) Syndrome associated with paresthesia of the lower jaw: case report, retrospective analysis of a representative Czech cohort and recommendations for the early diagnosis of the disease

Milan Hubáček [1], Tereza Kripnerová [1], Michaela Němčíková [2], Anna Křepelová [2], Alena Puchmajerová [2], Marcela Malíková [2], Markéta Havlovicová [2], Jana Čadová [3], Roman Kodet [4], Milan Macek Jr. [2], Tatjana Dostálová [1]

1 Department of Stomatology, Charles University 2nd Faculty of Medicine and University Hospital in Motol, Prague, Czech Republic
2 Department of Biology and Medical Genetics, Charles University 2nd Faculty of Medicine and University Hospital in Motol, Prague, Czech Republic
3 Department of Dermatology, Charles University 2nd Faculty of Medicine and University Hospital in Motol, Prague, Czech Republic
4 Department of Pathology and Molecular Medicine, Charles University 2nd Faculty of Medicine and University Hospital in Motol, Prague, Czech Republic

Correspondence to: Prof. Tatjana Dostálová, MD., DSc.
Department of Stomatology
Charles University 2nd Faculty of Medicine and University Hospital Motol,
V Uvalu 84, 150 06, Prague 5, Czech Republic.
TEL: +420 728 970 059; FAX: +420 224 433 120; E-MAIL: tatjana.dostalova@fnmotol.cz

Submitted: 2016-06-29 Accepted: 2016-09-08 Published online: 2016-09-30

Key words: **Gorlin-Goltz syndrome; basal cell nevus syndrome (BCNS) syndrome; odontogenic keratocyst; paresthesia, dentistry; paresthesia, genetics**

Neuroendocrinol Lett 2016; **37**(4):269–276 **PMID:** 27857042 NEL370416C02

Abstract

OBJECTIVES: Identification of early presenting signs of the Basal Cell Nevus (BCNS; synonyme Gorlin-Goltz) syndrome, which is associated with a principal triad of multiple basal cell nevi, jaw odontogenic keratocysts, and skeletal anomalies, in stomatological and neurological practices. Proposal of multidisciplinary diagnostic algorithm comprising other medical specialists, including pathology, imaging, laboratory and molecular analyses based on the study outcomes.
DESIGN: Case report of a male patient reporting paresthesia of their lower jaw, with right facial asymmetry (maxilla and mandible) and radiological detection of large osteolytic lesions in both jaws, including a retrospective analysis of a representative Czech cohort with BCNS from within the last decade. **SETTING:** Clinical, imaging and laboratory analyses were carried out at a national tertiary centre. **RESULTS:** A multidisciplinary clinical approach followed by surgical management lead to the identification of odontogenic cysts, which were substantiated by histological examination. DNA sequencing of the *PTCH1* gene detected a c.2929dupT resulting in p. Tyr977Leufs*16 pathogenic variant. This finding confirmed the clinical and laboraoty diagnosis of BCNS. Parental DNA analysis showed that this causal genetic defect arose *de novo*. Surgical management and orthodontic therapy were successful.

CASE REPORT

CONCLUSIONS: Analysis of the reported case and retrospective data analysis provided evidence that paresthesia of the lower jaw should be considered as one of the early presenting signs of this rare disorder in stomatological and neurological practice. Obtained results allowed us to formulate recommendations for diagnostic practice in stomatology and neurology.

INTRODUCTION

In 1960 Gorlin and Goltz (ICD-10: Q87.8; MIM#109400. ORPHA: 377) defined a syndrome with a principal triad of multiple basal cell nevi, jaw odontogenic keratocysts (OKC), and skeletal anomalies (Hegde *et al.* 2012). Other clinical characteristics include macrocephaly, ectopic calcifications, plantar and palmar pits, central nervous system and ocular lesions, and fairly typical facial features with frontal bossing and hypertelorism (Shear *et al.* 2007). Additionally, several cases of fetal rhabdomyoma have also been reported in association with the syndrome (Yang *et al.* 2001).

This syndrome has been given several alternative names. It is sometime called nevoid basal cell carcinoma syndrome (NBCCS), but it is also known as "basal cell nevus syndrome" (BCNS), "nevoid basal cell carcinomas syndrome," and "multiple basal epithelioma, jaw cysts and bifid rib syndrome" (Ortega García de Amezaga *et al.* 2008). Current medical literature mainly uses the abbreviation BCNS according to OMIM.org and Orpha.net catalogues.

The estimated prevalence of BCNS ranges from 1:57,000 to 1:256,000 and affects both genders equally (Leger *et al.* 2011). BCNS is inherited in an autosomal dominant manner and is associated with a strong pathogenic variant penetrance. According to recent molecular genetic studies, approximately 35–50% of cases result from *de novo* germline mutations (Sirous *et al.* 2011). It is estimated that 30–50% of patients suffering from BCNS are not aware of any other affected family member (Ortega García de Amezaga *et al.* 2008).

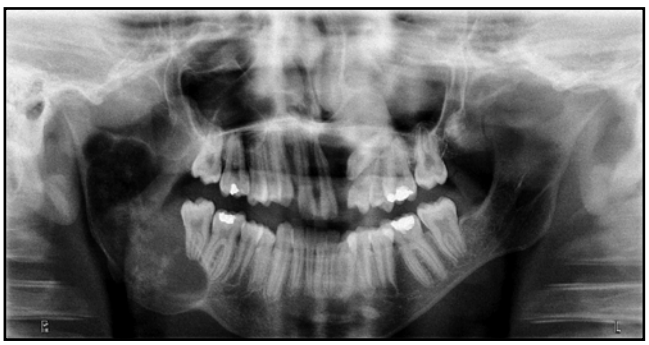

Fig. 1. Orthopantomographic (OPG) radiograph before surgery: a large cyst in the right ramus of the mandible, extending from the apex of tooth 46 cranially to the column of the mandible, including the coronoid process.

The gene responsible for this syndrome was mapped to chromosome 9q22.32, where the tumor suppressor gene *PTCH1* is located. *PTCH1* acts as a receptor for SHH ligands in the Sonic hedgehog (SHH) signaling pathway, which is implicated in the formation of embryonic structures during human development (Kitsiou-Tzeli *et al.* 2011). *PTCH1* is also involved in homeostatic maintenance of mature tissues, tissue repair during chronic inflammation, and tumorigenesis (Borgonovo *et al.* 2011). Protein patched homolog 1 (PTCH1) is a transmembrane protein that inhibits another transmembrane protein known as smoothened (SMO). When SHH and PTCH1 bind together, the inhibition of SMO is interrupted, leading to signal transduction and nuclear activation of Gli proteins, which regulate respective target genes (Beach *et al.* 2011). Based on this model, the inactivation of PTCH1, or the constitutive activity of SMO or SHH, could lead to over activity of SMO, resulting in neoplasia (Joshi *et al.* 2012).

BCNS has a wide variety of clinical forms. In order to assess its phenotypic variants radiologic protocols, which enable a more precise diagnosis, are required. In this regard panoramic radiography to detect multiple jaw cysts, skull radiography for the evaluation of CNS calcifications, chest radiography to detect bifid-, fused- or splayed ribs, and computed tomography (CT), as well as magnetic resonance (MR) to find further abnormalities are utilized (Bronoosh *et al.* 2011). The diagnosis of BCNS also relies, to a large degree, on molecular genetic analysis of the *PTCH1* gene.

Neurological symptoms have also been observed i.e. sudden-onset right-sided hemiparesis, supranuclear facioparesis, and motor aphasia (Budinčević *et al.* 2014). Additionally, familial central nervous system tumors with neuro-oncologic manifestation (Hottinger *et al.* 1996), meduloblastoma (Crawford *et al.* 2009), or multiple spinal osteochondromata and osteosarcoma (Sadek *et al.* 2013) have been observed, and meningeal calcification was found to be the cause of a yearlong headache (Nail *et al.* 2013).

Here we present a description of a Czech case with typical clinical features. This patient was diagnosed by the presence of odontogenic cysts associated with paresthesia of the lower jaw. The aim of our study is to highlight the need for awareness of early signs of the syndrome in stomatological and neurological clinical practice, whereby paresthesia of the lower jaw should not be disregarded as a benign sign.

PATIENTS

Case report

A twelve-year old boy presented with right facial asymmetry (maxilla and mandible) and has been reporting lower jaw paresthesia. Since radiological examination detected large osteolytic lesions in both jaws he was referred to our tertiary stomatological centre by a col-

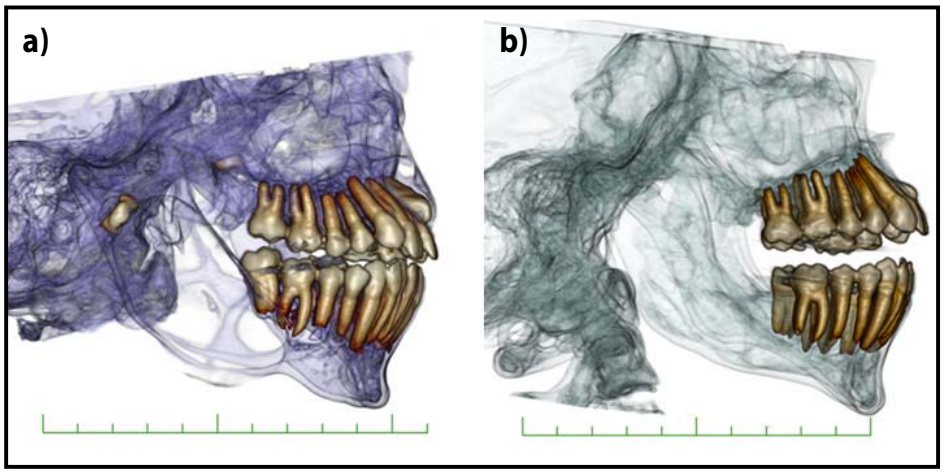

Fig. 2. a) A CT scan (3D reconstruction) before surgery: cyst on the right ramus of the mandible with resorption of both lateral and medial compact bone; retained tooth 23, surrounded by a cystic lesion; resorption of the right tuber of the maxilla caused by the cyst in that location; **b)** CT 3D reconstruction 1 year after treatment.

laborating orthodontist. The patient was asymptomatic and his dentition was within normal limits, with anodontia of the upper lateral incisors and retention of the upper left canine. Panoramic radiographic examination revealed a large, well-circumscribed radiolucency distal to the second right lower molar and a second cyst within the ramus of the left mandible (Figure 1). These radiographic findings prompted an incisional biopsy followed by a broader surgical procedure. CT revealed an osteolytic lesion centered well within the mandible, trespassing from the right ramus of mandible to the apex of the lower right molars (46, 47). The germ of the third molar was displaced cranially under the condylar process. The size of the cystic lesion was 90×45 mm. Other lesions were found in the right maxilla near tooth 18 (cystic lesion, surrounding the germ of the tooth, size = 30×20 mm) and left maxilla near tooth 23 (retention and dystopia of tooth 23, surrounded by a cystic lesion, size = 40×30 mm) (Figures 2a). Paresthesia of the left side of lower jaw, mainly surrounding n. mentalis loco foramen mentale, was substantiated by additional neurological examination.

Differential diagnosis

Differential diagnosis of well circumscribed, radiolucent lesions of the maxilla and mandible comprised several types of pathology, including OKC and tumors, non-odontogenic tumors, and other non-neoplastic conditions (Hutton *et al.* 2012). OKC are more common than odontogenic neoplasms. OKC affect the mandible 75% of the time and exhibit a strong propensity for the posterior mandible (Myoung *et al.* 2001). Odontogenic tumors are often present, as well as circumscribed radiolucencies, which suggests that this lesion could be one of a variety of odontogenic neoplasms, such as ameloblastoma, odontogenic myxoma, etc. (appearing as a "soap bubble" in radiographs) (Li *et al.* 2006). Our patient is unique in that he is significantly younger than the average age of diagnosis for ameloblastoma, which usually occurs during the mid- to late thirties (Reichart *et al.* 1995). Non-odontogenic mesenchymal neoplasms should also include differential diagnostic consideration of neurofibroma, desmoplastic fibroma of the bone, and vascular lesions. Primary mucoepidermoid carcinoma must also be considered (Hutton *et al.* 2012).

The patient underwent surgical treatment under general anesthesia. An incision was made on the right side from tooth 47 cranially to the ramus of the mandible. Lifting of the mucoperiosteal flap was complicated by adhesion of the cyst to the underlying soft tissues. Following extirpation of the cyst and extraction of the displaced third molar, the neurovascular bundle was

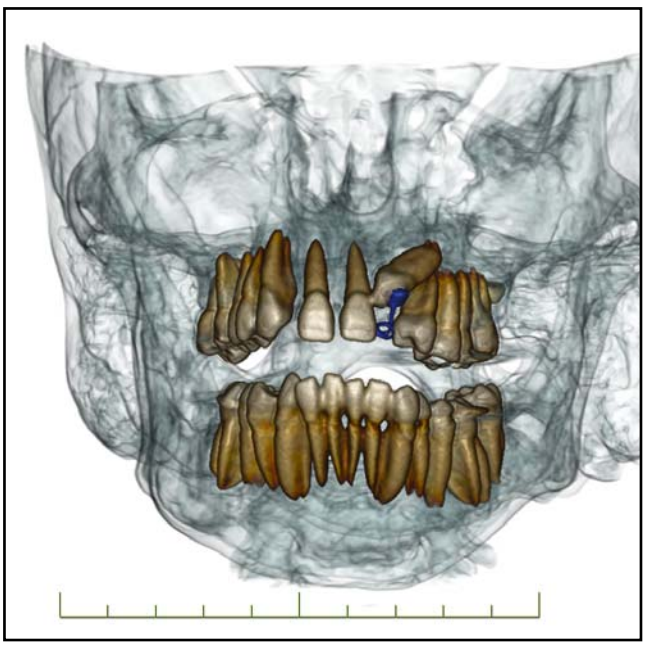

Fig. 3. Anodontia associated with tooth 12, 22, retention of canine.

carefully removed. Autologous spongious bone grafts were then taken from the right iliac crest and the defect was filled with Surgicel® and Spongostan (Ethicon, Norderstedt, Germany). Grafts were ground in a bone mill and used to augment the defect in the mandible, following which the surgical wound was hermetically closed. The cyst associated with tooth 48 was then extirpated. The mucoperiosteal flap was subsequently lifted via the intraoral approach from tooth 11 to tooth 24, which gave access to the cyst. Subsequently, the cyst was extirpated and tooth 23 was left to undergo spontaneous eruption or bonding, including attachment of an orthodontic bracket and future force application (Figure 3). The final part of the procedure involved the cyst associated with tooth 18. The germ of tooth 18 was extracted.

Incisions were close and post-operative recovery proceeded normally, with only a minor set-back. Two months after surgery, inflammatory complications appeared in the right ramus of the mandible, caused by the loss of vitality of tooth 47. This was followed by extraction of tooth 47 under local anesthesia and excochleation of the inflamed tissues. The wound was hermetically sutured, antibiotics were prescribed, and the lesion subsequently healed without any further complications. Two years after the surgery a control X-ray and CT scan were performed (Figure 2b). The images show that all defects, including the large defect in the right ramus of the mandible, had healed. Paresthesia spontaneously improved during the 6-month period following surgery. The patient is now XX months post-op and receiving regular follow-ups.

Retrospective analysis of additional cases treated at our center within the last decade

In addition to this case, we have managed seven additional cases of BCNS (Table 1) at our clinic over the last decade. This has enabled us to retrospectively reanalyze a total of 32 OKC (Table 2 and 3) with the following conclusions:

Tab. 1. Clinical and laboratory features of studied Czech BCNS cases.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Presented case (Patient 6)	Patient 7
Pathogenic Variant	c.2703+1G>C	c.2726delAinsTGC (p.Asp909Valfs*16)	c.838delG (p.Glu280Lysfs*3)	c.2309-2311delGAGinsA (p.Arg770Hisfs*19)	c.2309-2311delGAGinsA (p.Arg770Hisfs*19)	c.2929dupT (p.Tyr977Leufs*16)	c.3181dupG (p.Ala1061Glyfs*84)
Sex	F	F	M	M	F	M	M
Age of evaluation	15y	9y	16y	13m	prenatally	15y	7y
Parental analysis (mother/father)	–/–	–/+	na	+/– (+ maternal grandfather and uncle)	+/– (+ maternal grandfather and uncle)	–/–	–/–
Macrocephaly	+	+	+	+	+	+	+
Jaw odontogenic keratocyst	+	+	+	+	+	+	+
Skin lesions	trichofolliculoma of upper lip, pigmented nevi, cutaneous *keratocyst*	basaliomas, pigmented nevi	basaliomas, pigmented nevi	basaliomas, pigmented nevi	pigmented nevi	basaliomas, pigmented nevi	pigmented nevi, nevus flammeus
Tumors	–	medulloblastoma	–	–	fibroma of left ventricle	–	–
Others	–	severe kyphoscoliosis and lordosis, cysts of eyelids, bone cysts in vertebraes	right kidney cyst, mitral and aortal regurgitation	pancreatic cyst, brain venous angioma, brain arachnoid cyst	strabism, posthypoxic encephalopathy after CPR, intellectual disability	VSD, mitral valve prolapse, arrhytmia, kyphoscoliosis	kyphosis, ribs and vertebral malformation, brain arachnoid cyst, hypermetropia
Treatment	*extirpation of* odontogenic keratocysts and excision of trichofolliculoma	*extirpation of* odontogenic keratocysts, *excision of basaliomas, resection and chemotherapy of medulloblastoma*	*extirpation of* odontogenic keratocysts, *excision of basaliomas*	*extirpation of* odontogenic keratocysts, *excision of basaliomas*	*extirpation of* odontogenic keratocysts, implantation of defibrillator	*extirpation of* odontogenic keratocysts, *excision of basaliomas*	*extirpation of* odontogenic keratocysts

Legend: na, not available, CPR, cardiopulmonar resuscitation, VSD, ventricular septal defect
Patient 1 and patient 2 are siblings.

Tab. 2. Overview of detected odontogenic cysts.

Patient	Number of cysts TOTAL–UJ–LJ	Localization (teeth)	Size (mm)	Size (% of jaw)	Age	
					Year	Month
1	5–2–3	23	30×23×25	15	11	3
		43	15×10×10	2	12	4
		37	17×13×10	3	13	8
		28	25×20×13	10	16	0
		48	11×9×5	1.5	16	0
2	9–4–5	13	35×15×15	11	11	1
		23	20×15×15	6	11	1
		33	30×20×10	12	11	1
		43	40×20×10	10	11	1
		47	25×10×10	3	11	1
		37	35×30×20	13	12	5
		17	10×10×7	2	13	3
		27	30×25×10	15.5	13	3
		47	14× 10×7	2	13	3
3	4–2–2	18	45×40×35	37	19	10
		28	30×20×15	12.5	19	10
		38	50×23×15	14.5	19	10
		48	60×20×15	15	19	10
4	4–1–3	43	30×27×15	10	8	1
		23	10×9×7	2	9	6
		37	25×16×15	5	9	6
		47	25×15×8	4.5	9	6
5	2–1–1	11	15×12×10	2	8	9
		47	15×10×10	2	6	9
6	6–4–2	18	20×10×10	4	12	5
		23	30×15×15	10	12	5
		48	65×25×20	20	12	5
		27	8×7×5	1.5	13	11
		48	20×15×8	4	14	7
		28	45×15×10	14	17	2
7	2–0–2	37	17×10×5	2	6	10
		43	30×24×12	9	6	10

Tab. 3. Number and localisation of odontogenic cysts.

Right Side	LOCATION LEFT / RIGHT AND UPPER / LOWER																	Left Side	TOTAL
5	**2**	**1**				**1**		**1**				**4**					**2**	**3**	9	14
	8	7	6	5	4	3	2	1	+ --	1	2	3	4	5	6	7	8		
12	**4**	**4**				**4**						**1**				**4**	**1**	6	18

Total R-Side	Location Summary Left / Right																	Total L-Side	TOTAL
17	6	5				5		1				5				6	4	15	32

1. OKCs are most common in the 4th to 6th stages of tooth development;
2. apparently only the germs of permanent teeth are affected, since we have not observed OKC in temporary teeth;
3. the most commonly affected tooth germs are in the 2nd molars (11×/34%), canines (10×/31.5%), and 3rd molars (10×/31.5%);
4. there were no differences in the distribution of OKC with regards to the gender (M:F=4:3), affected jaw (upper:lower=14:18), or side (right:left=17:15) in analyzed patients.

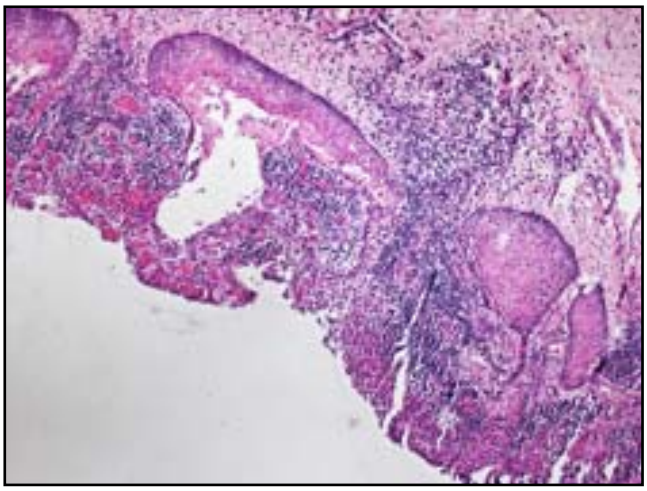

Fig. 4. Microscopic image shows two cysts. Both are typically lined by squamous epithelia, the lumen of one of the cyst is filled with keratinized acellular debris.

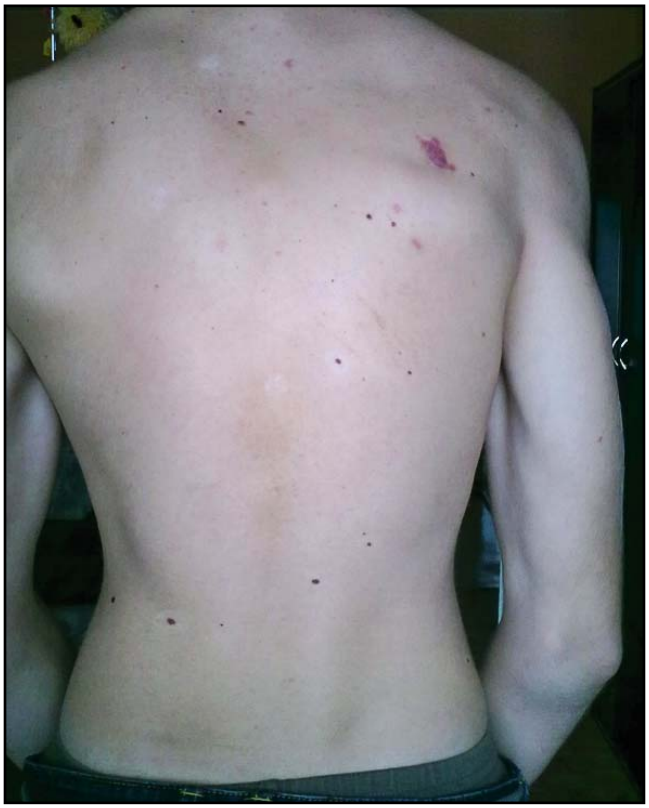

Fig. 5. Medium degree pigmentation.

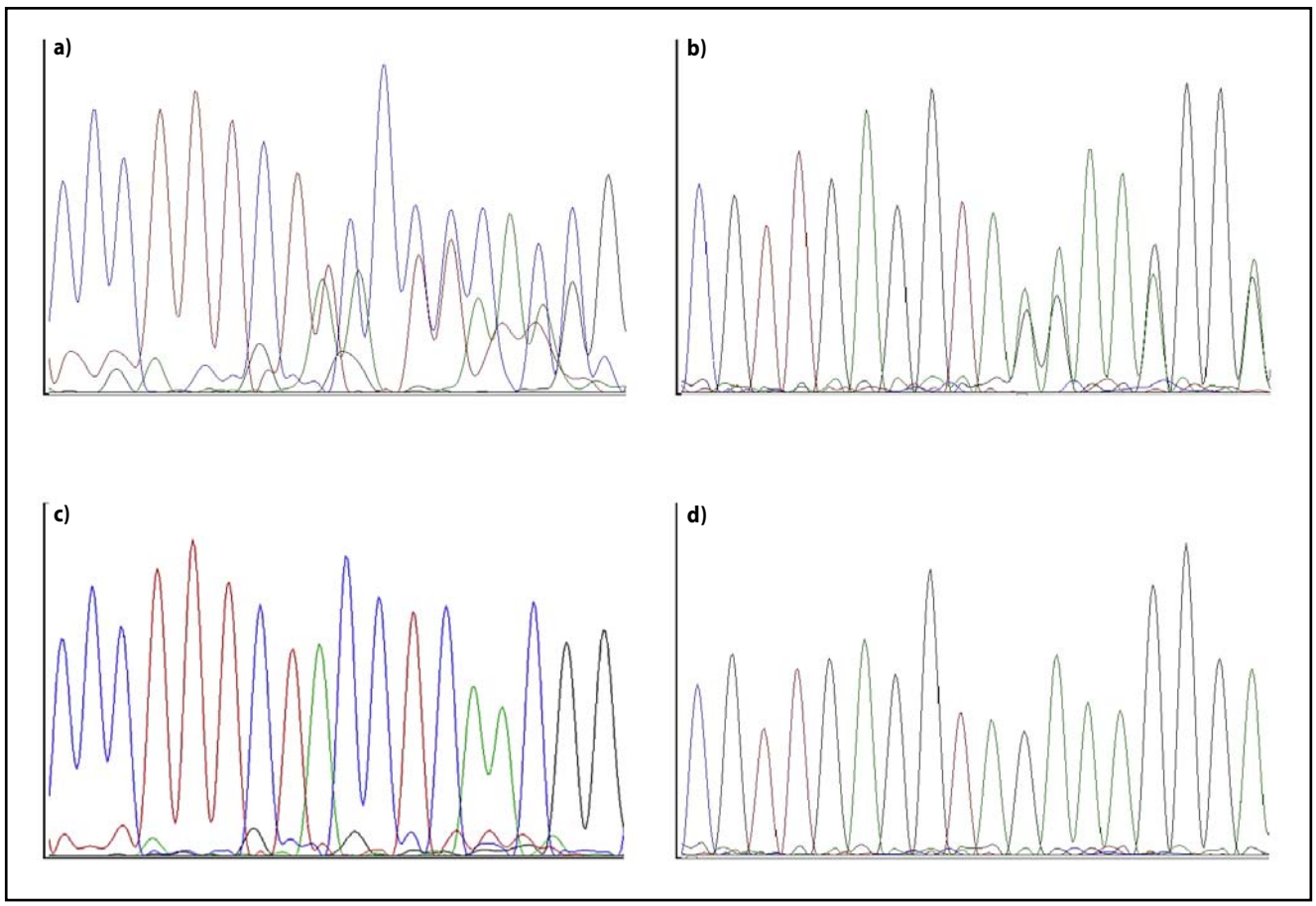

Fig. 6. Electrophoregram demonstrating mutation c.2929dupT (p.Tyr977LeufsTer16) in the *PTCH1* gene in a patient with BCNS (Ref.Seq. GenBank NM_000264.3). **a)** patient, forward, **b)** patient, reverse, **c)** negative control, forward, **d)** negative control, reverse.

METHODS

Histological diagnosis

Histological examination confirmed the diagnosis of OKC in all instances. These were typically lined with squamous epithelia and the lumen of one of the cyst was filled with keratinized acellular debris (Figure 4).

Clinical genetics

The proband was of normal stature for his age, with unblemished skin, medium-degree pigmentation (Figure 5), macrocephalic head with right facial asymmetry, fair hair, normal eyes, nose and mouth, slightly asymmetrical earlobes, symmetric neck and chest, normal male genitalia, limbs, and palm lines were normal. No other apparent phenotypic alternations were detected. The presence of multiple pigmented nevi on the skin increased the diagnosis of BCNS highly likely.

Molecular genetics

Following normal cytogenetic examination (46, XY), DNA Sanger sequencing (ABI3130xl gene sequencer, ThermoFischer Scientific; USA) of the *PTCH1* gene (MIM#601309) revealed a c.2929dupT predicting a p.(Tyr977Leufs*16), which, based on parental DNA analysis, appeared *de novo* in the germline. This result confirmed the clinical diagnosis of BCNS (Figure 6).

RESULTS AND DISCUSSION

Hereby, we present a typical case report and retrospective analysis of a representative cohort of BCNS cases seen at our stomatological center within the last decade. The reported case is currently under observation, with regular follow-up examinations scheduled at six-month intervals. The patient and his relatives have been informed of the possibility of developing other features of BCNS and the importance of careful monitoring.

Multiple OKC usually occur as a component of BCNS, Orofacial digital syndrome #MIM 311200), Noonan syndrome (#MIM 163950), Ehler–Danlos syndrome (#MIM 130000), Simpson-Golabi-Behmel syndrome (#MIM 312870), or other rare syndromes as reviewed by Kurdekar (2013). Our patient was apparently healthy, with no suggestive family history and no physical features suggestive of the aforementioned syndromes, such as orofacial maxilla and mandibular defects, stunted growth, bleeding diathesis, hyper-extensible skin or hypermobile joints, or other congenital anomalies associated with overall growth disturbances. However, multiple pigmented nevi on the skin helped confirm the diagnosis of BCNS.

From the histological point of view, para-keratinization, intramural epithelial remnants, and satellite cysts are more frequent in cases of multiple OKC associated with BCNS than solitary keratocysts (Woolgar *et al.* 1987). In our patient, both findings were observed. The cysts were typically lined by squamous epithelia and the lumen some were filled with keratinized acellular debris.

The biological behavior of multiple OKC associated with BCNS is more aggressive and these cysts have higher recurrence rates (82%) compared with solitary keratocysts (61%) (Dominguez *et al.* 1988). The mechanisms of origin and growth of OKC are based on cyst initiation and formation and on keratocyst growth. In this case, the presence of paresthesia was atypical and directly connected with keratocyst growth. After the surgery and healing period, the mental nerve recovered its functionality and the patient was without unpleasant sensations. A similar clinical manifestation has not been reported in the literature. Another interesting finding in our patient was the concomitant occurrence of anodontia associated with tooth 12 and 22, associated with an impacted canine in the maxillary right quadrant, which is a very rare finding in itself. It is well-known that dentigerous cysts associated with unerupted teeth are relatively rare, whereas unerupted teeth are common occurrences, which suggest that a genetic predisposition could be possible.

Obtained results allowed us to formulate the following recommendations for clinical practice in stomatology:

1. X-ray examination (panoramic radiograph) of jaws at age 6, 10, and 15 years, especially in cases reporting numbness and paresthesia;
2. In established cases of BCNS, follow-up radiographs are recommended at least once a year;
3. Following OKC extirpation, augmentation of jaw bone defects is not recommended in children, instead spontaneous bone healing is preferred, since bone regeneration and remodeling in children is much faster than in adulthood;
4. Unless there is a large bone defect, leaving the tooth in place, with more frequent check-ups, is worth considering. In addition, if needed the tooth can be straightened later in cooperation with an orthodontist. However, this does not apply to third molars where early germectomy is recommended instead.

In conclusion, awareness of BCNS among medical specialists who may encounter these patients in the first place (e.g. orthodontists, dentists, radiologists, neurologists) is important for its early diagnosis. Patients reporting lower jaw paresthesia should not be disregarded. The long-term consequences of the BCNS are associated with server morbidity and markedly decreased quality of life in patients. In this regard, early diagnosis represents an opportunity for effective management of this severe and progressive rare disorder.

ACKNOWLEDGEMENTS

Supported by CZ.2.16/3.1.00/24022OPPK, "Conceptual development project of research organization 00064203" (University Hospital Motol, Prague), European Regional Development Fund Prague (CZ.2.16/3.1.00/24022OPPK), LM2015091, 15-30880A, Norway Grants (NF-CZ11-PDP-3-003-2014) and COST-LD14073 to T.D. and M.M. The authors would like to thank Drs. S. Vejvalková, M. Simandlová and M. Koudová for their assistance with clinical genetic analysis of reported cases, Drs. Š. Čapková and L. Paroulková for the dermatological analyses.

Conflict of interest declaration: *The authors have no conflict of interest that could influence the content or processing of this manuscript.*

REFERENCES

1 Beach DF, Somer R (2011). Novel approach to Gorlin syndrome: a patient treated with oral capecitabine. Journal of Clinical Oncology. **29**: e397–401.
2 Borgonovo AE, Di Lascia S, Grossi G, Maiorana C (2011).Two-stage treatment protocol of keratocystic odontogenic tumour in zouny patients with Gorlin–Goltz syndrome: Marsupialization and later enucleation with peripheral ostectomy. A 5-year-follow-up experience. International Journal of Pediatric Otorhinolaryngology. **75**: 1565–1571.
3 Bronoosh P, Shakibafar AR, Houshyar M, Nafarzade S (2011). Imaging findings in a case of Gorlin-Goltz syndrome: a survey using advanced modalities. Imaging Science in Dentistry. **41**: 171–175.
4 Budinčević H, Starčević K, Bielen I, Demarin V (2014). Gorlin-Goltz syndrome and stroke: a case report. Acta Dermatovenerol Croat. **22**: 209–12.
5 Crawford JR, Rood BR, Rossi CT, Vezina G (2009). Medulloblastoma associated with novel PTCH mutation as primary manifestation of Gorlin syndrome. Neurology. **72**: 1618.
6 Dominguez FV, Keszler A (1988).Comparative study of keratocysts, associated and non-associated with nevoid basal cell carcinoma syndrome. J Oral Pathol. **17**: 39–42.
7 Hegde S, Shetty SR (2012). Radiological features of familial Gorlin-Goltz syndrome. Imaging Science in Dentistry. **42**: 55–60.
8 Hottinger AF, Khakoo Y (2007). Update on the management of familial central nervous system tumor syndromes. Curr Neurol Neurosci Rep. **7**: 200–7. Review.
9 Hutton SB, Kalamchi S, Wright JM (2012). An incidentally discovered radiolucency in the posterior mandible. Oral Surg Oral Med Oral Pathol Oral Radiol. **113**: 17–20.
10 Joshi PS, Deshmukh V, Golgire S (2012). Gorlin-Goltz syndrome. Dental Research Journal, Dent Res J (Isfahan). **9**: 100–106.
11 Kitsiou-Tzeli S, Willems P, Kosmadaki M, Leze E, Vrettou C, Kanavakis E, Katsarou A (2011). Nevoid basal carcinoma syndrome (Gorlin syndrome) and pronounced androgenic alopecia in a woman with a novel mutation p.Leu1159fsx32 in the PTCH gene. The Journal of Dermatology. **38**(12): 1205–8.
12 Kurdekar RS, Prakash J, Rana AS, Kalra P (2013). Non-syndromic odontogenic keratocysts: A rare case report. Natl J Maxillofac Surg. **4**: 90–93.
13 Leger M, Quintana A, Tzu J, Yee H, Kamino H, Sanchez M (2011). Nevoid basal cell carcinoma syndrome. Dermatology Online Journal. **15**(17): 23.
14 Li TJ, Sun LS, Luo HY. (2006). Odontogenic myxoma: a clinicopathologic study of 25 cases. Arch Pathol Laboratory Med. **130**: 1799–1806.
15 Myoung H, Hong SP, Hong SD, Lee JI, Lim CY, Choung PH, Lee JH, Choi JY, Seo BM, Kim MJ (2001). Odontogenic keratocyst: review of 256 cases for recurrence and clinicopathologic parameters. Oral Surg Oral Med Oral Pathol Oral Radiology Endod. **91**: 328–333.
16 Nair PP, Khilari M, Peddawad D, Chandrashekhar L (2013). Meningeal calcification in basal cell nevus syndrome. BMJ Case Rep. **28** ;2013
17 Ortega García de Amezaga A, García Arregui O, Zepeda Nuño S, Acha Sagredo A, Aguirre Urizar JM (2008). Gorlin-Goltz syndrome: clinicopathologic aspects. Med Oral Patol Oral Cir Bucal. **13**: E338–343.
18 Reichart PA, Philipsen HP, Sonner S (1995). Ameloblastoma: biological profile of 3,677 cases. Eur J Cancer B Oral Oncol. **31:** B86–99.
19 Sadek AR, Vajramani G, Barker S, Walker M, Kennedy C, Nader-Sepahi A (2014).Multiple spinal osteochondromata and osteosarcoma in a patient with Gorlin's syndrome. Clin Neurol Neurosurg. **118**: 5–8.
20 Shear M, Speight PM (2007). Cysts of the oral and maxillofacial regions. Blackwell Munksgaard, 4th ed., Copenhagen, 223 p.
21 Sirous M, Tayari N. (2011). A case report of Gorlin–Goltz syndrome as a rare hereditary disorder. Journal of Research in Medical Science.**16**: 836–840.
22 Woolgar JA, Rippin JW, Browne RM (1987). The odontogenic keratocyst and its occurrence in the nevoid basal cell carcinoma syndrome. Oral Surg Oral Med Oral Pathol. **64**: 727–730.
23 Yang S, Zhao C, Zhang Y, Liao S (2011). Mediastinal fetal rhabdomyoma in nevoid basal cell carcinoma syndrome: a case report and review of the literature. Virchows Arch. **459**: 235–238.