Primary ciliary dyskinesia: Kartagener syndrome with central giant cell granuloma. A case report

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This paper describes a clinical case of both giant cell granuloma and Kartagener syndrome in a 15-year-old male patient, with emphasis on the radiographic aspects of this extremely unusual pathology. To our knowledge, the presence of these 2 rare clinical conditions in the same patient has not been previously reported. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;110:e49-e56)

Primary ciliary dyskinesia (PCD) is an autosomal recessive disorder that represents a significant subgroup of the multisystem disease ciliopathy1 that affects the cilia, the microtubule-based hair-like organelles that extend from the surface of almost all cells in the human body.2 In ~50% of cases, PCD presents with sinusitis, bronchiectasis, and mirror image arrangement (situs inversus, in which the internal organs are located on the opposite side of the body from their normal position3) in a condition known as Kartagener syndrome.

Cilia are subdivided into 2 main types: epithelial cilia and primary cilia. Epithelial cilia are hair-like appendages that line the human respiratory tract and contribute to the mucociliary defense mechanism.2 Primary cilia consist of both sensory cilia and nodal cilia. Nodal cilia have an embryologic function in the determination of laterality. Effective nodal flow is proposed to be a key element in the asymmetric expression of developmental genes involved in left-right determination, which explains the association of situs inversus with ciliary abnormalities.2

PCD affects the activity of proteins important to the movement of cilia, especially in the respiratory tract, which results in retention of mucus and bacteria.4 Secondary to a failure in the mucociliary defence mechanism, PCD patients experience recurrent respiratory tract infections that begin in early childhood and lead to chronic bronchitis and/or bronchiectasis, chronic rhinosinusitis, and otitis media.2,5 Moreover, the congenital reduction or absence of ciliary function responsible for situs inversus explains the association between this condition and Kartagener syndrome.1,2,6,7 Patients with Kartagener syndrome also have a greater incidence of congenital cardiovascular defects.7

Recent literature has emphasized the importance of early diagnosis and appropriate treatment of PCD in preventing permanent sequelae, such as chronic rhinosinusitis and bronchiectasis and lung damage.1,6 The diagnosis should also be considered in older children with severe otitis media, bronchiectasis, or atypical asthma.2

Despite the substantial research on Kartagener syndrome that exists in the medical literature,4,5,8-10 the dental literature contains few reports on the disease. In a case report of a male patient presenting with Kartagener syndrome, Casanova et al.3 emphasized the radiographic aspects and stressed the importance of early diagnosis by an oral radiologist. Merrett and Durning11 reported on the unusual dental morphology associated with the Kartagener syndrome, and Giusto and Sciuumba12 reported on the oral findings in 2 siblings diagnosed with the syndrome. To our knowledge, there is no previous report on the simultaneous occurrence of Kartagener syndrome and giant cell granuloma, another rare clinical condition, in the same patient.

Giant cell granuloma is an uncommon bony lesion in the head and neck region that most commonly affects the maxilla and mandible and is usually treated with surgery. Although it is a benign disease process, it can also be locally destructive.13 The disease has a very low incidence among the general population and occurs mainly in individuals <30 years of age.14

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The present paper describes a clinical case of both giant cell granuloma and Kartagener syndrome in a 15-year-old male patient, with emphasis on the radiographic aspects of this extremely unusual pathology.

**CASE REPORT**

**Clinical and laboratory findings**

A 15-year-old male patient applied to the Oral Diagnosis and Radiology Department of the Faculty of Dentistry with complaints of swelling on the right side of the maxilla. Written informed consent was obtained before examination and treatment. Extraoral examination revealed swelling on the right side of the face resulting in facial asymmetry. There was no history of trauma, the skin was normal, and there was no elevation in local temperature at the site of the swelling. A complete lymph node examination of the cervical, submandibular, submental, supraclavicular, axillary, and epitrochlear sites revealed positive lymphadenopathy in the submandibular lymph nodes, but no pain on palpation.

Intraoral examination identified a swelling in the right maxillary labial sulcus that was extending palatally and included the first molar, first and second premolars and canine. There was no fluctuation on palpation or paresthesia. The right maxillary canine and first and second premolars were slightly displaced from their sockets and highly mobile; however, the teeth were insensitive to percussion, and the patient reported no pain. Electrical and thermal pulp vitality tests were performed by using an electrical pulp tester (Digitest; Parkell, Farmingdale, NY, USA) and solid carbon dioxide (CO₂ ice). A negative response was obtained from all of the examined teeth. The patient exhibited poor oral hygiene, but had no history of smoking or systemic drug use.

**Family history, history of disease, and imaging**

A detailed history identified consanguinity of the patient’s parents. The patient also reported a long-standing moist cough, postnasal mucopurulent secretion, nasal congestion, and rhinitis, but no chronic secretory otitis media. An initial panoramic radiograph showed a large radiolucent lesion in the right maxillary region and displacement of the right maxillary premolar and molar teeth.

To obtain a more precise location and definition of the pathologic features of the lesion, cone-beam computerized tomography (CBCT) images were taken using an Iluma Ultra CBCT scanner (Imtec Imaging, Ardmore, OK, USA) with a 24.4 × 19.5 cm amorphous silicon flat-panel image detector and a cylindrical voxel size of 0.09 mm and an exposure time of 40 seconds. An axial CBCT scan showed a large expansive lesion in the right maxilla, and axial, coronal, and sagittal images revealed total nasal obstruction and pannusitis. A panoramic reconstruction of CBCT images also showed expansile lesions extending from the right side of the maxilla to the left premolars (Fig. 1).

The lesion and surrounding soft tissue was examined using T₁-, T₂-, and fat-saturated T₂-weighted (W) magnetic resonance imaging (MRI). Images were taken with a 1.5T imaging unit (Magnetom Vision, Siemens, Erlangen; TR/TE 500/9, 4,126/98, 512 × 256 matrix, 23° × 23° field of view, 2-mm slice thickness, number of excitations (NEX) 1, 15.6 kHz band width). Coronal fat-saturated T₂-W images exhibited heterogeneous signal intensity around the maxilla and maxillary sinus and high signal intensity in the ethmoid region, whereas a coronal T₁-W image showed hypointense signal intensity at the maxillary and ethmoid region, with a slightly increased signal at the periphery of the lesions. A gadolinium-enhanced T₁-W image revealed patchy irregular contrast enhancement involving the maxillary sinus and increased signal intensity in the ethmoid region, and an axial T₂-W image clearly exhibited high signal intensity that was interpreted as sinusitis (Fig. 2).

Based on patient history and clinical and radiographic examination, the differential diagnosis included odontogenic cyst, odontogenic fibroma, odontogenic keratocyst, brown tumor, and unilocular ameloblastoma. Central giant cell granuloma (CGCG) was also considered in this case, because of the maxillary location of the lesion. An aspiration biopsy was performed, and histopathologic examination confirmed a CGCG of the maxilla. Based on this finding, a treatment plan was decided on that consisted of surgical excision of the lesion and a partial maxillectomy. Figure 3 shows the pre- and postoperative appearance of the CGCG. A definitive diagnosis was obtained through postsurgical histopathologic analysis. Microscopic examination (×40 and ×100) of the H&E-stained specimen revealed reactive bone and giant cells in a fibroblastic stroma with extravagated red blood cells (Fig. 4).

Because of the possibility of a genetic disorder implied by the consanguinity of the patient’s parents, Diagnostic Services was consulted, and the patient was referred to a chest consultant and then to a genetic consultant. Blood tests revealed a PTH level of 37 pg/mL and no abnormalities, which omitted a brown tumor from the differential diagnosis. A chest radiograph revealed situs inversus with dextrocardia, with the cardiac anatomy positioned in a mirror image of the normal anatomy (Fig. 5). Nasal nitric oxide measurements found low levels for both nasal and exhaled nitric oxide, and a ciliary beat frequency measurement and pattern analysis found a slow beat frequency. Radiologic images of paranasal sinuses demonstrated mucosal thickening, opacified sinus cavities, and hypoplastic frontal sinuses, and a nasal mucosa biopsy was found to be compatible with PCD. Based on the classic triad of situs inversus, bronchiectasis, and sinusitis, the case was defined as Kartagener syndrome. There was no family history of the syndrome or dental abnormalities in this case.

Surgical excision of the lesion and a hemi-maxillectomy were performed under general anesthesia. In view of the patient’s bronchiectasis, pulmonary status and cardiac structure and function were assessed prior to surgery in order to avoid pulmonary complications, and the patient received prophylactic antibiotic treatment because of the possibility of abnormal neutrophil chemotaxis. Due to the relative contraindication of anticholinergic and antitussive medications and nasal tubes, intubation anesthesia was performed using thiopental, nitrous oxide, enflurane, and succinylcholine, as reported by Etzel et al.
Postsurgery analgesics and antibiotics were prescribed, and the patient received oral hygiene instructions and was referred to a private clinic for further antibiotic treatment of chronic respiratory infections. Follow-up clinical and radiographic examinations are being conducted on a 6-month basis to track the healing process and inspect the surgical site for possible sequelae.

Fig. 1. Cone-beam computerized tomography (CBCT). a, Axial image demonstrates large expansive lesion in the right maxilla (arrows). b, c, d, Axial, coronal, and sagittal images show total nasal obstruction and pansinusitis of the sinuses. e, Panoramic reconstruction also shows expansile lesions involving from right side of the maxilla to left side premolar teeth (arrows).

Fig. 2. Magnetic resonance imaging. a, b, Coronal fat-saturated T2-weighted (W) images reveal heterogeneous signal intensity around maxilla and maxillary sinus and high signal intensity in the ethmoid region. c, d, Coronal T1-W image shows hypointense signal intensity for maxillary and ethmoid region with slight increased signal in the periphery of the lesions. e, After gadolinium enhancement, T1-W image reveals patchy irregular contrast enhancement involving maxillary sinus and increased signal intensity in the ethmoid region. f, Axial T2-W image shows clearly high signal intensity sinusitis.
recurrences. Good healing and no recurrence at the operation site were observed at the first follow-up visit (Fig. 6). Additional treatment plans include an interim obturator for maxillary resection to regain function and esthetics.

**DISCUSSION**

CGCG of the jaw usually presents clinically as a painless slow-growing swelling of the jaw and radiographically as a radiolucent expansion.\(^1\) The incidence of the disease is rare, and it has been reported to be highest among male individuals aged 10-14 years. Pain and sensory disturbances are rare.\(^1\) Differential diagnosis may include radicular cysts, adenomatoid odontogenic tumors, brown tumor,\(^1\) fibrous dysplasia, and calcifying epithelial odontogenic cysts, as well as more uncommon odontogenic neoplasms, such as ameloblastomas, keratocystic odontogenic tumors, and myxomas. The ultimate diagnosis relies on histopathology. Histologically, CGCGs appear as foreign body–type giant cells with irregular distribution and vacuolation. Their hallmarks are multinucleated giant cells that are clustered or diffusely distributed, especially in hemorrhagic areas, and possess collagenized or edematous stroma.\(^1\)
CGCGs can be radiologically differentiated from other entities containing giant cells, such as giant cell tumors (GCTs),
cherubism, brown tumor of hyperparathyroidism, and aneurysmal bone cysts. Like CGCGs, GCTs usually present as an aggressive, eccentric, lytic lesion centered on the metaphysis and extending to the subchondral bone with expansive remodeling; however, they lack the internal mineralization seen in CGCGs. Soft tissue involvement is frequently found in GCTs. Although cherubism is microscopically indistinguishable from CGCG, clinicopathologic correlation (children, autosomal dominance, bilateral multilocular jaw lucencies) can provide helpful clues to distinguish cherubism from CGCG. Brown tumors of hyperparathyroidism can occur in multiple areas within 1 bone or as a polystotic process. Whereas a brown tumor of hyperparathyroidism histologically resembles a CGCG, bone changes associated with hyperparathyroidism, such as generalized demineralization of the medullary bones of the jaws and loss of lamina dura around the roots of the teeth can help differentiate a brown tumor from a CGCG, and in cases of doubt, serum calcium, phosphorus, and alkaline phosphatase levels can be measured for a differential diagnosis. Aneurysmal bone cysts appear as trabeculated osteolytic lesions, associated with cortical thinning, with a “blow out” appearance. In the present case, an aspiration biopsy was performed and the lesion histologically identified as a CGCG of the maxilla. Definitive diagnosis of CGCG requires histopathologic analysis.

The literature includes several case reports describing CGCG of the maxilla involving the palate. Roberts et al. reported a case of an 18-year-old man initially treated with a partial maxillectomy that achieved a near-total debulking of the mass and immediate cosmetic improvement. Steroid injections were initially able to stall any reappearance of the residual disease; however, the patient experienced a recurrence 8 months after surgery. As a result, a bilateral total inferior maxillectomy was performed using a facial degloving approach, and the patient was subsequently fitted with an obturator. The authors concluded that a combination of partial surgical resection and intraleisional steroid injections may not be adequate for the treatment of large CGCGs of the maxilla and suggested that complete surgical resection should be considered for the initial treatment, particularly in aggressive cases. Ciorba et al. also described a case that involved the maxilla which was treated with surgical excision, followed by local injection of steroids. Dos Santos et al. have dealt with the usefulness of CT in the evaluation of this lesion.

A recurrence rate of up to 70% has been reported, mainly for lesions that display an aggressive biologic behavior. An aggressive and extensive behavior of the present lesion with radiographic evidence of perforation of cortex required a more radical excision, i.e., partial maxillectomy. Follow-up sessions are very important, because the recurrence rate is reported to be high, with most occurring within the first 2 years of the

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**Fig. 5.** Chest radiograph shows dextrocardia.

**Fig. 6.** Postoperative (a) 3-month and (b) 6-month panoramic radiographs showing no recurrence and good healing of the operation site.
Kartagener syndrome, which may have implications for disorders of the dentition, because the developing dentition may be affected by any alteration in the bone architecture within which the developing tooth germs are contained. The patient had been diagnosed with the syndrome at 8 years of age, and the authors suggested that the treatment of respiratory tract infections with numerous courses of antibiotics may have played a role in the development of this unusual dental morphology and that the high incidence of caries experienced by the patient may have been related to the infections themselves. Several studies have mentioned disorders of the bone system associated with Kartagener syndrome, which may have implications for disorders of the dentition, because the developing dentition may be affected by any alteration in the bone architecture within which the developing tooth germs are contained. Giusto and Sciubba documented a patient with the syndrome and his sibling who expressed an oligosymptomatic form of the syndrome, both displaying identical dental findings: impacted maxillary cuspids, a “gothic” or high-arched palate, and a Bolton tooth-size discrepancy. According to those authors, further research is required to determine whether the dental finding is associated with the syndrome to a higher degree; however, the difficulty in ascertaining this information relates to the syndrome being noted so infrequently, and finding affected patients who would agree to have a panoramic radiograph taken. Researchers also noted that the patients’ mother could not recall any other family members afflicted with the syndrome, therefore an accurate family history and pedigree analysis to trace the lineage of the trait was not possible. In contrast to the study mentioned above, the present patient showed no unusual dental morphology, including congenitally missing teeth or other abnormalities.

Apart from intraoral findings, Casanova et al. mentioned that the oral radiologist must consider the image of the paranasal pansinusitis in association with nasal polyposis. A high-resolution CT of the paranasal sinuses reveals pansinusitis. The examination shows mucosal thickening and opacified maxillary, ethmoid and frontal sinus cavities, besides the total nasal obstruction. More recently, the presence of rhinitis, chronic otitis, nasal polyposis, and opacified sinus cavities has been described. Chest radiography may be performed to confirm the syndrome components. Early detection can reduce or even prevent the occurrence of severe respiratory infections, thus contributing to a better prognosis and an increase in the patient’s quality of life.

Gorham and Merselis observed the triad associated with Kartagener syndrome in 2 young adult siblings, both of whom had had symptoms since early childhood. The authors traced the family through 4 generations and reviewed the literature regarding familial incidence, discovering 6 cases of familial incidence, all of which involved siblings only. This was in keeping with the finding of the authors’ own cases; all 4 generations were free of symptoms. The Kartagener triad appeared to have a high familial incidence but appeared only in 1 generation, and suggesting that rather than a genetic factor, an environmental factor present during embryonic development may be responsible for the appearance of the triad.

In contrast to this assumption, a recent study by Geremek et al. concluded that PCD was a mainly autosomal-recessive genetic disorder that showed extensive genetic heterogeneity and identified 4 genes with a proven pathogenetic role in PCD. However, none of the variations alone could explain the occurrence of the disease in these patients. The authors concluded that more families need to be examined to establish the exact Kartagener syndrome region. Casanova et al. mentioned that the disorder is inherited as an autosomal recessive trait. Male and female individuals are affected equally. The complete syndrome has high familial evidence, appearing only in 1 generation, and multiple siblings may have various combinations of its components, which do not appear in their children. These features and the high incidence of consanguinity among the apparently normal parents of affected children support the contention that the genetic abnormality is carried as an autosomal recessive gene. Casanova et al. reported no family history of the syndrome referred by their patient. In the present case, an extensive family history covering first- and second-degree kinship revealed no sign of Kartagener syndrome among any other family members.

The detection of a very low nasal nitric oxide output may also be useful in diagnosing PCD in older children. The finding of immotile or dyskinetic cilia by phase-contrast microscopy allows PCD to be diagnosed...
with high sensitivity.\(^5\) Completion of the human genome sequence has accelerated the identification and characterization of disease genes and should provide new insight into the molecular mechanisms involved in the assembly and function of cilia, which in turn may promote the development of new methods for the diagnosis, prevention, and treatment of PCD, such as specific protein or gene therapy.\(^2\) However, few patients with PCD carry a well established diagnosis, which reflects the limited ability to diagnose this disorder.\(^7\) According to Bush et al.\(^1\) and Barnes,\(^8\) although respiratory disease and mirror image arrangement may suggest the presence of PCD, diagnosis is often delayed, in part because PCD presents with symptoms, such as rhinitis, secretory otitis media, and coughing, that are common among children. Casanova et al.\(^3\) mentioned that the oral radiologist must consider the image of the paranasal pansinusitis in association with nasal polyposis and the patient’s clinical data. Chest radiography may be performed to confirm the syndrome components. General pediatricians and pediatric nurses must be alert to the condition, because early diagnosis is essential for the prevention of permanent lung damage.\(^2,8\) The present case highlights the role that dentists can play in early diagnosis with appropriate consultations and referrals.

**CONCLUSION**

CGCG of the jaws is a rare benign tumor of uncertain etiology that accounts for up to 7% of all tumors in the mandible and the maxilla.\(^38,39\) The etiology of CGCG is still not clear, except that trauma or inflammation have been mentioned as important factors. Once considered to be a local reparative response of the bone, possibly to intramedullary hemorrhage or trauma,\(^40,41\) the finding of CGCGs in patients with anomalies with a known genetic origin, such as neurofibromatosis type 1, cherubism, Noonan syndrome, or hyperparathyroidism, suggests the possibility of a genetic-related etiology.\(^14\) Kartagener syndrome itself comprises a triad of symptoms associated with an autosomal-recessive inherited disease, and although there is insufficient proof to confirm a connection between CGCG and Kartagener syndrome, we believe a possible relationship exists between them. In light of the present case report, it is recommended that new studies be conducted to confirm a possible genetic connection between CGCG and Kartagener syndrome. Despite the rarity of the disease, oral and maxillofacial radiologists should be aware of these lesions. Moreover, the presence of CGCG in conjunction with Kartagener syndrome requires additional radiographic examinations.

**REFERENCES**


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