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PRIKAZ SLUČAJA
*CASE REPORT*

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# Oralne i maksilofacijalne manifestacije Gardnerova sindroma: prikaz slučaja

# *Oral and Maxillofacial Manifestations of Gardner's Syndrome: Case Report*

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**Sažetak**
Gardnerov sindrom rijedak je genetski poremećaj koji karakterizira trijada nasljedne polipoze, multipli osteomi i tumori mekog tkiva. U svim se tim slučajevima javlja maligna transformacija polipa debelog crijeva u rak debelog crijeva te zbog toga oboljeli imaju lošu kakvoću života. Muškarca u dobi od 27 godina na naš je odjel poslala obližnja medicinska ustanova kako bismo mu izvadili drugi donji lijevi kutnjak. Na priloženim ortopantomografskim snimkama bila je vidljiva karijesno destruirana kruna zuba, impaktirani donji očnjaci na donjem rubu mandibule i multipli osteomi mandibule. Iz anamneze je bilo jasno da pacijent boluje od Gardnerova sindroma i da je bio podvrgnut različitim kirurškim postupcima. Svrha ovog prikaza jest opisati oralne i maksilofacijalne simptome Gardnerova sindroma i njegove moguće stomatološke implikacije.

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## Uvod

Gardnerov sindrom (GS) rijedak je genetski poremećaj. Naziv je dobio prema Eldonu J. Gardneru koji je prvi opisao njegova svojstva godine 1951. Sindrom karakterizira trijada nasljedne polipoze, multipli osteomi i tumori mekih tkiva (1-5). Bolest uzrokuje mutacija gena APC-a lociranog na kromosomu 5q21, a to je gen mutant prisutan kod nasljedne adenomatozne polipoze (FAP-a). Iz tog se razloga Gardnerov sindrom smatra fenotipskom varijantom FAP-a (1).

## Introduction

Gardner syndrome(GS) is a rare genetic disorder. The syndrome is named by Eldon J. Gardner who first described the characteristics of syndrome in 1951. The syndrome is characterized by the triad of familiar polyposis, multiple osteomas and tumors of soft tissues (1-5). GS is caused by mutation of the APC gene located at chromosome 5q 21.,which is the same gene mutant in familial adenomatosis polyposis(FAP). For this reason Gardner's syndrome is considered as a phenotypical variant of FAP (1).

Bolest ima visoku stopu penetracije i varijabilnu ekspresivnost s incidencijom između 1:8.000 i 1: 14.000 živorođenih (1). Za Tursku nema točnih podataka.

Većina aficiranih pojedinaca ima obiteljsku anamnezu opterećenu tom patološkom pojavom, ali se 25 posto pacijenata javlja s novom kliničkom slikom svježe dominantne mutacije te mogu biti prvi aficirani članovi svoje obitelji (2,6).

Iako je maligna pretvorba u rak prisutna u svim slučajevima (1,3), najvažniji nalaz kod toga sindroma su crijevni polipi. Najčešći su u debelom crijevu i rektumu, no mogu se razviti i u cijelom gastro-intestinalnom traktu, uključujući želudac, dvanaesnik i terminalni ileum. Polipi se počinju javljati u pubertetu, a posebice tijekom drugog i trećeg desetljeća života kada se njihov izgled pojačava (3). Tijekom kolonoskopije može se ustanoviti broj polipa u rasponu od nijednog do više od 7.000 vidljivih u crijevima kod rijetkih pacijenata (3). Maligna transformacija samo je pitanje vremena. U pubertetu je malignitet 5 posto i povećava se prema 100 posto kod pacijenata u dobi iznad 50 godina (3,7).

Drugo važno svojstvo Gardnerova sindroma jest nalaz multiplih osteoma (3,4). To su benigne osteogene lezije sa sporom proliferacijom na kompakte medularne kosti. Njihova je lokalizacija u facijalnim kostima i kraniju, iako se mogu pojaviti i na bilo kojoj drugoj kosti. Prisutnost im je najčešće asimptomatska, ali klinički mogu uzrokovati oteklinu i asimetriju, posebice ako su smješteni periferno.

Tumori mekih tkiva kod GS-a uključuju fibrome, fibromatitis, rak štitnjače, te epidermoidne i lojne ciste (3-5). U većem dijelu populacije epidermoidne ciste čest su benigni nalaz, ali se nikada ne javljaju u pubertetu. Kod pacijenata s Gardnerovim sindromom češće se javljaju i ranije ih se nalazi, dakle i u doba puberteta.

Udjel od 75 posto pacijenata s Gardnerovim sindromom ima kongenitalnu hipertrofiju pigmentnog epitela mrežnice, što se s lakoćom može detektirati postupkom oftalmoskopije. Takve su lezije rijetke kod zdravih pojedinaca (3-5).

## Prikaz slučaja

Muškarca u dobi 27 godina na naš je odjel poslala obližnja medicinska ustanova radi ekstrakcije drugog donjeg lijevog kutnjaka. Kliničkim pregledom potvrđen je bol senzitivnim odgovorom na test vertikalne perkusije.

Na priloženim ortopantomografima (Sl.1) vidjela se kruna zuba destruirana karijesnom lezijom te

It has a high dominant penetrance and variable expressivity with incidence between 1:8.000 and 1:14.000 live births (1). There is no precise data for Turkey.

The majority of individuals have a family history of this pathology, but 25% of patients can present with a new dominant mutation and be the first member of their family (2,6).

Through the malignant transformation to the cancer in all cases(1,3),intestinal polyps are the most important findings in this syndrome.Their localization is mostly in colon and rectum, however they may develope through the gastro-intestinal tract,including stomach, duodenum and the terminal ileum.The polyps start to appear in puberty, especially during the second and third decades of life, their appearance is intensive (3). The number of polyps can range from no detectable polyps at colonoscopy to more than 7.000,which are seen on resected specimens of bowel (3). Malignant transformation of polyps is a matter of time.İn puberty the incidence of malignancy is 5%, increasing to 100% for the patients more than 50 years of age (3,7).

Multiple osteomas are the second most important features of Gardner syndrome.(3,4) Osteomas are benign osteogenic lesions characterized by slow proliferation of compact or medullary bone. Their localization is in facial bones and cranium, however they can involve any other bone.Their presence is mostly asymptomatic,but clinically they can produce tumefaction and asymmetry especially if they are located peripherally.

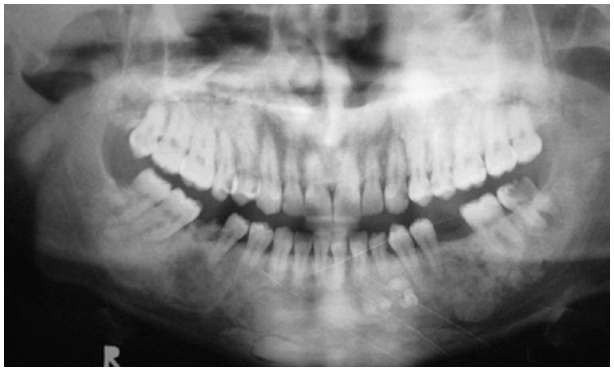
Tumours of soft tissues including fibromas, fibromatisis, thyroid cancer, epidermoid and sebaceous cysts are also seen at the patients with GS (3-5). Epidermoid cysts are common benign findings in general population, but they never occur in puberty. At the patients with Gardner's syndrome their presence is more frequently and starts before and during puberty.

75%of Gardner syndrome patients have congenital hypertrophy of the retinal pigment epithelium (CHRP), easily detected on ophtalmoscopy. In healthy persons these lesions are rare (3-5).

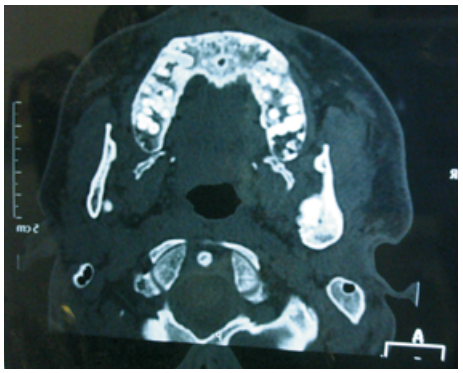
## Case report

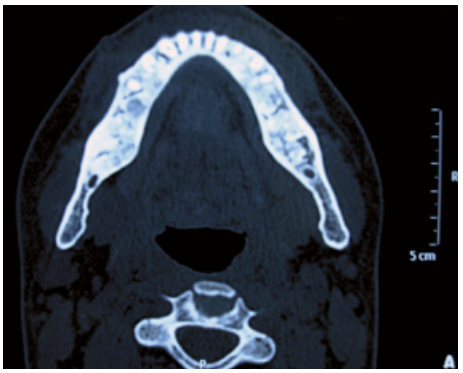
A 27-years old male was reffered to our department from a nearby medical centre for extraction of lower left mandible second molar tooth. On clinical examination the pain was confirmed by sensitivity on vertical percussion.

The panoramic radiographs (Figure 1) disclosed a tooth crown destroyed with caries lesion, impacted

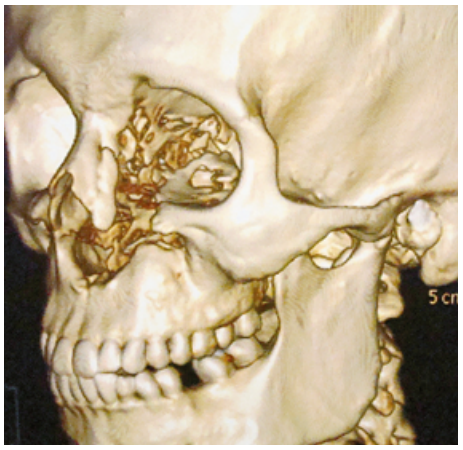


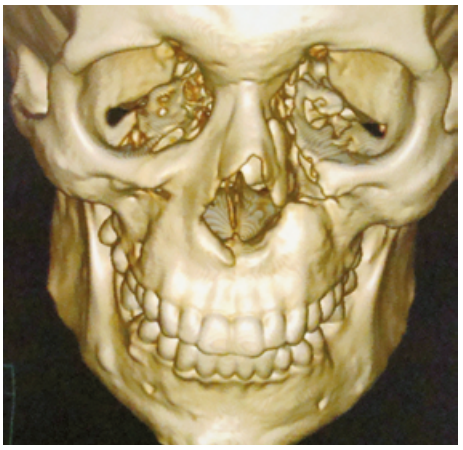
**Slika 1.** Ortopantomogram s vidljivim multiplim osteomima i impaktiranim očnjakom na donjem rubu mandibule
**Figure 1** The panoramic radiographs showing multiple osteomas and an impacted canine tooth in the inferior border of the mandible



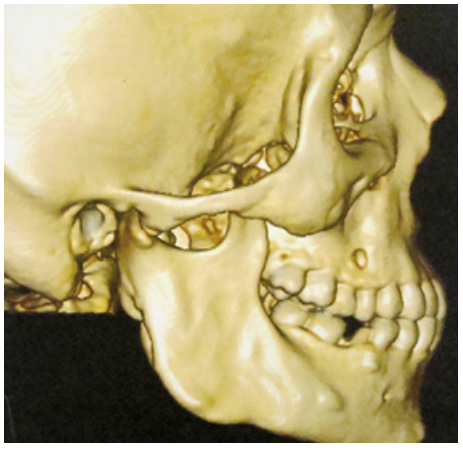


**Slika 2.a,b** Na aksijalnoj CT-snimci vidljive su radio nepropusne mase smještene obostrano u mandibuli i maksili
**Figure 2a,b** Axial CT shows multiple radio opaque masses located in mandible and maxilla for both sides





**Slika 3.a,b** Na 3D CT snimci uočljiv je defekt na lateralnoj granici nosne šupljine, što je posljedica kirurškog postupka
**Figure 3a,b** On 3 D CT can be noticed a defect on the lateral wall of the nose as a result of surgical procedure



**Slika 4.** Lateralna 3 D CT snimka otkriva prisutnost osteoma u obliku ekzostotskih formacija.
**Figure 4** Lateral 3 D CT from right side shows a presence of osteomas as the exostotic formations.

impaktirani donji očnjaci smješteni na donjoj granici mandibule, uz multiple osteome s obje strane mandibule i maksile.

Iz anamneze je bilo jasno da pacijent boluje od Gardnerova sindroma (GS-a) i da je bio podvrgnut različitim kirurškim postupcima, poput profilaktične kolektomije i uklanjanja nazalnih i mandibularnih osteoma. Simptome rektalnog krvarenja imao je od 20. godine. Nakon daljnjih pregleda dijagnosticiran mu je Gardnerov sindrom.

Pacijent je naveo kiruršku korekciju asimetrije na lijevom angulusu mandibule prije tri godine, a bila je obavljena postupkom osteotomije.

Njegova obiteljska anamneza bila je negativna, tj. on je bio prvi član iz obitelji s Gardnerovim sindromom.

Od godine 2001. do 2007. pacijent je bio na sedam operacija, a dvije su uključivale enukleaciju osteoma u maksilofacijalnoj regiji. Ostalih pet rezultiralo je totalnom kolektomijom.

Ekstraoralnim pregledom nisu bile ustanovljene ni asimetrija ni limfadenopatija.

Krvni nalazi – uključujući i hemogram i testove koagulacije - bili su normalni. Pacijent se savjetovao s liječnicima s odjela opće kirurgije te interne medicine i otorinolaringologije, i nije bilo kontraindikacija za kirurški ili koji drugi postupak.

Priložene su bile slike triju dimenzija CT-snimanja na kojima se vide multipli osteomi smješteni u medularnoj kosti (spužvastoj) s obje strane maksile i mandibule. Osteomi su se nalazili i u kondilima mandibule. Istodobno su uočeni i uklonjeni defekti u regiji maksilo-nazalne strukture, frontalnih nastavaka maksile, medijalne stijenke maksilarnog sinusa te srednjih i donjih nosnih hodnika (Sl.2).

Dijagnosticirani su bili i kronični sinuitis sfenoidnih maksilarnih i etmoidalnih sinusa te multiple formacije osteoma.

Pacijentu smo objasnili njegovo zdravstveno stanje i moguće posljedice liječenja, te je on iz straha odbio terapiju. Dakle, liječenje je bilo ograničeno na palijativnu skrb. Ekstrahiran mu je bio prvi donji lijevi kutnjak i bio je pod nadzorom idućih šest mjeseci.

## Rasprava

Multipli osteomi općenito se javljaju u adolescenciji i to najčešće u čeljusti, facijalnom skeletu i frontalnim kostima, ali mogu istodobno zahvatiti i bilo koju drugu kost (poput tibije ili femura) (3,4). Općenito, osteomi u facijalnim kostima i kraniju nilower canine teeth located in inferior border of mandible and multiple jaw osteomas located in mandible and maxilla from both sides.

From patient's history we found out that patient was suffering from GS and had undergone surgical procedures such as a prophylactic colectomy and had nasal and mandibular osteomas removed**.** The onset of symptoms like bleeding from rectum, manifested itself at the age of 20. Following the examinations the diagnosis was Gardner's syndrome.

The patient reported the presence of asymmetry on the left side of angulus mandible which was corrected 3 years ago with osteotomy.

The family pedigree was negative,which means that the patient is the first member of his family affected with Gardner's syndrome.

From 2001-2007 the patient had undergone seven operations of which two included enucleation of osteomas in the maxillofacial region. The other five resulted in complete colectomy.

On extraoral examination there was no facial asymmetry or lymphadenopathy.

The blood tests, which included hemogram and coagulation tests, were normal. Patient was consulted with General Surgery, Internal Medicine and Otolaryngology Departments, there was no contraindication for surgery or other treatment

The 3 dimension CT's presented multiple osteomas located into the medular (spongious) bone of the corpus of maxilla and mandible from both sides. They were also present in the mandibular condyles.

At the same time there were noticed the defects in the regions of maxillo-nasal suture, maxillary frontal processes, medial wall of the maxillary sinus, medial and inferior concha, which were the results of surgical enucleations of osteomas located there (Figure 2).

Chronic sinusitis in sphenoidal, maxillary and etmoidal sinuses, together with multiple osteoma formations, were dıagnosed, too.

After we have informed the patient about his state of health and possible consequences of therapy, he refused the treatment due to fear he was feeling. Therefore, therapy was limited to palliative care. Lower left mandible first molar tooth was extracted and the patient is for 6 months under follow up.

## Discussion

Multiple osteomas generally appear in adolescence and mainly involve the jaws, facial skeleton and frontal bones**,** but at the same time they can involve any other bone (long bones such as tibia or femur) (3,4). The presence of osteomas in facial

su česti, pa ako se i pojave to su uglavnom mandibularni osteomi, a oni su i najveći (3,5).

Kod bolesnika s GS-om opisani su slučajevi multiplih osteoma u paranazalnim sinusima (frontalni i etmoidni sinusi češće su zahvaćeni od maksilarnih ) (3). Kod našeg pacijenta osteomi su uglavnom bili smješteni u maksilarnim i etmoidnim sinusima.

U prosjeku se osteomi detektiraju 17 godina prije polipa debeloga crijeva (8). Iako ih ne moramo ekstirpirati, često se uklanjaju zbog njihova izgleda i tegoba kod pokretljivosti. Novi se osteomi javljaju već nakon nekoliko mjeseci do nekoliko godina (5).

Oralni radiološki nalazi GS-a obuhvaćaju multiple impaktirane i prekobrojne zube s multiplim osteomima čeljusti (na panoramskim radiografima izgledaju poput vatiranog pamuka) (3).

Kod našeg pacijenta bili su uočeni impaktirani donji očnjaci te multipli osteom u medularnoj kosti maksile i mandibule.

Odontogene ciste nisu obilježje toga poremećaja, ali se mogu razviti iz zubnih folikula.

Ekstrakcija zuba kod pacijenata s GS-om opisana je kao vrlo teška jer imaju iznimno gustu alveolarnu kost, a parodontni prostor im je jako tijesan zbog hipercementoze (9). Tijekom ekstrakcija zuba kod našeg pacijenta nije bilo poteškoća.

Uloga stomatologa opće prakse vrlo je važna, jer oni trebaju točno i pravodobno dijagnosticirati mnoga patološka stanja, uključujući i sindrome poput Gardnerova. Za svakog je pacijenta vrlo važno imati dobru i iscrpnu anamnezu, jasne ortopantomograme te obaviti kliničke preglede. Stomatolozi mogu biti prvi u detekciji ranih simptoma mnogih bolesti vezanih za maksilofacijalno područje.

Terapija GS-a mora biti simptomatska. Ponekad se, kao u našem slučaju, javljaju estetske i funkcijske tegobe u maksilofacijalnoj regiji, no one mogu upozoriti na prisutnost osteoma. U dijagnostičke svrhe dostatan je nalaz impaktiranih i prekobrojnih zuba te više od tri osteoma.

Razdoblje kontrole obuhvaća kliničke i rendgenske preglede svakih šest mjeseci. Najbolja tehnika za snimanje osteoma jest CT ili 3DCT.

Kako se polipoza obično javlja nakon osteoma (3), stomatolozi moraju najprije posumnjati na Gardnerov sindrom. Na taj način mogu pomoći u ranom postavaljanju dijagnoze i uputiti pacijenta na preventivne medicinske preglede.

bones and cranium is not common in general population, but if they appear mandibular osteomas are the commonest and largest (3,5).

There are cases which describe the presence of multiple osteomas at the GS patients in the para-nasal sinuses (frontal and etmoid sinuses are more affected than maxillary sinuses)(3). In the case of our patient, osteomas were located mostly in maxillar and etmoid sinuses.

On the average, osteomas are detected 17 years before appearance of colon polyps (8). Although osteomas do not need to be extirpated, they are often removed, due to their appearance and the interference contributed by their mobility. New osteomas can appear after a few months or years (5).

Oral radiological findings of GS include multiple impacted and supernumerary teeth with multiple jaw osteomas present as 'cotton-wool 'on panoramic radiographs (3).

In our case was noticed the presence of impacted lower canine tooth and multiple osteomas in the medular bone, both the maxilla and mandible .

Dentigerous cysts are not characteristic for this disorder, but they can appear arising from the follicles of teeth.

Tooth extractions in patients with GS have been reported to be very difficult, because of the extremely dense nature of the alveolar bone and the almost complete absence of the periodontal space caused by hypercementosis (9). In our patient the extraction was not difficult.

The role of general dental practitioners is very important for proper and early diagnosis of many pathological states including many syndromes such as Gardner`s. After doing a good anamnesis from the patient, clear dental panoramic radiographs and clinical examinations, the general dental practitioners can be in the position to first detect the early symptoms of many diseases connected with maxillofacial area.

The therapy of the GS has to be symptomatic. Sometimes esthetic and functional disturbances in the maxillofacial area can point to the presence of osteomas, as it was in our case. The presence of impacted and supernumerary teeth and more than three osteomas is enough for a diagnosis.

Follow up period include clinically and radiographically examinations every six months. The best imaging technique for the diagnosis of an osteomas is CT or 3 DCT.

Considering that polyposis normally develops after the osteomas (3), the general dental practitioners should firstly assume it as Gardner's syndrome. In this way they can help in early diagnosis of GS referring the patient to preventive medical examinations.

**Abstract**
Gardner syndrome is a rare genetic disorder characterized by the triad of familiar polyposis , multiple osteomas and tumors of soft tissues. Malignant transformation of colonic polips to colon cancer occurs in all cases, the disease is distinctive with poor qualıty of life.The 27-year old male was referred to our department from a nearby medical centre for extraction of lower left mandibular second molar tooth. The panoramic radiographs disclosed a tooth crown destroyed with caries lesion, impacted lower canine teeth located in the inferior border of mandible and multiple jaw osteomas. From the patient's history we found out that the patient was suffering from Gardner's syndrome and had undergone different surgical procedures. The aim of this case report is to describe oral and maxillofacial symptoms of Gardner syndrome and its potential dental implications.

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**Key words**
Gardner Syndrome; Tooth, Impacted; Osteoma

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