

Human and Feline Invasive Cervical Resorptions: The Missing Link?—Presentation of Four Cases

Thomas von Arx, Prof Dr med dent,* Peter Schawalder, Prof Dr med vet,[†] Matthias Ackermann, Prof Dr med vet,[‡] and Dieter D. Bosshardt, PD Dr sc nat*

Abstract

This report describes 4 patients presenting with multiple teeth affected by invasive cervical resorption (ICR). The cases came to our attention between 2006 and 2008; previously, no cases of multiple ICR (mICR) had been reported in Switzerland. Characteristics common to all 4 cases included progression of disease over time, similar clinical and radiographic appearance of lesions, and obscure etiology. The histologically assessed teeth showed a similar pattern of tooth destruction, with resorptive lesions being confined to the cervical region. Howship's lacunae and multinucleated, tartrate-resistant acid phosphatase-positive odontoclasts were detected. None of the teeth presented with internal resorption. The positive pulp sensitivity corresponded to the histologic findings, indicating that the pulp tissue resisted degradation even in advanced stages of resorptive lesions. Although mICR is rare in humans, a similar disease known as feline odontoclastic resorptive lesions (FORL) is common in domestic, captive, and wild cats. The etiology of FORL, like that of mICR, remains largely unknown. Because FORL has been associated with feline viruses, we asked our mICR patients whether they had had contact with cats, and interestingly, all patients reported having had direct (2 cases) or indirect (2 cases) contact. In addition, blood samples were taken from all patients for neutralization testing of feline herpes virus type 1 (FeHV-1). Indeed, the sera obtained were able to neutralize (2 cases) or partly inhibit (2 cases) replication of FeHV-1, indicating transmission of feline viruses to humans. Future studies on mICR (and FORL) should evaluate the possible role of a (feline) virus as an etiologic (co-)factor in this disease. (*J Endod* 2009;35:904–913)

Key Words

Cat, etiology, feline herpes virus, feline odontoclastic resorptive lesion, histology, human, multiple invasive cervical resorption, virus transmission

Invasive cervical resorption (ICR) is a clinical term used to describe a relatively uncommon, insidious, and often aggressive form of external tooth resorption that might occur in any tooth in the permanent dentition (1). The clinical presentation of ICR varies considerably, and detection of lesions is often made incidentally. In some early lesions, a slight irregularity can be evident in the gingival contour. In advanced lesions, the crown will display a pinkish color, mimicking an internal resorption of the crown (2). ICR is usually painless because the pulp resists the degradation process, possibly because of the thin and protective predentin layer (3). Radiographically, ICR is characterized by well-demarcated, undermining defects that extend from the cervical root area (tooth neck) into the dentin, eventually amputating the crown. Three-dimensional imaging techniques, such as cone beam computed tomography (CBCT), can be useful in the diagnosis and management of ICR, because the true extent of the defects cannot always be estimated from conventional radiographs (4).

Only one single study with a large number of ICR patients has been published (5). That study analyzed potential predisposing factors in 222 patients with a total of 257 teeth displaying varying degrees of ICR. Several predisposing factors were identified, with orthodontics (in 24.1%) and trauma (in 15.1%) being the most frequent sole factors. In combination with other factors, trauma (in 10.6%) and intracoronal bleaching (in 9.7%) were found to prevail. However, in 16.4% of the analyzed cases, no predisposing factor could be identified.

Although the study of Heithersay (5) and many case reports have addressed ICR associated with a single tooth or with up to 3 teeth, only a few cases with multiple invasive cervical resorption (mICR) have been described (6–9). Liang et al (6) presented a systematic review of cases with idiopathic mICR, adding 4 cases to a list of 14 previously presented. In 7 of the 18 patients, only 1–3 teeth were initially involved, whereas ultimately the number of involved teeth per patient ranged from 5–24. Cases included were not associated with the conditions generally accepted as causative factors.

With regard to the pathogenesis, many authors believed ICR to be a type of progressive external inflammatory resorption maintained by infection (10–13). However, the lesion's invasiveness and relative aggressiveness, coupled with its histopathologic appearance, raise questions as to its nature (14). Interestingly, early researchers in this field considered ICR to be a benign neoplasm or fibrous dysplasia, reflecting a rather aggressive but noninflammatory root-resorptive process that is consistent with the histology of many such lesions. In the early stage of development, the resorption cavity contains a mass of fibrous tissue, numerous blood vessels, and clastic resorbing cells adjacent to the dentin surface. Clastic cells lining the resorptive cavities are generally mononuclear, but some multinucleated cells can also be identified. The resorbing tissue is usually devoid of acute or chronic inflammatory cells unless the lesion has been invaded with oral microorganisms. These early lesions contain fibrovascular tissue, but they appear to progress to fibro-osseous lesions through the deposition of ectopic

From the *Department of Oral Surgery and Stomatology, School of Dental Medicine, [†]Division of Small Animal Surgery, Orthopedics and Stomatology, Department of Clinical Veterinary Medicine, University of Bern, Bern; and [‡]Institute of Virology, Vetsuisse-Faculty, Veterinary Medicine, University of Zurich, Zurich, Switzerland.

Address requests for reprints to Prof Dr Thomas von Arx, Department of Oral Surgery and Stomatology, School of Dental Medicine, University of Bern, Freiburgstrasse 7, 3010 Bern, Switzerland. E-mail address: thomas.vonarx@zmk.unibe.ch. 0099-2399/\$0 - see front matter

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bone-like calcifications within the resorbing tissue and directly onto the resorbed dentin surface.

ICR also occurs in domestic, captive, and wild cats, and the disease is known as neck lesions or feline odontoclastic resorptive lesions (FORL) in the veterinary field (15, 16). The etiology of FORL, like that of mICR, remains largely unknown. Suggested etiologic or predisposing factors include furcation anatomy of feline teeth, mechanical stress, diet texture and nutrient content, oral acid levels related to diet or vomitus, irregularities of calcium homeostasis, excess vitamin D, and viral infections (17, 18). Some authors also reported a significantly lower occurrence of root replacement resorption by alveolar bone (type II) in cat teeth with resorptive lesions, with the latter presenting roots with a normal radiographic appearance without replacement resorption (type I) (19, 20).

Interestingly, the clinical, radiologic, and histopathologic features of ICR and FORL appear to be analogous (21–23). It seems unlikely that the pathogenesis of ICR in humans and of FORL in the feline population, respectively, would be substantially different. Analysis of the dental literature shows an increase in the number of case reports dealing with mICR since 1986 (6, 7). It is also interesting that FORL was rarely documented in the veterinary literature before the 1980s (24).

Our objective in presenting these case reports is to highlight a possible but as yet unrecognized relationship between ICR in humans and FORL in cats.

Case Presentations

These cases are presented in the order that they were seen by the principal author.

Case 1

A 50-year-old female patient was referred by her private dentist in May 2006 because he had detected extended cervical lesions in teeth #8, 9, and 10 on periapical radiographs (Figs. 1–5). He had seen the patient previously in October 2005, without any evidence of such lesions. The medical and dental history was noncontributory (later the patient reported that she had had a bicycle accident with arm and shoulder injuries, but she was not aware of traumatized teeth). On presentation in our department in May 2006, tooth #10 was sensitive to percussion, but no periodontal or caries lesions were present, and all teeth (except the root canal–treated #3) reacted normally to CO₂. The radiographic evaluation with periapical radiographs and CBCT showed cervical lesions in 5 teeth in the maxilla (#8, 9, 10, 11, 12). A diagnosis of mICR with unknown etiology was made, and the patient was scheduled for extraction of teeth #8, 9, 10, and 11 (as a result of circumferential cervical lesions) and for restorative treatment of #12. On removal of these teeth, it was found that the lesion in tooth #12 had progressed, and tooth #7 now also presented with ICR. Both teeth were removed 4 weeks later. A reexamination in March 2007 revealed new ICR lesions in teeth #5, 6, 13, 14, and 15, and the teeth were surgically removed 1 month later. Within a year, the remaining maxillary teeth #2, 3, and 4 all developed new ICR and were subsequently also removed. On extraction, all teeth fractured at the cervical level. The extracted teeth presented with circumferential and deep resorption cavities in the cervical area, and most had an intact thin layer of dentin around the pulp. Some teeth were subjected to histologic analysis.

Histologic and Histochemical Processing. Immediately after extraction, the tooth samples were immersed in 4% buffered formalin for at least 48 hours. Thereafter, the specimens were processed for the production of undecalcified ground sections. Briefly, the specimens were rinsed in running tap water, dehydrated in

ascending concentrations of ethanol, and embedded in methylmethacrylate (MMA). The embedded tissue blocks were cut horizontally from the coronal to the apical aspect by using a slow-speed diamond saw (Varicut VC-50; Leco, Munich, Germany). After mounting on acrylic glass slabs, the sections were ground and polished to a final thickness of about 100 μ m (Knuth-Rotor-3; Struers, Rodovre/Copenhagen, Denmark) and surface-stained with fuchsin and toluidine blue/McNeal. Digital photography was performed with a Progress C5 digital camera (Jenoptik, Jena, Germany) attached to a Zeiss Axioplan microscope (Zeiss, Jena, Germany). To evaluate the activity of tartrate-resistant acid phosphatase (TRAP) in multinucleated giant cells, some sections were treated with azo staining by using naphthol AS-TR phosphate coupled with fast red violet TR salt. Positive TRAP staining of multinucleated giant cells allows classification of these cells as osteoclast-like cells.

Histology. The histologic evaluation showed that the teeth presented with resorptive lesions that were confined to the cervical region. Consecutive horizontal sections revealed a decrease in hard tissue destruction from the cemento-enamel junction in the coronal direction. The resorptive lesions were characterized by the presence of a jagged surface contour of dentin. None of the teeth showed internal resorption or loss of dentin in the apical half of the root.

A typically affected tooth is shown in Fig. 3. Part of the crown dentin is resorbed, yet the 2 pulp chambers are still intact. At the dentin–soft tissue interface, numerous Howship's lacunae are present, some of which are lined by intensely stained, multinucleated cells resembling odontoclasts. The soft tissue is fibrous and lacks an inflammatory cell infiltrate. Howship's lacunae and multinucleated cells are also seen in the enamel but are restricted to the region of the dentino-enamel junction. Numerous TRAP-positive cells are present along the resorbed dentin surface.

In all teeth, the resorbed dentin was partially covered with repair cementum. The repair cementum was thicker apically than coronally and in teeth that were extracted later. The presence of an inflammatory cell infiltrate in the lamina propria of the gingiva was common. In mid-root and apical root regions, however, the periodontal ligament revealed healthy, noninflamed conditions. In most teeth, the dental pulp apical to the resorptive lesion was structurally normal. Even when the resorptive lesion was close to the dental pulp, there were no signs of inflammation and resorption evident in the pulp tissue.

Human–Feline Link. The patient was contacted 5 weeks after the last extractions and questioned about possible contact with cats. The patient confirmed that she had lived with 2 cats for 14 years, but both had died about 1 year after she had been referred to our department. One of the cats had had some broken teeth and problems with eating hard food.

Case 2

A 58-year-old female patient was referred to our department in October 2007. The patient's private dentist wrote in his report that he had had to extract tooth #24 in June 2006 because of a deep cervical resorption (Fig. 6). In the meantime, he noted multiple cervical resorptions in other mandibular teeth, which prompted him to refer the patient. The patient's medical history revealed a car accident 8 years previously, with involvement of the vertebral column. The clinical examination in October 2007 showed slight recession of the facial gingiva (teeth #4, 5, 10, 11, 12, 20, 21, 27, and 28) and angular cervical defects (teeth #20 and 28). No probing depths >3 mm or active carious lesions

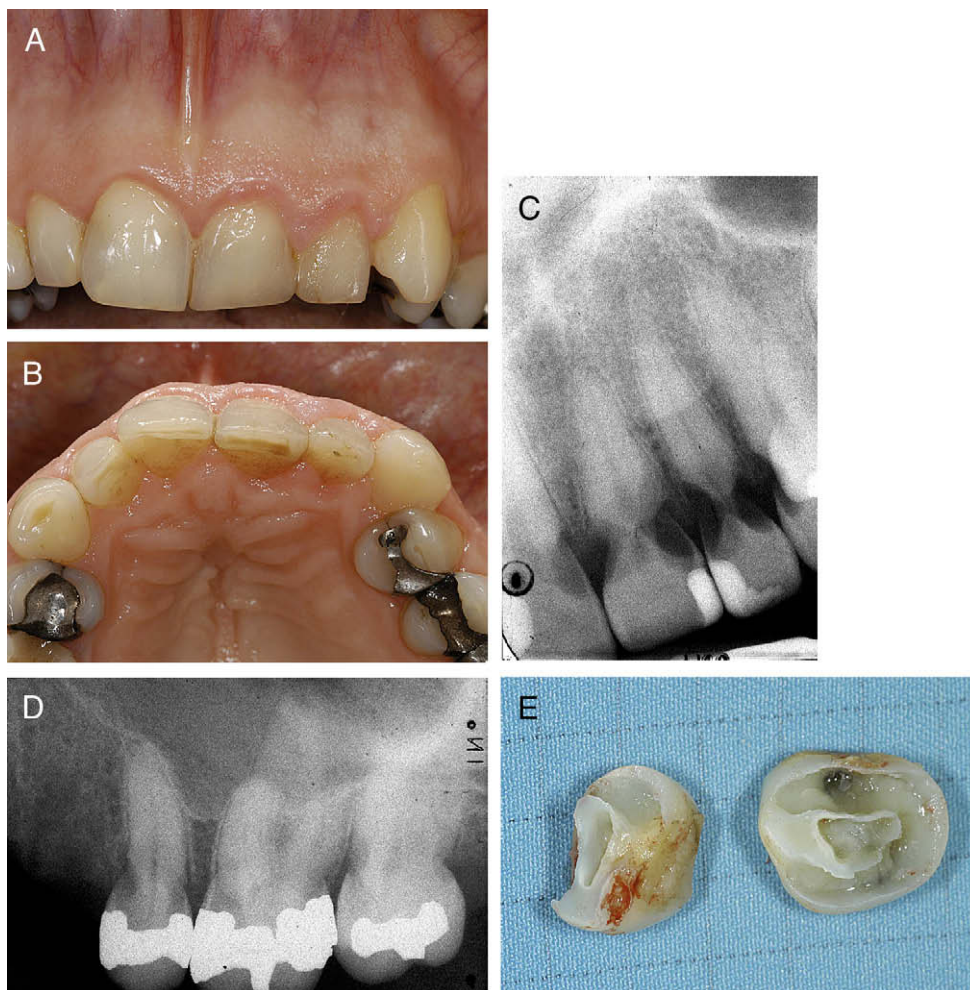


Figure 1. Clinical appearance of the anterior maxillary teeth of case 1. (A) Frontal view shows slightly inflamed free gingiva in teeth #8, 9, and 10, with some irregularities of the gingival margin facial of #9 and mesiofacial of #10. (B) “Pink lesions” shimmering through the enamel can be seen on the palatal aspects of #9 and 10 in the occlusal view. (C) The periapical radiograph demonstrates invasive cervical lesions of teeth #8, 9, 10, and 11. (D) A periapical radiograph of the left posterior maxilla shows cervical lesions of all teeth. It is interesting to note that the alveolar bone adjacent to the affected teeth appears to be intact on both radiographs. (E) The crowns of teeth #13 and 14 demonstrate extensive and circumferential cervical resorption, but with a thin intact dentin layer around the pulp cavity.

were detected. All remaining teeth except the root canal–treated tooth #4 reacted normally to CO₂ testing of pulp sensitivity.

The comprehensive radiographic examination (panoramic radiograph, periapical radiograph of mandibular teeth, CBCT) showed that all remaining mandibular teeth except tooth #28 had cervical lesions, mainly located on mesial, distal, or lingual aspects. None of the cervical defects was circumferential. None of the remaining maxillary teeth were affected. The patient was subsequently referred to the Department of Restorative Dentistry for conservative, restorative treatment of the mICR lesions.

The patient was reexamined in July 2008. In the meantime, the restorative dentist had tried to treat the defects in the left mandible with the method published by Heithersay (25). However, a recurrent lesion was found apical to the restoration at the distal aspect of tooth #21. The restorative dentist also reported that he was unable to treat the defect at the distolingual aspect of tooth #20 as a result of the difficult access and depth of the defect. This tooth was subsequently extracted and subjected to histologic analysis.

Histology. The histologic processing was similar to that described above. The histologic evaluation of tooth #20 showed massive dentin

resorption. Most of the dentin loss had occurred right at the level of the cemento-enamel junction. From there, the loss of dentin decreased in both the coronal and apical directions. The tooth showed histologic features similar to those of the other teeth from case 1, with a few exceptions. First, histologic signs of deep scaling were evident down to the mid-root region. Second, the crown dentin adjacent to the amalgam filling appeared carious, and an inflammatory cell infiltrate was observed in the coronal pulp.

Human–Feline Link. The patient was contacted 8 months after the initial examination (in June 2008) and questioned about possible contact with cats. She confirmed that she lives with several cats and reported that one (a 6-year-old female) had had severe drooling, and that 2 teeth had had to be removed by the veterinarian in April 2008. The veterinarian was contacted by telephone and confirmed that both teeth had presented with neck lesions, presumably FORL.

Case 3

A 68-year-old male patient was brought to our attention in July 2008 by the Division of Fixed Prosthodontics. The patient had been referred by his private dentist in April 2007 because of multiple cervical

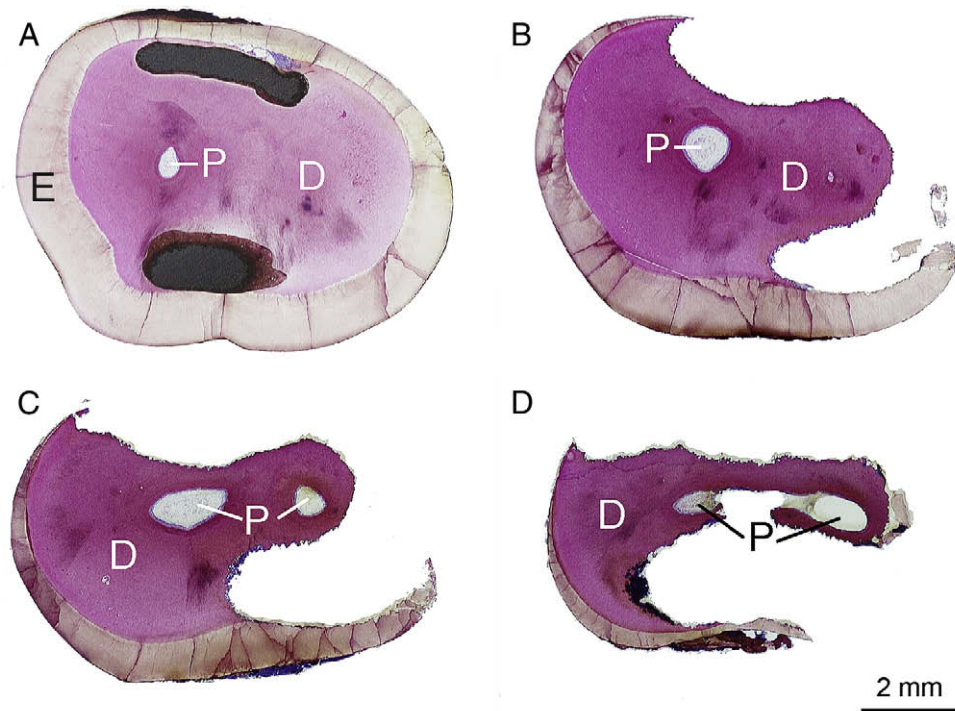


Figure 2. Consecutive horizontal sections from coronal (A) to apical (D) illustrating the apically increasing extension of the resorptive lesion. The apical portions of an amalgam filling are seen in (A). Although there are no signs of hard tissue resorption at the level of the pulp (P) horns (A), the more apically located sections reveal clear signs of past resorptive activity, as indicated by a significant loss of dentin (D) and the presence of a scalloped dentin border (C, D). The enamel (E) is slightly resorbed as well. An intact pulp chamber is seen in (A–C).

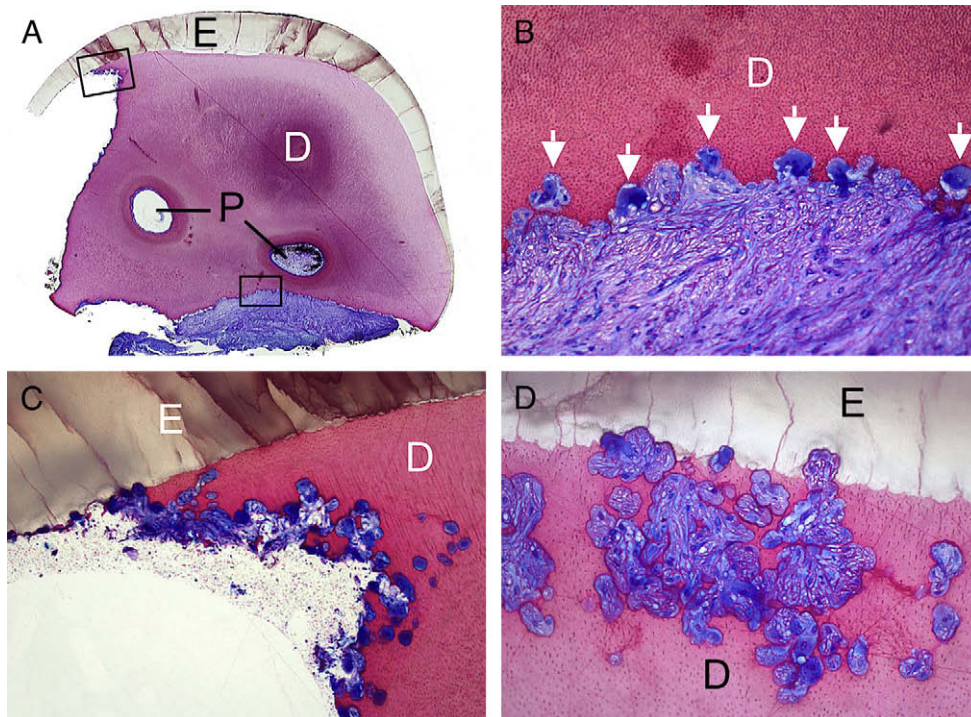


Figure 3. Horizontal ground sections illustrating the cervical region of a tooth with a resorptive lesion that has almost reached the dental pulp (P). The lower and upper areas outlined in (A) are enlarged in (B) and (C), respectively. Numerous Howship's lacunae, some of which are lined by odontoclasts (arrows), are present along the border of the resorbed dentin (D) (B, C). Resorption cavities are also seen at the dentinoenamel junction, where they slightly extend into the enamel (E) (C, D).

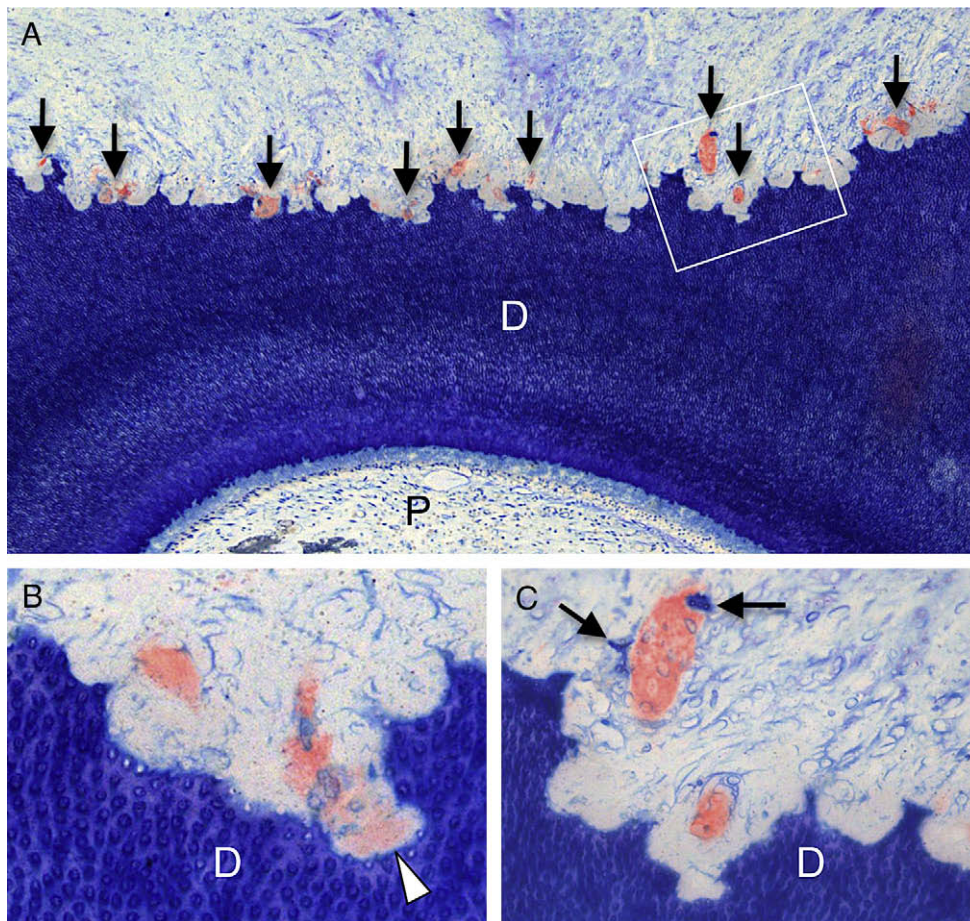


Figure 4. (A) Many TRAP-positive cells (arrows) are present along the resorbed dentin (D) surface. The dentin facing the pulp (P) lacks both resorption and TRAP-positive cells. The boxed area is enlarged in (C). (B) Some TRAP-positive cells occupy the space of a Howship's lacuna (arrowhead). (C) Other TRAP-positive cells appear to be not in contact with the dentin surface. However, dentin particles (arrows) can be seen at the cell periphery.

resorptions of teeth #7, 8, 28, 29, and 30 (Fig. 7). The dentist reported that all affected teeth reacted positively to pulp sensitivity testing. Bite-wing radiographs taken in August 2004 showed no resorptive lesions. The examination with periapical radiographs in May 2007 showed multiple cervical lesions in teeth #5, 6, 7, 8, 9, 10, 26, 27, 28, 29, and 30. The attending dentist suggested either to wait and observe the situation or to remove all affected teeth. A few days later, the crown of tooth #7 fractured and was stabilized with interdental composite to the adjacent teeth. The patient was first seen in our department in July 2008 for a follow-up examination. A clinical and radiographic examination was carried out. The patient reported having no pain whatsoever. None of the teeth had a probing depth >3 mm, and all teeth reacted positively to pulp sensitivity testing except the root canal-treated teeth (#4, 11, 31) and tooth #27. The panoramic radiograph and the CBCT demonstrated invasive cervical lesions in the same teeth as in May 2007, but new lesions were detected in teeth #24, 25, and 31. In addition, bony ingrowth from the adjacent crestal bone into the resorptive defect was observed in several CBCT images.

Human–Feline Link. The patient reported having had no direct contact with cats for 10 years. However, he regularly picked up feline feces from stray cats in his garden, and he also reported having contact with feline feces when mowing the lawn because he never wore garden gloves. The patient had been a blood donor for many years. In February 2007 he was informed by the blood donation authorities in a written

report that autoantibodies had been detected in his blood after blood donation in December 2006, and that possibly he had had a viral infection.

Case 4

A 66-year-old male patient with mICR was referred to our department in September 2008. Bite-wing radiographs taken in February 2006 by the private dentist showed developing cervical lesions in teeth #20 and 21 (Fig. 8). The patient had no pain whatsoever, and clinically, no probing depths deeper than 3 mm were measured. No carious lesions or plaque accumulation were seen. A pink lesion of the crown of tooth #8 was noted at the facial gingival margin. The panoramic radiograph showed cervical lesions in teeth #6, 7, 8, 9, 10, 11, 12, 13, 14, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, and 31.

Human–Feline Link. The blind patient (congenital glaucoma) had been living with guide dogs for years and said that he might have had indirect contact with domestic cats.

Neutralization of Feline Herpes Virus Type 1. Because of the possibility of virus transmission from cats to humans and the fact that all 4 patients had had direct, or possibly indirect, contact with domestic cats, the patients were invited to give blood samples in November 2008. Ten milliliters of venous blood was collected from each patient, centrifuged, and analyzed for the presence of neutralizing antibodies

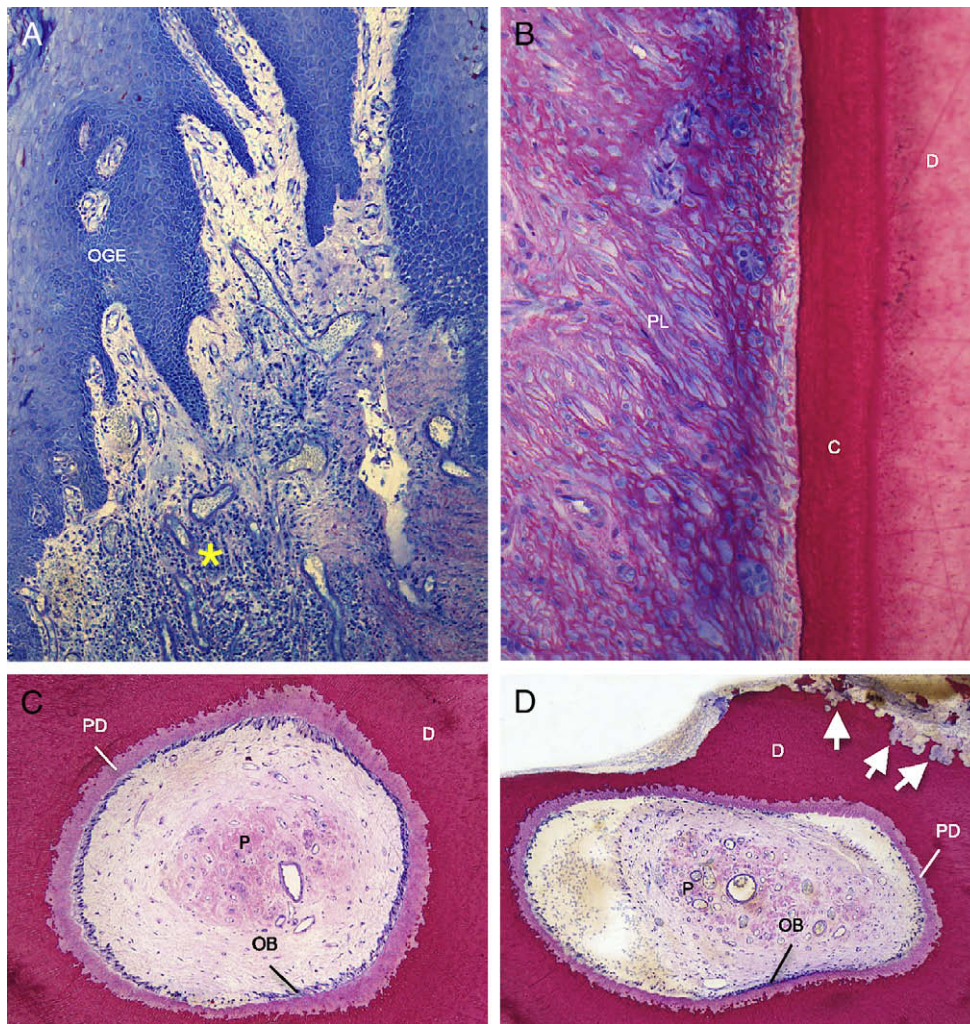


Figure 5. Longitudinal (A) and horizontal (B–D) ground sections of teeth and periodontal tissues affected by mICR. (A) An inflammatory cell infiltrate (asterisk) is seen in the lamina propria of the gingiva (OGE, oral gingival epithelium). (B) Apical to the resorptive lesion, the dentin (D), acellular extrinsic fiber cementum, and the periodontal ligament (PL) reveal normal structures with connective tissue fibers inserting into the cementum layer. (C) Apical to the resorptive lesion, the dental pulp shows normal structural elements with pre-dentin (PD), odontoblasts (OB), blood vessels, and nerve bundles. (D) Even in close proximity to a resorptive lesion (arrows point to Howship's lacunae), the pulp space exhibits preservation of structural elements. Note that in (C) and (D) there are no inflammatory cells and no signs of internal resorption.

against feline herpes virus type 1 (FeHV-1). For the virus neutralization assay, 10 median tissue culture infective dose (TCID₅₀) of FeHV-1 in a volume of 50 μ L were mixed with an equal volume of patient serum and incubated at 37°C for 1 hour before being inoculated onto a monolayer of Crandell feline kidney cells (CrFK). A second serum sample was diluted 1:10 before being subjected to the same procedure. The sera from 3 humans of similar age but without contact to cats or history of mICR were used as controls. Each sample was assayed in quadruplicate. Three days later, the monolayers were observed for the occurrence of typical cytopathic effects (CPE) caused by FeHV-1. Presence of full CPE at that time indicated unrestricted replication of FeHV-1 in the cell culture and absence of FeHV-1 neutralizing antibodies, whereas absence of CPE was interpreted as demonstration of neutralizing antibodies against FeHV-1 in the sera. Indeed, the sera from 2 patients (cases 1 and 2) were able to neutralize FeHV-1, presenting a titer of <10. The sera of patients 3 and 4 were able to partly inhibit replication of FeHV-1. In contrast, the sera obtained from the controls did not show any neutralizing activity against FeHV-1. Thus, although FeHV-1 is not known to infect human cells, the sera of at least 2 of the mICR patients

contained low titers of neutralizing antibodies against FeHV-1. These antibodies might be due to FeHV-1 itself or a serologically related virus.

Discussion

The present report points at a possible link between mICR in humans and FORL in cats. Whereas single ICR has been associated mainly with dental trauma, orthodontics, intracoronal bleaching of teeth, and dentoalveolar surgery (5), the etiology of mICR remains obscure (6, 7).

The parallels between mICR and FORL are striking; unknown etiology, similar clinical, radiographic, and histopathologic features. Yet, surprisingly, none of the authors of mICR case reports have ever addressed a possible link between humans and cats, ie, by taking a history of possible (physical or other) contact between a patient affected with mICR and a cat. Previous and recent studies have evaluated and documented a possible viral etiology of FORL, but none of the studies/case reports in humans have looked at such a cause for mICR. Whereas FORL is a relatively frequent finding in domestic cats (prevalence rates of up to 67% have been reported [21]), the finding of mICR in humans is extremely rare.

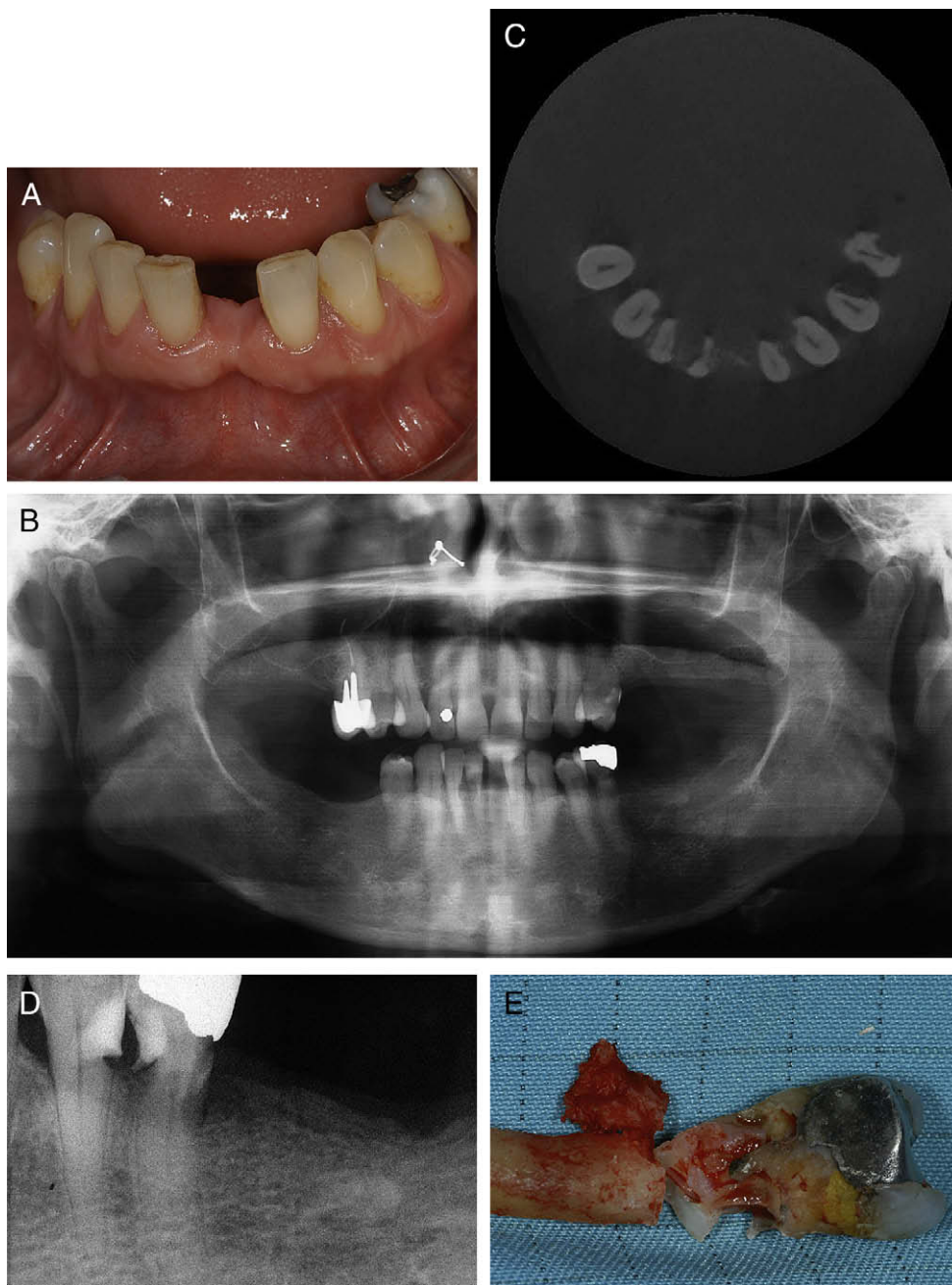


Figure 6. (A) The clinical view of the anterior mandible of case 2 demonstrates the single tooth gap, some occlusal wear of the incisors, and wedge-like defects of the premolars. The gingiva presents only minimal inflammatory signs. (B) The panoramic radiograph demonstrates multiple cervical lesions in the mandibular teeth, but no resorptive lesions are present in the maxillary teeth. (C) The occlusal CBCT image shows the true extent of the numerous cervical lesions in all remaining mandibular teeth except the right second premolar. (D) A periapical radiograph taken after restorative treatment shows persisting lesions in both left mandibular premolars. (E) The mandibular left second premolar was extracted, and a large cervical lesion can be seen at the distolingual aspect.

The principal author, who has been working for 25 years in governmental institutions and has been a member of a university teaching faculty for 10 years, had not seen a single case with mICR before 2006. Interestingly, between May 2006 and July 2008, three patients with mICR were referred to our School of Dental Medicine, and an information campaign aimed at dentists in Switzerland resulted in the referral of another patient in September 2008. Common characteristics of all 4 cases included progression of disease over time, similar clinical and radiographic appearance of cervical lesions, no clear etiologic factors (such as trauma, orthodontic treatment, bruxism, bleach-

ing), and direct (cases 1 and 2) or indirect (cases 3 and 4) contact with domestic cats. On the basis of the patients' reports, it is likely that the cats of cases 1 and 2 had FORL. Interestingly, these 2 patients presented with positive titers of neutralizing antibodies against FeHV-1 in their blood samples. In the context of FORL, various feline viruses have been discussed to play a pertinent role in the pathogenesis of cervical resorptive lesions (26, 27).

With regard to the location of cervical resorptive lesions, the port of entry is situated immediately below (apical to) the epithelial attachment. The latter appears to prevent surface resorption, as has been

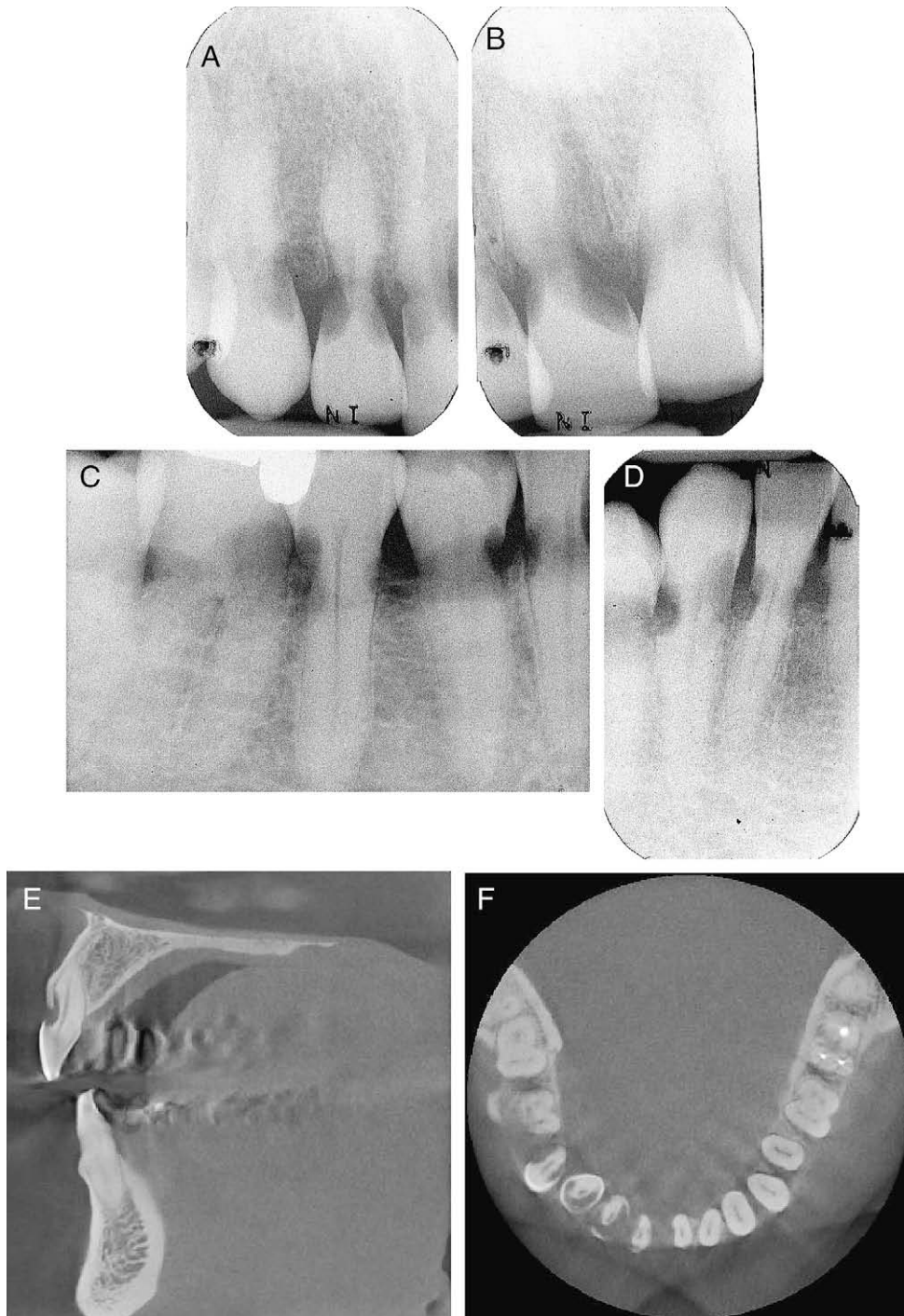


Figure 7. (A–D) The periapical radiographs of case 3 show multiple cervical lesions mainly affecting teeth on the patient's right side. Note again that the adjacent alveolar bone presents with only minimal radiographic changes. (E) The orofacial view (sagittal CBCT image) of tooth #8 demonstrates that the alveolar bone on the facial root aspect has grown into the cervical resorption cavity. (F) The occlusal view (axial CBCT image) of the mandibular teeth shows the typical radiographic appearance of cervical invasive resorption. The lateral incisor, the canine, and both premolars on the patient's right side present with cervical lesions that develop around the pulp chamber.

demonstrated in an experimental animal model (28). In that study, experimental cavities were created at root necks in monkey teeth. Cavities covered with a thin plastic foil presented a dentin surface devoid of epithelial coverage, and resorption cavities were found. In contrast, cavities without plastic foil were all covered with a thin squamous epithelium and did not show resorptive lesions. Antiresorptive biologic

control mechanisms originating in the periodontal ligament and possibly exerted by epithelial cells of the rests of Malassez have also been addressed (1, 29–31).

With regard to the cementum-covered root, osteoclasts are unable to initiate resorption until the thin layer of matrix lying on top of all calcified tissue is removed. External agents (perhaps viruses?) might provide

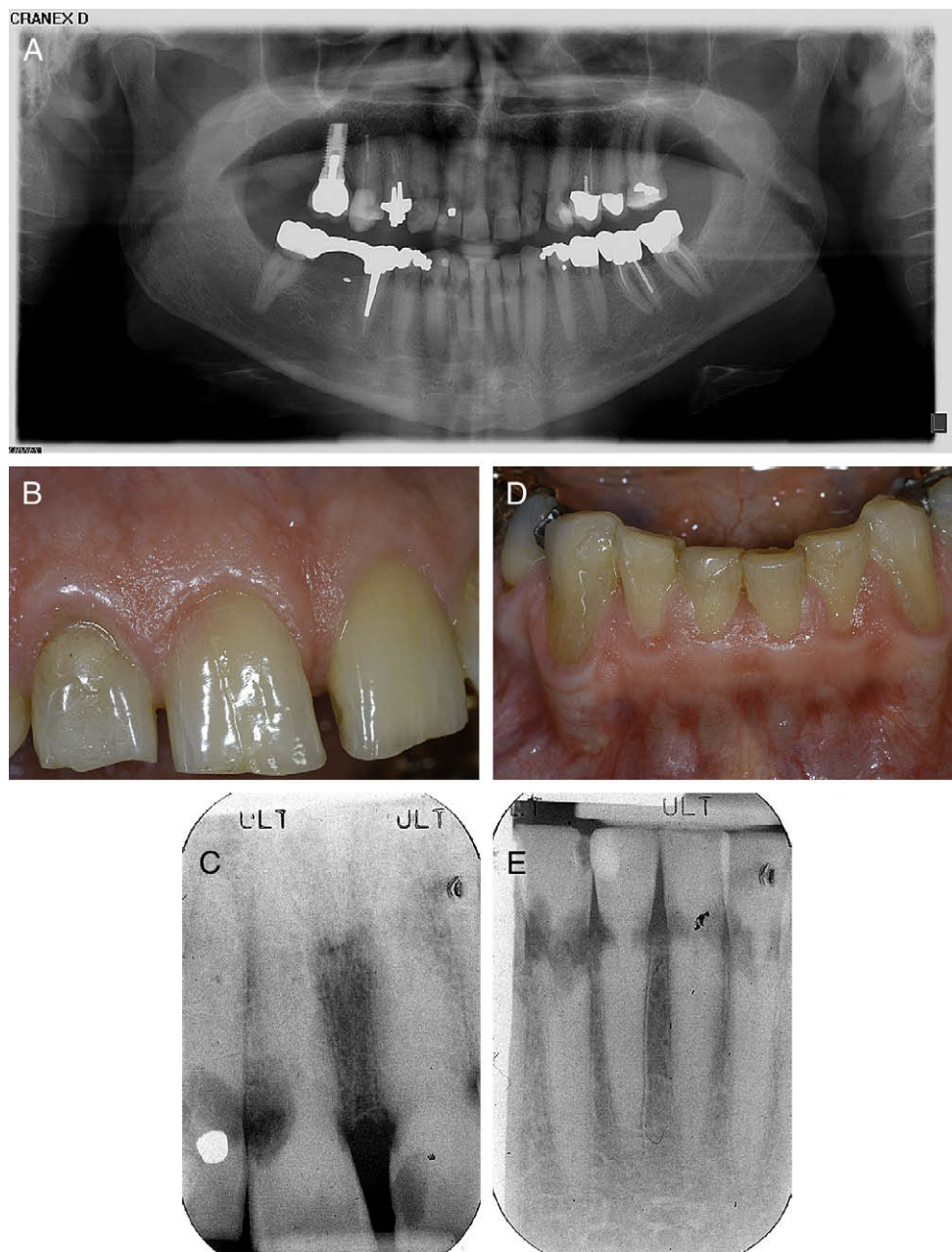


Figure 8. (A) The panoramic radiograph of case 4 illustrates mICRs affecting maxillary and mandibular teeth. (B) The clinical picture of the maxillary incisors shows a pink lesion at the distofacial aspect of tooth #8 close to the gingival margin. (C) The corresponding periapical radiograph depicts a profound cervical lesion at the distal aspect of tooth #8, initial lesions at the mesial aspect of tooth #8 and on mesial and distal aspects of tooth #9, but also a profound cervical lesion in tooth #7. (D) With regard to the gingival contour in the anterior mandibular teeth, a slight irregularity of the gingiva can be seen at the facial aspect of tooth #26. (E) The corresponding periapical radiograph shows multiple profound cervical lesions in the anterior mandibular teeth.

the molecular structures that are accepted by receptors on periodontal ligament cells, enabling these cells to recruit osteoclast precursor cells and at the same time enhance the production of collagenases, which, by destroying the surface layer of protein on cementum, exposes the bone morphogenetic proteins to the osteoclasts, thereby increasing both their number and activity (32). Viruses might also indirectly stimulate osteoclastogenesis via immunologic cells (B-cells, T-cells, RANK-RANKL-OPG system). In recent years there have been significant advances in the understanding of osteoclast differentiation and activation as a result of the analysis of a number of factors involved in a receptor activator of nuclear factor kappa B (RANK) signaling network in osteoclasts

(33). Other key regulators of remodeling of mineralized tissue include osteoprotegerin (OPG) and osteopontin (OPN).

From an endodontic perspective, it is interesting that all teeth affected with mICR in the presented 4 cases showed normal pulp sensitivity on thermal stimulation with carbon dioxide snow. This is in line with other reports on cases with mICR that found resorbed teeth to be vital by pulp testing (7, 9). The histologic evaluation described above in the first of the 4 case reports clearly documented that the pulp might remain free of inflammation and internal resorptive activity even in an advanced stage of ICR. With regard to treatment of advanced and/or circumferential lesions, no conclusive recommendations can be

made, and such resorbed teeth often have to be extracted. In contrast, repair of resorptive lesions by ingrowth of mineralized tissue has been reported (34). Interestingly, such bony repair was also observed in case 3 of the present article. Likewise, in cases 1 and 2, repair tissue formation was observed histologically on the resorbed dentin surface. In these 2 cases, however, the repair tissue was root cementum and not bone. Spontaneous repair cementum formation is common in many kinds of resorptive root lesions (35). In many situations, overcompression of the periodontal ligament is the main reason for root resorption, and the resorptive activity is transient and ceases soon after the disappearance of the stimulus. The findings of the present study indicate that repair can also occur in teeth affected by mICR. However, the repair period appears to be transient, possibly because of the persistence of the etiologic agent.

Although the presented case reports highlight possible transmission (viral infection) from cats to humans, a possible viral etiology still has to be proved. Future studies should, therefore, take into consideration the involvement of feline viruses as causative agents of mICR and of FORL.

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