CASE REPORT

Journal of Pre-Clinical and Clinical Research, 2018, Vol 12, No 3, 95-99
www.jpccr.eu

Mandibular odontogenic cysts associated with basal cell carcinoma in a patient with Gorlin-Goltz syndrome – Case Report

Anna Gaweda[1], Jolanta Wojciechowicz[1], Sara Dweik[2], Mateusz Wachowicz[2], Agnieszka Kałuża[2]

[1] *Department of Maxillofacial Surgery, Medical University, Lublin, Poland*
[2] *Medical University, Lublin, Poland*

Gaweda A, Wojciechowicz J, Dweik S, Wachowicz M, Kałuża A. Mandibular odontogenic cysts associated with basal cell carcinoma in a patient with Gorlin-Goltz syndrome – Case Report. J Pre-Clin Clin Res. 2018; 12(3): 95–99. doi: 10.26444/jpccr/93554

Abstract

Gorlin-Goltz syndrome (GGS) is a genetic disease of autosomal dominant inheritance. It is characterized by the presence of multiple basal-cell carcinoma foci, odontogenic keratocysts and anomalies of the skin, eyes, bones, nervous and endocrine system. Patients are predisposed to various neoplasms, such as medulloblastoma and fibrosarcoma. Rare incidence of the syndrome and multi-organ manifestations require providing patients with multi-specialist care, in particular, with dermatologists, dentists and surgeons. This is a case report of a 63-year-old patient with Gorlin-Goltz syndrome treated for odontogenic keratocysts of the mandible and basal-cell carcinoma. The report includes an extensive review of the GGS with regard to its etiology, features, clinical examination, diagnostic criteria and treatment modalities.

Key words

odontogenic jaw cysts, basal-cell carcinoma, Gorlin-Goltz syndrome

INTRODUCTION

Gorlin syndrome, also known as Gorlin-Goltz syndrome (GGS), nevoid basal-cell carcinoma syndrome (NBCCS), jaw cysts syndrome or fifth phakomatosis, is a rare genetic disease of autosomal dominant inheritance. Mutation of human Patched gene PTCG1 is responsible for the occurrence of the disease [1, 2, 3].

The gene is located on chromosome 9 (q22-q31) and its most likely position is between D9S12 and D9S53 DNA markers. Although its occurrence among family members is an important diagnosing criterion, it has been found that between 20–40% of cases result from a *de novo* mutation of the PTCH1 gene [1, 4, 5]. According to some researchers, new mutations occur in 35–50% of patients [4, 6, 7]. In this group of patients, GGS may occur spontaneously and reveal phenotype in various ways. According to the current state of knowledge, mutations of other genes, such as Patched2 (PTCH2), Smoothened (SMO) and Sonic Hedgehog (SHH), are also observed in relation to basal-cell carcinoma and medulloblastoma [5, 7], and they can influence the occurrence of the syndrome. The cause of the syndrome is a complete loss of PTCH1 gene action [8]. The protein encoded by the PTCH1 gene acts as a transmembrane receptor and contributes to the regulation of development and proliferation of stem cells in the skin, skeletal and central nervous system [8, 9]. Homozygotes to PTCH1 mutations have predispositions for such neoplasms as basal-cell carcinoma, medulloblastoma, cystic adenoidal epithelioma, esophageal and urinary bladder cancer [1, 2, 3, 6, 7, 10, 11].

Nevoid basal cell carcinoma syndrome (NBCCS) affects all ethnic groups but occurs most frequently in white patients with comparable frequency in both genders from 1/56000 [6], 1/57000 [4], 1/164000 [10] to 1/256000 [12]. NBCCS is characterised by multi-organ involvement and an increase in the risk of occurrence of basal-cell carcinoma. Other symptoms of Gorlin syndrome include keratocystic odontogenic tumour, palmar and plantar pits, intracranial defects, medulloblastoma, calcification of the dura mater, cysts of mesenteric lymph nodes and ovarian or cardiac fibroma.

Lesions in the craniofacial region include frontal and temporoparietal bossing, strongly marked superciliary arches, wide base of the nose, hypertelorism, low occipital position, cleft lip or palate, opthalmic anomalies ranging from congenital blindness to corneal opacity, strabismus and retinitis [1, 2, 3, 6, 7, 10, 11]. The pathognomonic symptom of GGS is multilamellar calcification of the falx cerebri, revealed by computed tomography [2, 13, 14].

Basal-cell carcinoma usually develops after puberty. The number of BCC lesions varies from several to thousands, their diameter ranges from 1 – 10 mm. They may have various forms, for instance, from skin-coloured nodules or papules to ulcerating plaques. They are usually located on the face, back and chest, but they may also be found on the skin unexposed to the sun. Aggressive forms of basal-cell carcinomas infiltrating the facial bones occur very rarely [11].

Another frequent symptom of GGS is keratocystic odontogenic tumour (KCOT), primarily defined as a keratocyst. This is a benign odontogenic tumour containing dental lamina without odontogenic ectomesenchyme, characterized by a high recurrence rate and high proliferation index. It destroys adjacent tissues and develops satellite micro-tumours responsible for frequent recurrences; it can also produce inflammatory symptoms of a developing cyst. In other circumstances, the tumour is often accidentally detected on X-ray examination. It is characterized by potential aggressivity more frequent in the maxillar than mandibular region) [3, 6, 7, 10]. The lesions occur in as many as 90% of patients above the age of 40 [15]. The KCOTs

Address for correspondence: Anna Gaweda, Department of Maxillofacial Surgery. Medical University of Lublin, The Medical University of Lublin, Staszica 11, 20-081 Lublin, Poland, 20-081 Lublin, Poland
E-mail: agaweda5@wp.pl; Received: 1 June 2018; Accepted: 19 July 2018

are divided into parakeratotic, orthokeratotic, and (rarely) mixed and solid lesions. They are differentiated based on a histological examination. The tumour consists of a thin fibrous external pouch the interior of which is lined with a stratified squamous epithelium of a parakeratotic (96%) type. The orthokeratotic form of tumour seldom occurs, has a milder course and considerably fewer recurrences. Therefore, according to the WHO stages, the orthokeratotic form of the lesion is classified as an odontogenic cyst, and the parakeratotic form is considered a benign neoplasm [5, 15]. The cavity of the tumour is filled with thick keratinous cells or straw-coloured fluid. An X-ray image of KCOT in its early stage shows a spherical or oval unilocular lytic bone lesion often involving a wisdom tooth. It is well circumscribed and has a well-defined osteosclerotic rim which may become less visible while the lesion grows and transforms into a multilocular form [6, 7, 15]. Gorlin-Goltz syndrome is diagnosed if two major criteria or one major and two minor ones are found [1, 2, 3, 6, 7, 10, 11, 14].

Major criteria include:
- more than two basal-cell carcinomas or one in a patient <20 years old)
- odontogenic keratocysts of the jaw;
- three or more palmar or plantar pits;
- calcifications of falx cerebri;
- fused, bifid or markedly spla;ed ribs
- a first-degree relative with GGS.

Minor criteria include:
- macrocephaly
- congenital anomalies: frontal bossing, coarse facies, hypertelorism, cleft lip or palate;
- skeletal anomalies: marked pectus deformity, marked syndactyly of the digits;
- radiologic anomalies: bridging of the sella turcica, flame-shaped lucencies of the hands and feet, vertebral anomalies;
- ovarian fibroma;
- medulloblastoma [1, 2, 3, 6, 7, 10, 11, 14].

CASE REPORT

A 63-year-old male patient reported to the Department of Maxillofacial Surgery of the Medical University of Lublin, Poland, in 2015 to have his bilateral cysts located in the body of the mandible treated. The patient complained of oedema in the vestibule of the oral cavity that persisted for two months and uncomfortable adjustment of the lower denture that he had already been using. In his past medical history, the patient reported surgical treatment of multifocal basal cell carcinoma that lasted for 10 years. The patient had had several tens of focuses/foci of epithelioma from the face, neck, trunk and thorax removed. In the systemic review, an elevated level of cholesterol, gastric ulcers, degeneration of the lumbar and cruciate vertebral column were reported.

Examination of the skin revealed two foci of basal cell carcinoma with a disameter of approximately 4 and 6 mm in the vicinity of a lesion in the left pre-aural region that had been removed surgically one year before (Fig. 1). The patient had numerous scars after the removal of epitheliomas of the face (Fig. 2) neck, trunk and thorax (Fig. 3, 4). There was a new focus of basal cell carcinoma on the cranial vault which was planned to be removed soon. Clinical examination showed a large head (circumference of 60 cm) with prominent frontal tubers and distinctly marked supraorbital ridges. The patient's mean interpupillary distance (IPD) was 75 mm (norm 60–65 mm), inner intercanthal distance equaled 40 mm (norm 30–32 mm) [16]. Intraoral examination revealed a bulge and deformity of the body of the mandible on the left side and moderate pain sensitivity of the left body of the mandible.

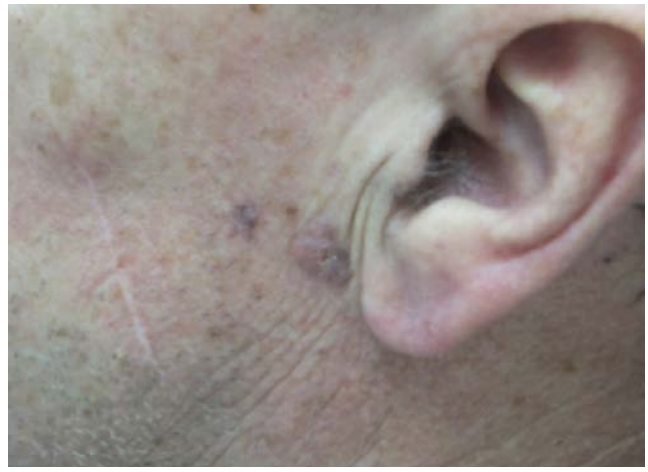

Figure 1. Scar after removing basal cell carcinoma (thin arrow) and two secondary foci (thick arrows)

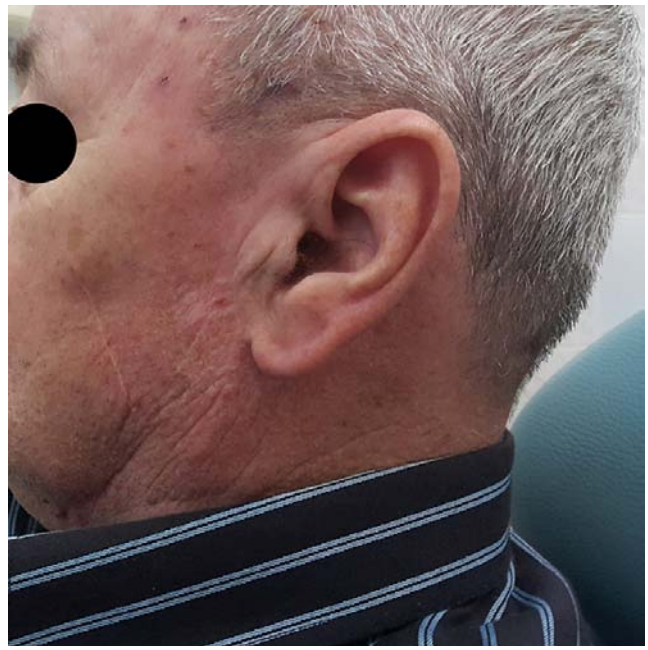

Figure 2. Condition after removing two foci of carcinoma in the left preauricular area

Panoramic radiograph (OPG) (Fig. 6) and computed tomography (CT) (Fig. 6,7) showed two oval areas of increased translucences that were well-differentiated with a marked osteosclerotic capsule. On the right, there is osteolytic defect from the 43 tooth at 44 mm and discontinuation of the bone lamella in the upper part of the mandibular alveolar process. On the left, there is the second area of mandible destruction from tooth 33 at 37 mm where the teeth 33 and 34 are in contact with the lesion. Discontinuation of the bone in the upper mandible is present.

Histopathological examination of the lesions revealed left-side keratocyst and right-side radicular cyst. Bilateral

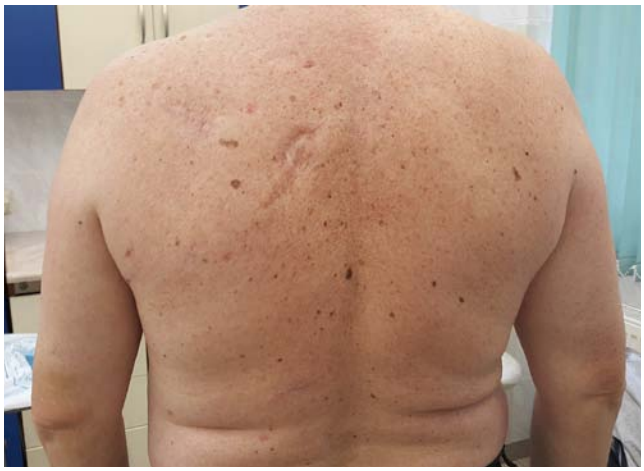

Figure 3. Numerous scars after the removal of basal cell carcinoma on the back

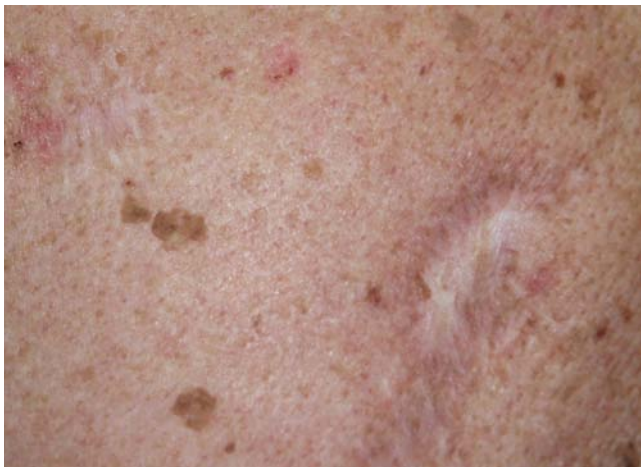

Figure 4. Two scars on the patient's back after removing basal cell carcinoma foci in 2006 and 2008

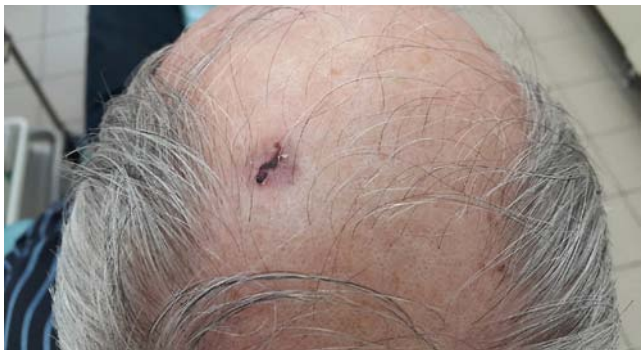

Figure 5. BCC focus on the cranial vault

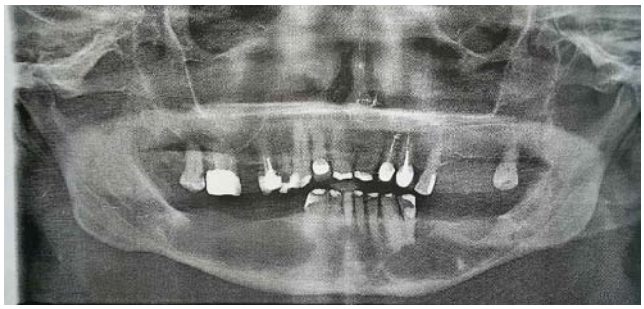

Figure 6. Panoramic radiograph – keratocyst on the left side and radicular cyst of the right side of the mandible

cystectomy under general anaesthesia was performed. The examination of the removed lesions confirmed the initial diagnosis.

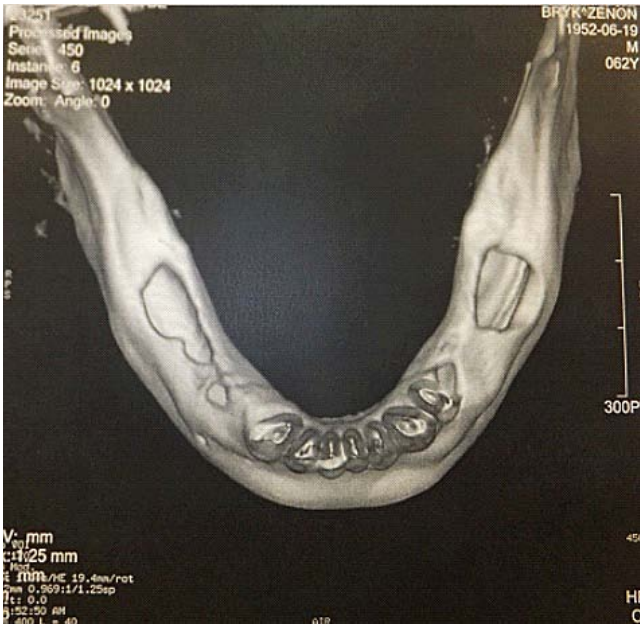

Figure 7. 3D CT of the mandible, visible two osteolytic defects with destruction of the mandibular compact bone lamella

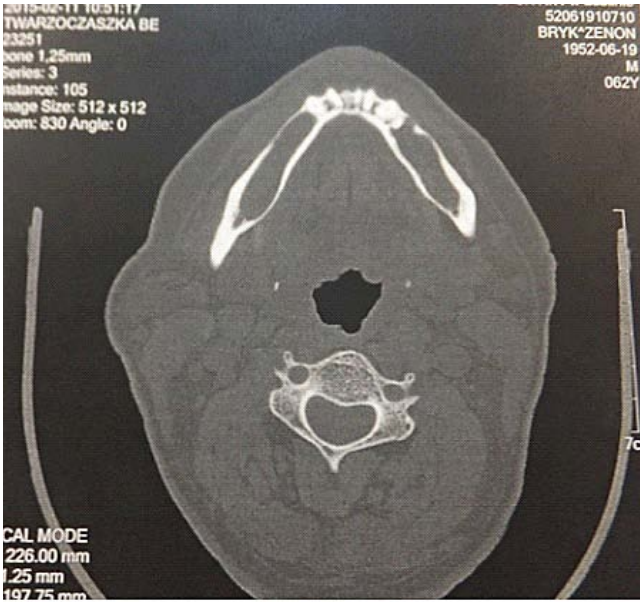

Figure 8. Axial projection CT, visible dentinogenerous cysts, left-sided keratocyst and right-sided radicular cyst of the body of the mandible

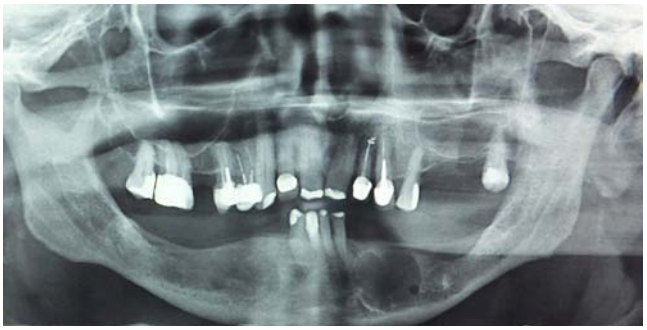

Figure 9. Panoramic X-ray recurrence of keratocyst on the left side and bone regeneration on the right side of the mandible

After 1.5 years, recurrence of the left-sided lesion and right-sided bone regeneration were observed (Fig. 9). New foci of basal cell carcinoma on the head and back were detected. Early removal of the lesions was planned (Fig. 10). Recurrence of the keratocyst was removed surgically (Fig. 11) and three weeks after the surgery, a complete healing of the intraoral lesions was observed (Fig. 12).

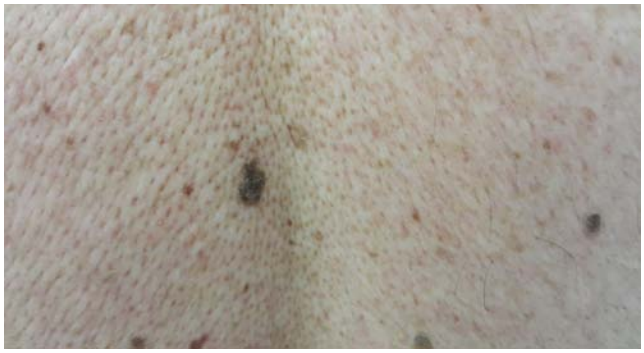

Figure 10. New foci of 2 BCC on the back

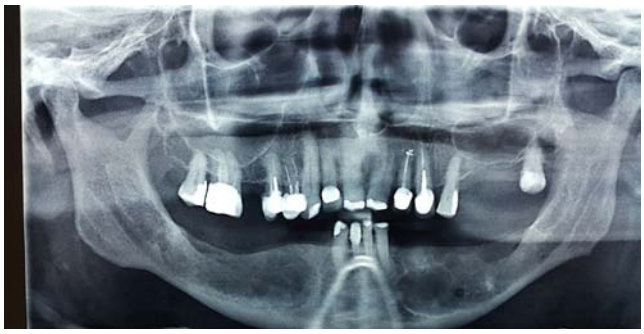

Figure 11. Control panoramic X-ray after removal of the left-sided KCOT recurrence, visible right-sided bone regeneration

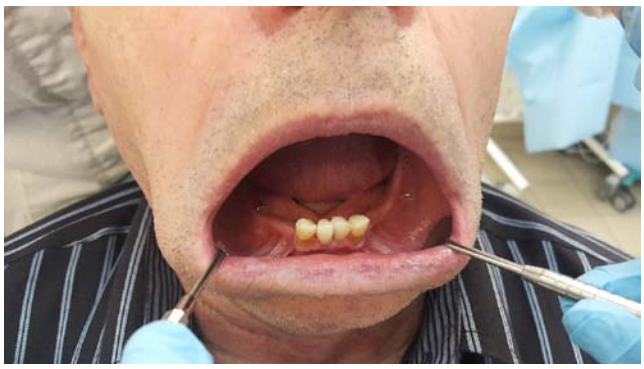

Figure 12. Healed mucosa after the treatment

DISCUSSION

Gorlin-Goltz syndrome is a hereditary disease. The condition is very difficult to diagnose in early childhood because its signs and symptoms appear gradually with different intensity as a child grows and are they are treated independently by different specialists [6, 7, 8]. More than 100 clinical abnormalities have been reported [10]. Symptoms of the disease should be diagnosed easily although it turns out to be difficult. Its variable expressiveness is proportional to the age of the patients. In most cases, GGS is detected using clinical major and minor criteria.

It is important to make an early diagnosis of GGS, especially in young people, due to predisposition to malignant degeneration [6]. Location of the gene for Gorlin syndrome offers the possibility that DNA markers can be used in risk estimation and presymptomatic identification of patients for surveillance. A detailed description of the gene that causes the syndrome may improve our understanding of the pathogenesis of basal cell carcinomas [2, 7, 8, 10, 13]. In the scientific lityerature there are many designations of the syndrome which often stem from its manifestations.

The following case report describes the syndrome with mandibular keratocysts and nevoid basal cell carcinomas of the face, neck and trunk. Moreover, minor signs and symptoms of GGS, such as telecanthus, hypertelorism and prominent frontal tubers, were found. According to the literature, the syndrome is more frequent in young middle-aged patients [1, 2, 15]. Other authors have observed clinical mainfestations of the syndrome in the first, second and third decade of life [6].

The 63-year-old patient described in the report had been treated for basal cell carcinoma for several years. Basal cell lesions of the skin are removed with a CO2 laser. In addition, classic surgical removal, cryosurgery and electrocoagulation are utilized [7, 13, 17]. In the case report, surgical removals with a margin of adjacent healthy tissue were performed several times, which enabled histopathological examination and confirmation of the initial diagnosis.

Surgical treatment of keratocysts depends on the patient's age, location and size of the lesions as well as the histopathological examination. In the case of keratocysts, a simple enucleation with the lesion curettage was performed. Other methods include direct application of Carnoy's solution or liquid nitrogen at -196°C after enucleation of the keratocyst [6, 7, 10, 15, 17], which were not applied in the patient due to the risk of damage of the inferior alveolar nerve. Greater keratocysts require partial or complete bone resection with immediate or delayed reconstruction [15]. According to Khaliq et al, KCOT is a frequent manifestation of GGS and can be its first sign. Among seven patients assessed from 2004 – 2015, there were 15 primary and two recurrent lesions [3]. Thus, follow-ups at regular intervals of six months up to five years after the operation, followed by annual check-ups for the entire life are recommended [17].

Physicians' knowledge of signs and symptoms, particularly such specialists as, maxillofacial surgeons, dentists and dermatologists, enables early diagnosis and referring patients to further diagnostic tests and treatment.

Patients should be educated about the disease, namely its causes, signs and symptoms, possible complications and available treatment. It is also vital to make patients aware of such risks as ionizing radiation (RTG, UV) that intensify the occurrence of basal cell carcinoma. Sun ray protection and Vitamin A may protect against skin cancer [1,7].

CONCLUSIONS

- Development of the odontogenic keratocysts of the jaws and basal-cell carcinoma of the skin suggest Gorlin-Goltz syndrome and require interdisciplinary diagnosis and treatment along with surgery.
- Rare incidence of the syndrome and multi-organ manifestations require providing patients with multi-specialist care.

REFERENCES

1. Manjima S, Naik Z, Keluskar V, Bagewadi A. Multiple jaw cyst-unveiling the Gorlin-Gotz syndrome, Contemp Clin Dent. 2015 Mar; 6(*Supp 1): 102–105.
2. Sirous M, Tayari N. A case report of Gorlin–Goltz syndrome as a rare hereditary disorder, J Res Med Sci. 2011 Jun; 16(6): 836–840 Available from: URL: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3214404/
3. Khaliq M, Shah A, Ahmad I,Hasan S, Jangam S, Farah. Keratocystic odontogenic tumors realted to Gorlin-Goltz syndrome: A clinico-pathological study, Craniofacial Research Foundation, 2016 May-Aug; 6(2): 93–100.
4. Farndon PA, Del MastroRG at al. Location of gene for Gorlin-Goltz syndrome. Lancet. 1992, 339–581–2.
5. Huang YF, Chen YJ, Yang HW: Nevoid basal cell carcinoma syndrome – case report and genetic study. J Dent Sciences, 2010; 5: 166–70 14.
6. Ramesh M., Krishanan R., Chalakkal P., Paul G. Gorlin-Goltz Syndrome: Case report and literature review. J Oral Maxillofac Path.2015, 19, 2:267–79.
7. Kiwilsza M, Sporniak-Tutak K. Gorlin-Goltz syndrome – a medical condition requiring a multidisciplinary approach, Med Sci Monit, 2012; 18(9); RA145–153.
8. Deneswari M, Reddy MSR. Genetic mutations in Gorlin-Goltz-syndrom. Indian J Hum.Genet.2013, 19,3,369–372.
9. Burdgorf WHC, Plewing G, Wolf HH, Landhaler M.Braun-FalcoDermatologia. Carcinoma basocellulare. Refenberg J.Ruzicka T.Wydaw.Czelej, Lublin 2011, 1378–1379.
10. Kulkarni GH, Khaji SI, Kulkarni R. Multiple keratocysts of the mandible in association with Gorlin-Goltz syndrome: A rare case report. Contemp Clin Dent. 2014 Jul-Sep; 5(3): 419–421.
11. Manfredi M, Vescovi P, Bonanini M, Porter S. Basal cell carcinoma syndrome: a review of the literature Int. J. Oral Maxillofac. Surg. 2004; 33: 117–124 Nevoid.
12. KimonisVE, Golddstein AM, Pastiakia B at al. Clinical manifestation in 105 persons with nevoid basal cell carcinoma syndrome. Am J Med Genet. 1997,69,299–308.
13. Alanna F. Bree and Maulik R. Shah for the BCNS Colloquium Group. 2011. Consensus Statement From the First International Colloquium on Basal Cell Nevus Syndrome(BCNS) Am J. of medical genetics Part A 155:2091–2097.
14. Borzecki A, Pilat P, Raszewska-Famielec M, Pilat J. Combination therapy of basal-cell carcinoma in 31-year-old patient with nevoid basal cell carcinoma syndrome – Case study, JPCCR, 2016, Vol 10, No 1, 66–68.
15. Brzozowski F, Wanyura H, Stopa Z, Kowalska K. Odontogenic keratocysts in the material of the Department of Craniomaxillofacila Surgery, Medical University of Warsaw. Czas Stomatol, 2010; 2: 69–78 24.
16. Booth PW, Schendel SA, Hausamen JE, Maxillofacial Surgery, Second Edition, Volume 1, Churchill Livingstone Elsevier, 2006.
17. Bahadure RN, Jain ES, Badole GP, Gorlin and Goltz Syndrome. A Case Report with Surgical Review, Int J Clin Pediatr Dent. 2013 May-Aug; 6(2): 104–108 Available from: doi: 10.5005/jp-journals-10005-1199.