Original Contributions

Case Report

Hardened exogenous material after extrusion of calcium hydroxide with barium sulfate

Case study and histopathologic and laboratory analyses

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ABSTRACT

Background and Overview. Although calcium hydroxide (Ca[OH]$_2$) paste associated with barium sulfate ($BaSO_4$) is considered a safe agent, there is a lack of clinical research on its effects on periodontal and submucosal tissues. The aim of the authors was to report the effects of extrusion of Ultracal XS paste (Ultradent Products) in 2 cases. The authors also analyzed the paste constituents and compared them with the proportion reported by the manufacturer and the material extruded.

Case Description. The authors present 2 cases in which root canals were restored with Ultracal XS paste after cleaning and shaping, and there was unintentional overextension of the paste into periradicular tissues, with a hardened exogenous material observed associated with inflammatory signs and symptoms. A biopsy was performed, and the material was subjected to histopathologic analysis and characterization through scanning electron microscopy, energy dispersive x-ray spectroscopy, Fourier transform infrared spectroscopy, and x-ray diffraction.

Conclusions. $BaSO_4$ and calcium carbonate ($CaCO_3$) were associated with a hardened material after Ultracal XS paste extrusion. The $Ca(OH)_2$ percentage on the Ultracal XS paste was approximately 2 times greater than the proportion reported by the manufacturer.

Practical Implications. $Ca(OH)_2$ with $BaSO_4$ paste application should be performed carefully, and its extrusion to periradicular and submucosal tissues should not occur. Its extrusion may result in the formation of a persistent exogenous material of hardened consistency associated with inflammatory signs and symptoms.

Key Words. Biopsy; dental materials; endodontic therapy; foreign bodies; root canal.

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Calcium hydroxide (Ca[OH]$_2$) intracanal medicament is widely used for its inhibitory properties on clastic activity through the formation of an alkaline environment, in addition to its biological activities as a mineralizer, anti-inflammatory, tissue-dissolution, and antimicrobial agent.[1-3] The antimicrobial activity of $Ca(OH)_2$ is achieved through the release of highly reactive hydroxyl ions in an aqueous environment, which primarily affects cytoplasmic membranes, proteins, and DNA.[4] Moreover, the effectiveness of chemomechanical preparation against endotoxins is clinically improved with the use of root-canal medicament.[5] In endodontic retreatment, its use has been associated with relief of postoperative pain in patients with previously symptomatic teeth as well as with a reduced frequency of flare-ups.[6]

The placement of $Ca(OH)_2$ paste should be limited to within the root canal, but unintentional overextension of $Ca(OH)_2$ paste into periradicular tissues is more likely to occur in canals with large and open apexes.[7] Overextension of the $Ca(OH)_2$-based medicament was previously supported because it is thought to have beneficial properties for promoting healing.[8] Once in contact with tissues, $Ca(OH)_2$ triggers superficial necrosis and subsequent inflammation, which encourages repair and active calcification.[4] Although $Ca(OH)_2$ paste is considered a safe agent,[9,10] adverse effects such as nerve and tissue lesions have been reported as a result of its extrusion.[11] The effect of $Ca(OH)_2$ paste on periodontal tissue is a controversial issue.[4]

$Ca(OH)_2$ paste is a mixture composed of the powder and a vehicle (aqueous, viscous, or oily). Radiopacifiers can be included to aid in radiologic assessment.[7] Commercial $Ca(OH)_2$ formulations are ready-to-use products and may also include radiopacifiers (for example, Vitapex, Neo Dental Chemical Products; Pulpdent Multi-Cal, Pulpdent; and Ultracal XS, Ultradent Products). According to the manufacturer, Ultracal XS consists of an aqueous solution of 30 through 35 percentage by weight $Ca(OH)_2$, 20 wt% barium sulfate ($BaSO_4$) or less, and an unidentified vehicle with a high pH (12.0-13.0). $BaSO_4$ is commonly used as a radiopacifier agent,[12] and its effects on tissues are questionable.[13-16] The overflow of $Ca(OH)_2$ powder mixed with $BaSO_4$ powder (ratio, 1:8) applied to periradicular tissues was previously associated with retardation and hindering of $Ca(OH)_2$ paste resorption.[7] Extrusion of this mix may cause several reactions, and to our knowledge, no researchers have reported on the effects of Ultracal XS paste extrusion on periradicular and submucosal tissues.

Our purpose in this study was to report the effects of unintentional extrusion of Ultracal XS paste on periradicular and submucosal tissue in 2 clinical cases in which signs and symptoms persisted. We also analyzed Ultracal XS paste constituents. We compared the results with the paste composition stated by the manufacturer and to the extruded material.

CASE 1

A 50-year-old man visited an endodontic specialist at a private dental office with the symptom of purulent exudate. His medical history was noncontributory, and he had no history of trauma. The intraoral examination revealed a sinus tract associated with the left maxillary central incisor (tooth no. 9) and extensive restoration and the presence of a carious lesion on the same tooth (Figure 1A). The tooth was tender to vertical percussion and palpation testing. A periapical radiograph revealed a J-shaped radiolucency surrounding the apex of tooth no. 9 and radiopaque structures consistent with a post and a previously treated root canal (Figure 1B). No deep periodontal pockets were present. On the basis of American Association of Endodontists terminology,[17] the specialist clinically diagnosed tooth no. 9 with a previously treated root canal (pulpal condition) and chronic apical abscess (apical condition). The specialist conducted nonsurgical endodontic retreatment. The specialist removed the post and the restoration material with the aid of a dental operating microscope and ultrasonic instruments. No crack was detected. The specialist completed the apical preparation with a no. 50 K-type hand file. After chemomechanical preparation, the specialist positioned a 29-gauge needle at 2 millimeters of its working length and slowly restored the canal with Ultracal XS paste up to the cementoenamel junction (Figure 1C). The access cavity was then sealed with composite resin (CR). At the next visit 15 days later, the specialist observed persistence of the sinus tract in association with a hardened material. Apical palpation provoked drainage of the exogenous material (Figures 1D and 1E). The interappointment medicament was removed. The specialist instrumented the canal again and restored it with $Ca(OH)_2$ powder mixed with a saline solution. The specialist resealed the access cavity with CR.

After 7 days, complete remission of the sinus tract was observed, and the patient reported no symptoms (Figure 1F). After removal of the $Ca(OH)_2$ paste, the specialist completed repreparation and performed obturation with gutta-percha and sealer using a continuous wave technique (Figure 1G).[18] The specialist then restored the crown with CR. The patient continued to be free of signs and symptoms after 8 months of follow-up (Figure 1H).

CASE 2

A 74-year-old woman reported a traumatic injury with extrusion of teeth nos. 9 and 10 (left maxillary central and lateral incisor, respectively), which she immediately repositioned herself. After cone-beam computed tomography (CBCT), a general dentist at a hospital dental clinic detected a maxillary alveolar fracture involving the buccal cortical portions of the left maxillary anterior teeth at the level of the apexes (Figure 2A). The dentist applied a semirigid splint and referred the patient to an endodontic specialist at a private dental office. The patient's medical history was noncontributory. At the intraoral examination, teeth nos. 9 and 10 were found to be misaligned. The crowns presented no signs of change in morphology and color. Mild swelling of the

ABBREVIATION KEY

Au: Gold.
Ba: Barium.
$BaSO_4$: Barium sulfate.
C: Carbon.
$CaCO_3$: Calcium carbonate.
$Ca(OH)_2$: Calcium hydroxide.
CBCT: Cone-beam computed tomography.
CR: Composite resin.
EDS: Energy dispersive x-ray spectroscopy.
FTIR: Fourier transform infrared.
IR: Infrared.
La: Lanthanum.
mag: Magnification.
Na: Sodium.
Nb: Niobium.
O: Oxygen.
S: Sulfur.
SEM: Scanning electron microscopy.
Ti: Titanium.
XRD: X-ray powder diffraction.

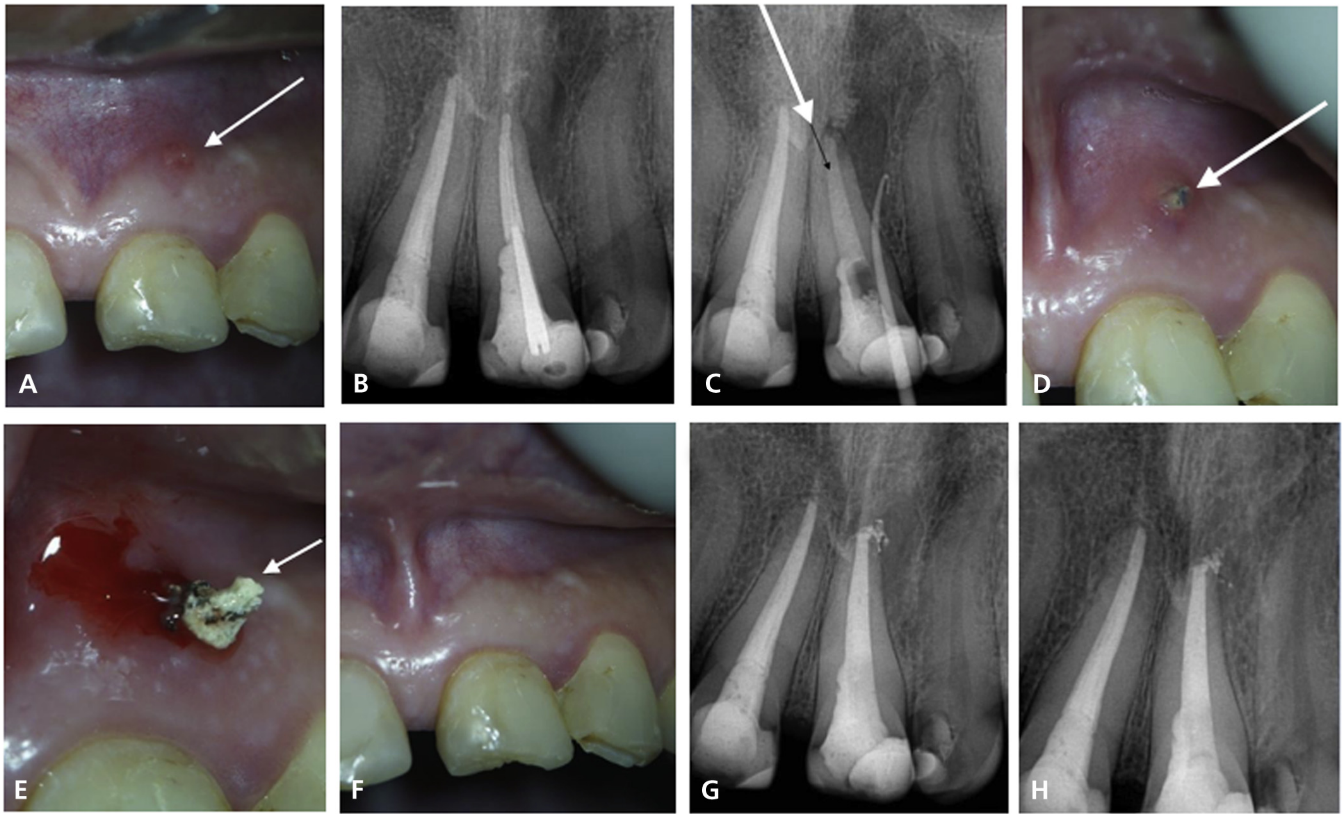

Figure 1. Case 1. **A.** Intraoral sinus tract (arrow) associated with tooth no. 9. **B.** Periapical radiograph revealed a J-shaped radiolucency surrounding the apex and radiopaque structures consistent with a post and previously treated root canal in tooth no. 9. **C.** No intracanal crack (arrows) was detected. After removal of the post and restoration material, the root canal was cleaned, shaped, and restored with Ultracal XS (Ultradent) paste. **D.** Hardened exogenous material (arrow) was observed in the sinus tract. **E.** Apical palpation provoked drainage of the material (arrow). **F.** Tissue repair. **G.** Periapical radiograph after root canal restoration. **H.** Follow-up at 8 months.

alveolar mucosa was also observed in the area. Teeth nos. 8 (right maxillary central incisor), 9, and 10 were tender to vertical percussion and palpation tests. Thermal pulp sensitivity tests (Endo Ice, Coltène/Whaledent) resulted in low-intensity pain with fast recovery after removal of the stimulus in those teeth. Periapical radiography revealed increased width of the periodontal ligament. The apex of tooth no. 10 exhibited morphologic radicular alteration (Figure 2B). After occlusal reduction of teeth nos. 9 and 10, the patient was advised to return in 4 weeks.

At the next visit, the specialist removed the splint, and the patient reported diffuse pain during biting and with apical palpation on teeth nos. 8, 9, and 10. Those teeth were nonresponsive to cold pulp testing with Endo Ice. The specialist made a clinical diagnosis of pulp necrosis and symptomatic apical periodontitis on all 3 teeth.[17] The specialist conducted nonsurgical endodontic treatments and completed apical preparation with a no. 40 K-type hand file (tooth no. 10) and a no. 50 K-type hand file (teeth nos. 8 and 9). After chemomechanical preparation, the specialist restored the canals with Ultracal XS paste, in the same manner as that in case 1, and sealed the access cavities with CR. Periapical radiography revealed a radiopaque area consistent with Ultracal XS paste extrusion at the apex of tooth no. 10, associated with morphologic alteration to the root (Figure 2C). A CBCT image suggested external apical resorption in the root of tooth no. 10 (Figure 2D). A soft-tissue swelling in proximity to the apical region of tooth no. 10 consistent with an acute apical abscess was also observed (Figure 2D).

After a month, the patient was asymptomatic to vertical percussion on teeth nos. 8, 9, and 10. However, palpation of the alveolar mucosa above the apex of tooth no. 10 still elicited mild pain. The specialist cleaned and shaped the root canals (teeth nos. 8, 9, and 10) and restored them with gutta-percha and sealer using a continuous wave of obturation technique. The specialist then sealed the access cavities with CR.

At the 12-month root canal treatments follow-up, periapical radiographic images revealed persistent evidence of exogenous material (Figure 2E). The patient still had mild pain on palpation

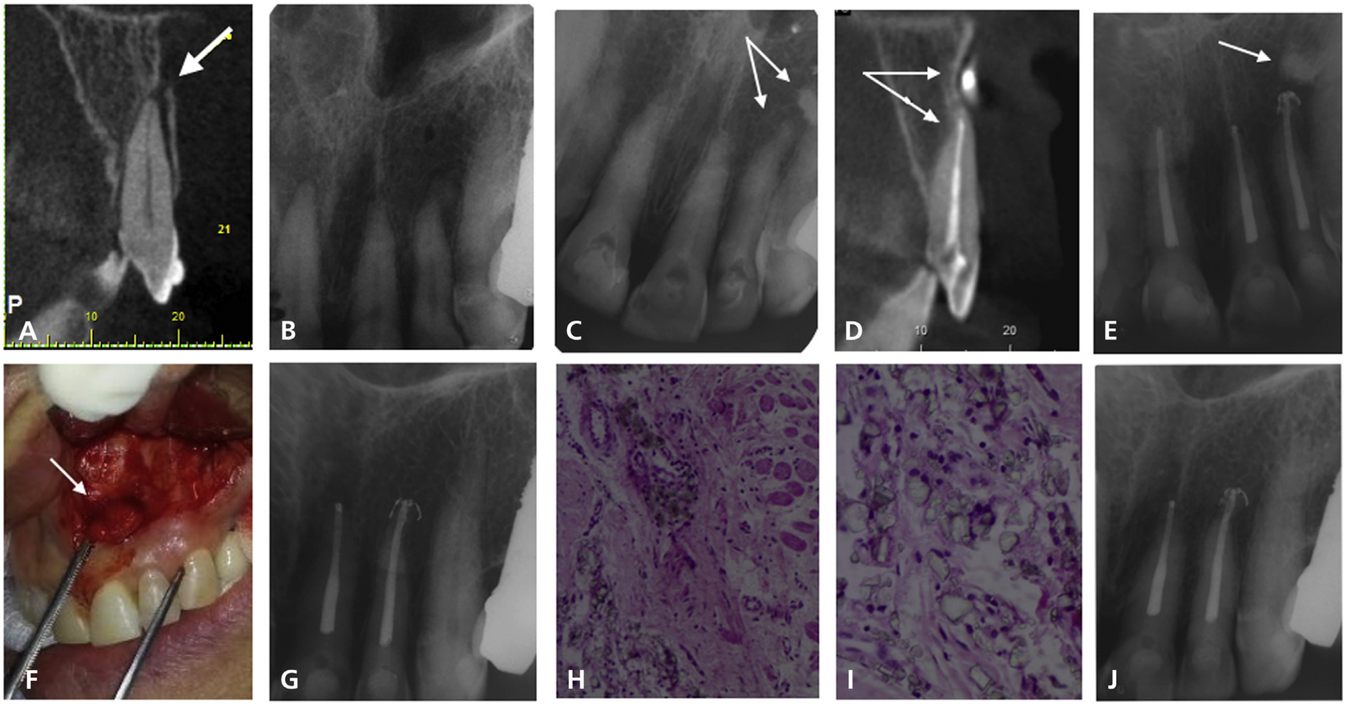

Figure 2. Case 2. **A.** A sagittal plane cone-beam computed tomographic (CBCT) scan revealed a maxillary alveolar fracture (arrow) involving the buccal cortical bone of tooth no. 9. **B.** Periapical radiographs suggest increased width of the periodontal space at the apex of tooth no. 10 with morphologic radicular alteration. **C.** A radiopaque area consistent with Ultracal XS (Ultradent Products) paste extrusion at the apex of tooth no. 10 (arrows), associated with morphologic alteration to the root. **D.** A cone-beam computed tomographic image suggested external apical resorption in the root of tooth no. 10 (arrows) and Ultracal XS paste extrusion to the soft tissue adjacent to the same tooth. **E.** Persistence of extruded material after root canal obturation (arrow). **F.** Material removed during biopsy procedure (arrow). **G.** Transoperative periapical radiograph revealed the absence of extruded material. **(H)** Photomicrographs of histologic sections taken from the hardened material (hematoxylin-eosin, original magnification ×100) and **(I)** photomicrographs of histologic sections taken from the hardened material (hematoxylin-eosin stain, original magnification ×200). **J.** Follow-up at 10 months after surgical procedure.

of the alveolar mucosa above the apex of tooth no. 10. Considering that the nonsurgical endodontic treatment was adequate, the specialist made a mutual decision with the patient to remove the exogenous material with surgical intervention, as reported in case 1 (Figure 2F).[19] Postoperative periapical radiography confirmed complete removal (Figure 2G). This material was immersed in fixative for histopathologic analysis and was submitted for further laboratory analyses and characterization.

For scanning electron microscopy (SEM) and energy dispersive x-ray spectroscopy (EDS) analysis, we applied a thin conductive coating of evaporated gold to the specimen with an ion coater (IC-50, Shimadzu). We then mounted it on carbon-coated aluminum stubs and viewed it under a scanning electron microscope (Quanta 200FEG, FEI). We performed elemental analysis by means of EDS (Figure 3A) and obtained morphologic characterization by means of SEM (Figure 3B).

We performed Fourier transform infrared (FTIR) spectrophotometry (Vertex 70, Bruker) using transmitted infrared (IR) spectroscopy. We compared and analyzed the data obtained from the Ultracal XS paste samples and the exogenous material using Origin software (OriginLab).

We carried out x-ray powder diffraction (XRD) phase analysis using a diffractometer (D8 Advance, Bruker) with x-ray emission in the alpha line in the K shell of copper atom radiation at 40 milliamperes and 40 kilovolts. We crushed the material using a mortar and pestle before testing. The sample was presented in powder form, and the detector was set to rotate at an angle of 2 theta ranging from 10° through 80°, a sampling width of 0.02°, and a time step of 1 second. We accomplished phase identification using HighScore Plus 4.1 search-match software (Panalytical).[20] We analyzed the Ultracal XS paste constituents and compared them with the proportion reported by the manufacturer and with the material extruded. We determined the presence and quantities of crystalline compounds by means of Rietveld refinement and quantification of crystalline phase material on the Ultracal XS sample.

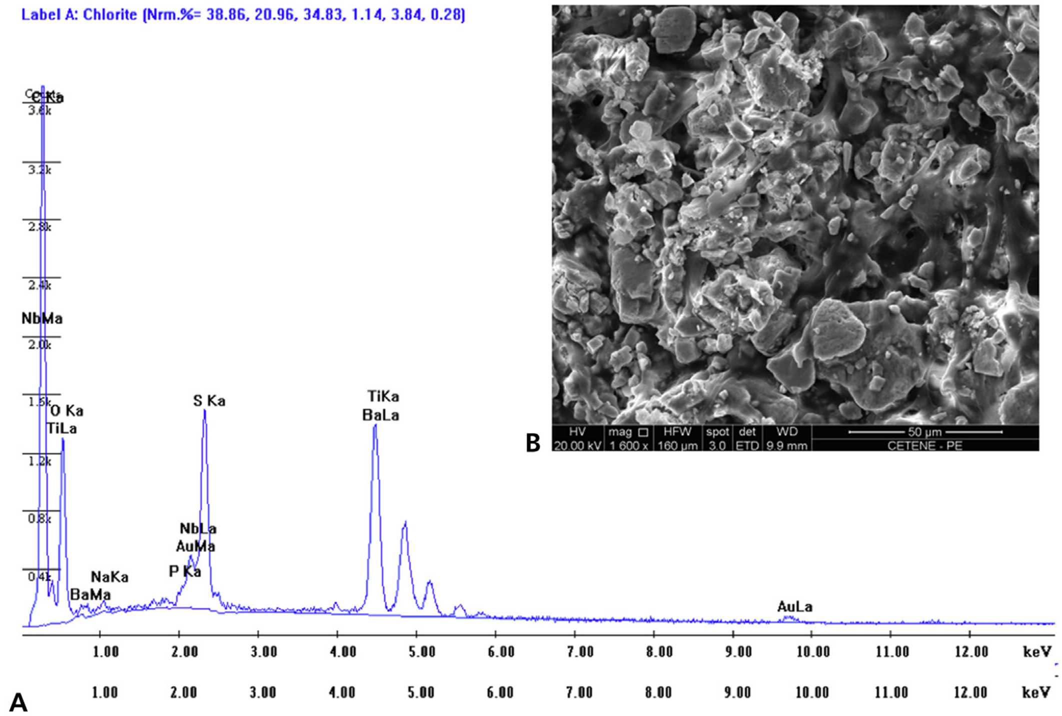

Figure 3. A. Energy dispersive x-ray spectroscopy analysis. **B.** Scanning electron micrograph of exogenous material (original magnification ×1,600). Au: Gold. Ba: Barium. C: Carbon. CETENE: Northeast Center for Strategic Technologies (PE, Brazil). det: Detector. ETD: Everhart-Thornley detector. HFW: Horizontal field width. HV: High voltage. Ka: X-ray emission in the alpha line in the K shell. keV: Kiloelectron volt. kV: Kilovolt. La: Lanthanum. Ma: X-ray emission in the alpha line in the M shell. mag: Magnification. µm: Micrometer. mm: Millimeter. Na: Sodium. Nb: Niobium. Nrm.%: Nonredundant masking. O: Oxygen. PE: State of Pernambuco, Brazil. S: Sulfur. Ti: Titanium.

Histopathologic analysis revealed fragments of connective tissue, brown crystalloid material, and rare mononuclear inflammatory cells (Figures 2H and 2I). We determined from the histopathologic report that the tissue had a connective and muscular origin with standard characteristics. We also noted the presence of exogenous material. After 10 months of surgical follow-up, the patient was asymptomatic (Figure 2J).

EDS showed elemental peaks of barium for the sample, and SEM analysis indicated a nonhomogeneous material (Figure 3). The data obtained by means of FTIR spectroscopy showed the presence of absorbed water molecules, with vibration mode centered at 3,380 centimeters^{-1} and 1,643 cm^{-1}. We observed no carbonate bands on the Ultracal XS sample. The sharp band at 3,640 cm^{-1} was related to the oxygen-hydrogen bond from the hydroxide group in $Ca(OH)_2$ (Figure 4B). The weak band at 985 cm^{-1} as well as the band centered at 1,204 through 1,070 cm^{-1} were caused by symmetrical vibration of the sulfate group.[21-23] The spectra of the extracted material did not show $Ca(OH)_2$ or $BaSO_4$ vibration modes; we observed only absorbed water molecule vibration modes. However, the band centered at 700 cm^{-1} may have been associated with the carbonate group of $CaCO_3$ (Figure 4C).[24,25]

The XRD analysis revealed $Ca(OH)_2$, $BaSO_4$, and $CaCO_3$ levels of 73.8%, 15.8%, and 10.4%, respectively (reference codes: $BaSO_4$, 96-101-0543; $Ca(OH)_2$, 96-100-8782; $CaCO_3$, 96-900-9669) (Figure 4A). XRD analysis of the exogenous material only presented the $BaSO_4$ crystalline phase, even after we analyzed several combinations with other compounds ($Ca[OH]_2$ and $CaCO_3$) (Figure 4B).

DISCUSSION

$Ca(OH)_2$ formulations are used in endodontics as interappointment intracanal medicaments and pulp-capping agents and during treatment of root perforations and root resorption because of their biological response as mineralization and antimicrobial agents.[4] In case 1, retreatment was initiated with the removal of the post and previous restoration material, followed by chemomechanical

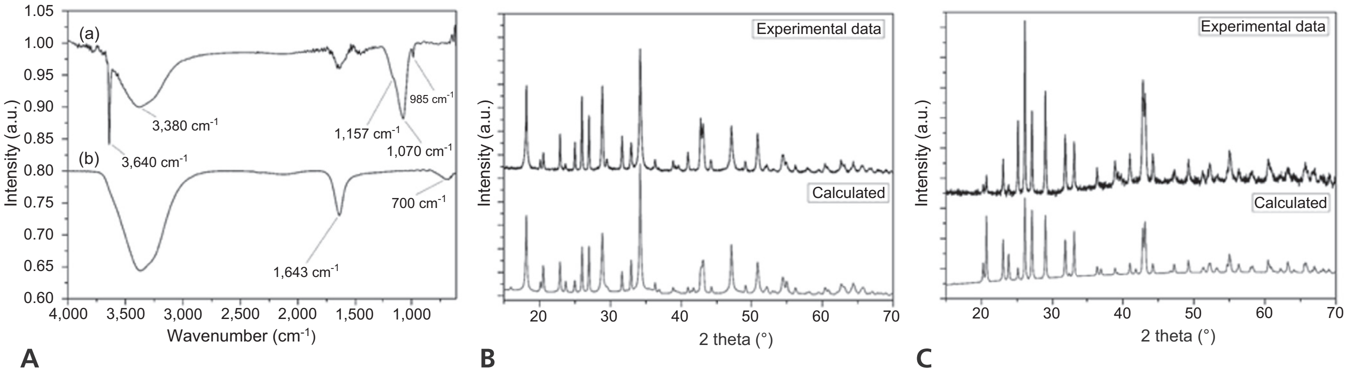

Figure 4. A. Comparison between the Fourier transformed infrared spectra of Ultracal XS (a) and exogenous material (b) samples. X-ray diffraction plots from **(B)** Ultracal XS and **(C)** exogenous material samples. a.u.: Arbitrary unit. cm: Centimeter.

preparation and restoration of the root canal with Ultracal XS paste. The presence of apical periodontitis after endodontic treatment is associated with either persistence of microorganisms or secondary infection.[26] As a complementary clinical strategy, the specialist chose intracanal medicament in an attempt to optimize disinfection and to promote the regression of clinical signs and symptoms. $Ca(OH)_2$-based intracanal medicament has a role in dental traumatology to control internal root resorption as well as inflammatory apical root resorption.[4]

In case 2, a traumatic injury led to extrusive luxation in teeth nos. 9 and 10. The pulpal diagnosis in both teeth was necrosis; this finding is expected in 43% to 98% of cases of extrusive luxation and is frequently observed in the first year after trauma.[27,28] Furthermore, treatment guidelines for luxation injuries indicate the use of $Ca(OH)_2$ as intracanal medicament whenever there is evidence of external inflammatory root resorption,[29] which was observed in tooth no. 10.

The effectiveness of $Ca(OH)_2$ paste dressing is directly associated with the complete restoration of the root canal.[30] It should be compacted and positioned as apically as possible.[31] Ultracal XS paste has low viscosity, and the manufacturer recommends $Ca(OH)_2$ delivery using an ultrathin needle (29 gauge, 0.013 inch) to facilitate the introduction of the medicament into the root canal. Flexible plastic tips sized 25 gauge (0.02 in) and 28 gauge (0.014 in) (Capillary tips, Ultradent Products) may be used for intracanal placement of $Ca(OH)_2$ paste[32]; however, care is needed because plastic tips tend to bind to the apical portion of the canal and cause extrusion. Consideration when selecting the size of the needle should include the fact that the force necessary to depress the plunger of a syringe increases as the diameter of the needle decreases.[33] Apical extrusion of $Ca(OH)_2$ has been observed in the use of injectable systems as the method of delivery.[11] $Ca(OH)_2$ is hydrosoluble,[34] and Ultracal XS has been shown to be biocompatible with rat subcutaneous tissue.[35] Overextension of $Ca(OH)_2$-based medicaments has been previously supported because of its beneficial properties in the context of healing.[8] However, although extrusion was unintentional, a reaction to the Ultracal XS paste was observed in both clinical cases presented here. The trauma with a subsequent vestibular cortical bone fracture in case 2 allowed extrusion of the Ultracal XS paste into the submucosal tissues, maintaining the inflammatory process in that region. The authors in previous case reports have described severe tissue necrosis resulting from $Ca(OH)_2$ paste displaced into an artery adjacent to the molar root apexes[36] and paresthesia of the inferior alveolar nerve associated with direct contact of $Ca(OH)_2$ with the neurovascular bundle.[37] Others have reported on the accidental displacement of $Ca(OH)_2$ beyond the apex into the maxillary sinus.[38] Care must be taken to gently backfill and not extrude the $Ca(OH)_2$ paste.

In this study, the proportion of $Ca(OH)_2$ in the Ultracal XS paste differed from that reported by the manufacturer. The XRD analysis revealed 73.8 wt% $Ca(OH)_2$ in contrast to 30 through 35 wt% $Ca(OH)_2$ reported by the manufacturer. Formulations containing 50% to 60% of $Ca(OH)_2$ and the ready-to-use Ultracal XS paste are recommended as endodontic interappointment medicaments because of their high antimicrobial efficacy.[39] Radiopacifiers such as $BaSO_4$ are added into the $Ca(OH)_2$ formulation to aid in radiologic assessment in identifying voids within the root canal space and its extrusion beyond the apex into tissues. Orucoglu and Cobankara[7] reported the extrusion of a mixture of $Ca(OH)_2$ powder, $BaSO_4$ powder, and distilled water into the periradicular tissues, where the paste did not resorb. The authors suggested that the $BaSO_4$ powder could be responsible for delayed healing. According to Alacam and colleagues,[40] many clinicians prefer a mixture of $Ca(OH)_2$ powder and vehicle without radiopacifier because they believe that the ingredients of commercial preparations can retard or delay the reparative process. The manufacturer formulation consists of 20 wt% $BaSO_4$ or less, consistent with the XRD analysis (15.8 wt%). In our study, $BaSO_4$ was the only component we found in the exogenous material using XRD. The effects of $BaSO_4$ are controversial. In some studies, researchers reported that $BaSO_4$ was deleterious for inducing bone resorption.[13,14] Other researchers, however, have reported that $BaSO_4$ appears to be biocompatible and osteoconductive.[15,16] In orthopedic surgery, $BaSO_4$ is added to the bone cement (polymethylmethacrylate), which is widely used for prosthesis adhesion to confer radiopacity on the cement and improve radiographic visualization.[16] Researchers in a previous study reported on the formation of agglomerates of these compounds within bone cement,[41] and this could be observed on the exogenous material found in the cases we present in this study (Figure 3B).

We found carbonate groups associated with $CaCO_3$ in the exogenous material by means of FTIR analysis; carbonate groups can be obtained by means of the reaction of $Ca(OH)_2$ with carbon dioxide.[42,43] $CaCO_3$ is an essential salt and when in contact with water can form carbon dioxide and $Ca(OH)_2$. On the basis of our findings in this study, we can infer that there was nondissociated $Ca(OH)_2$ in the surgically removed material.

The encapsulated exogenous material from case 2 pointed to a natural behavior consistent with normal tissues. However, it was associated with symptoms on palpation. This is in contrast with the work of Orucoglu and Cobankara,[7] who reported no symptoms related to paste extrusion. Here, the complete remission of signs and symptoms occurred after the removal of the exogenous material through the sinus tract in case 1 and surgery in case 2. The presence of radiopaque material in the apical region can hinder radiographic interpretation of the bone reparative process in cases of apical periodontitis. Even after the periradicular radiolucency disappears, complete paste resorption does not always occur.[7,44]

We used different methodologies to investigate the microstructure and to determine the chemical composition of the Ultracal XS paste and the exogenous material. These methods are complementary. EDS identifies different elements, whereas we confirmed the specific phases by means of XRD, which gives specific peaks for different phases in the samples. XRD is based on the intrinsic properties of crystalline solids, providing a unique pattern to each phase. Thus XRD analysis detects conventional structures (crystals) in the sample composition, but amorphous structures cannot be identified.[45] FTIR is a nonspecific technique that identifies only functional groups on chemical compounds because each functional group absorbs at a particular wavelength in the IR region. Thus the radiation intensity frequency graph (spectrogram) allows for the characterization of functional groups of standard or unknown materials.[46]

CONCLUSIONS

We can conclude that Ultracal XS paste application should be performed carefully, and its extrusion to periradicular and submucosal tissues should be avoided. Extrusion of the material may result in the formation of a persistent exogenous material of hardened consistency, which we observed to be associated with inflammatory signs and symptoms. Barium sulfate and calcium carbonate were associated with the hardened material. Finally, we determined that the proportion of $Ca(OH)_2$ in Ultracal XS paste was approximately 2 times greater than the proportion reported by the manufacturer. ■

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1. Bystrom A, Claesson R, Sundqvist G. The antibacterial effect of camphorated paramonochlorophenol, camphorated phenol and calcium hydroxide in the treatment of infected root canals. *Endod Dent Traumatol*. 1985;1(5):170-175.

2. Slutzky-Goldberg I, Hanut A, Matalon S, Baev V, Slutzky H. The effect of dentin on the pulp tissue dissolution capacity of sodium hypochlorite and calcium hydroxide. *J Endod*. 2013;39(8):980-983.

3. Siren EK, Kerosuo E, Lavonius E, Meurman JH, Haapasalo M. Ca(OH)2 application modes: in vitro alkalinity and clinical effect on bacteria. *Int Endod J*. 2014;47(7):628-638.

4. Mohammadi Z, Dummer PM. Properties and applications of calcium hydroxide in endodontics and dental traumatology. *Int Endod J*. 2011;44(8):697-730.

5. Sousa EL, Martinho FC, Nascimento GG, Leite FR, Gomes BP. Quantification of endotoxins in infected root canals and acute apical abscess exudates: monitoring the effectiveness of root canal procedures in the reduction of endotoxins. *J Endod*. 2014;40(2):177-181.

6. Yoldas O, Topuz A, Isci AS, Oztunc H. Postoperative pain after endodontic retreatment: single- versus two-visit treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2004;98(4):483-487.

7. Orucoglu H, Cobankara FK. Effect of unintentionally extruded calcium hydroxide paste including barium sulfate as a radiopaquing agent in treatment of teeth with periapical lesions: report of a case. *J Endod*. 2008;34(7):888-891.

8. Maalouf EM, Gutmann JL. Biological perspectives on the non-surgical endodontic management of periradicular pathosis. *Int Endod J*. 1994;27(3):154-162.

9. Martin DM, Crabb HS. Calcium hydroxide in root canal therapy. A review. *Br Dent J*. 1977;142(9):277-283.

10. Ribeiro DA, Marques ME, Salvadori DM. Lack of genotoxicity of formocresol, paramonochlorophenol, and calcium hydroxide on mammalian cells by comet assay. *J Endod*. 2004;30(8):593-596.

11. Olsen JJ, Thorn JJ, Korsgaard N, Pinholt EM. Nerve lesions following apical extrusion of non-setting calcium hydroxide: a systematic case review and report of two cases. *J Craniomaxillofac Surg*. 2014;42(6):757-762.

12. Ordinola-Zapata R, Bramante CM, Garcia-Godoy F, et al. The effect of radiopacifiers agents on pH, calcium release, radiopacity, and antimicrobial properties of different calcium hydroxide dressings. *Microsc Res Tech*. 2015;78(7):620-625.

13. Ingham E, Green TR, Stone MH, et al. Production of TNF-alpha and bone resorbing activity by macrophages in response to different types of bone cement particles. *Biomaterials*. 2000;21(10):1005-1013.

14. Wimhurst JA, Brooks RA, Rushton N. The effects of particulate bone cements at the bone-implant interface. *J Bone Joint Surg Br*. 2001;83(4):588-592.

15. Acarturk O, Lehmicke M, Aberman H, et al. Bone healing response to an injectable calcium phosphate cement with enhanced radiopacity. *J Biomed Mater Res B Appl Biomater*. 2008;86(1):56-62.

16. Khandaker M, Vaughan MB, Morris TL, White JJ, Meng Z. Effect of additive particles on mechanical, thermal, and cell functioning properties of poly(methyl methacrylate) cement. *Int J Nanomedicine*. 2014;9:2699-2712.

17. American Association of Endodontists. AAE consensus conference recommended diagnostic terminology. *J Endod*. 2009;35(12):1634.

18. Buchanan LS. The continuous wave of obturation technique: "centered" condensation of warm gutta percha in 12 seconds. *Dent Today*. 1996;15(1):60-62, 64-67.

19. Ioannidis K, Thomaidis V, Fiska A, Lambrianidis T. Lack of periradicular healing and gradually increasing swelling two years after intentional extrusion of calcium hydroxide into periapical lesion: report of a case. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2010;109(6):e86-e91.

20. Degen T, Sadki M, Bron E, König U, Nénert G. The HighScore suite. *Powder Diffraction*. 2014;29(suppl 2):S13-S18.

21. Saraya MEI, Bakr IM. Synthesis of BaSO4 nanoparticles by precipitation method using polycarboxylate as a modifier. *American Journal of Nanotechnology*. 2011;2(1):106-111.

22. Ramaswamy V, Vimalathithan RM, Ponnusamy V. Synthesis of monodispersed barium sulphate nanoparticles using water-benzene mixed solvent. *Advanced Materials Letters*. 2012;3(1):29-33.

23. Patel CM, Chakraborty M, Murthy ZVP. Study on the stability and microstructural properties of barium sulfate nanoparticles produced by nanomilling. *Advanced Powder Technology*. 2014;25(1):226-235.

24. Vagenas NV, Gatsouli A, Kontoyannis CG. Quantitative analysis of synthetic calcium carbonate polymorphs using FT-IR spectroscopy. *Talanta*. 2003;59(4):831-836.

25. Gu W, Bousfield DW, Tripp CP. Formation of calcium carbonate particles by direct contact of $Ca(OH)_2$ powders with supercritical CO_2. *Journal of Materials Chemistry*. 2006;16(32):3312-3317.

26. Siqueira JF Jr., Rocas IN. Clinical implications and microbiology of bacterial persistence after treatment procedures. *J Endod*. 2008;34(11):1291-1301.e3.

27. Dumsha T, Hovland EJ. Pulpal prognosis following extrusive luxation injuries in permanent teeth with closed apexes. *J Endod*. 1982;8(9):410-412.

28. Lee R, Barrett EJ, Kenny DJ. Clinical outcomes for permanent incisor luxations in a pediatric population. II. Extrusions. *Dent Traumatol*. 2003;19(5):274-279.

29. Diangelis AJ, Andreasen JO, Ebeleseder KA, et al. International Association of Dental Traumatology guidelines for the management of traumatic dental injuries: 1. Fractures and luxations of permanent teeth. *Dent Traumatol*. 2012;28(1):2-12.

30. Oztan MD, Akman A, Dalat D. Intracanal placement of calcium hydroxide: a comparison of two different mixtures and carriers. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2002;94(1):93-97.

31. Deveaux E, Dufour D, Boniface B. Five methods of calcium hydroxide intracanal placement: an in vitro evaluation. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2000;89(3):349-355.

32. Torres CP, Apicella MJ, Yancich PP, Parker MH. Intracanal placement of calcium hydroxide: a comparison of techniques, revisited. *J Endod*. 2004;30(4):225-227.

33. Moser JB, Heuer MA. Forces and efficacy in endodontic irrigation systems. *Oral Surg Oral Med Oral Pathol*. 1982;53(4):425-428.

34. Rehman K, Saunders WP, Foye RH, Sharkey SW. Calcium ion diffusion from calcium hydroxide-containing materials in endodontically-treated teeth: an in vitro study. *Int Endod J*. 1996;29(4):271-279.

35. Andolfatto C, da Silva GF, Cornelio AL, et al. Biocompatibility of intracanal medications based on calcium hydroxide. *ISRN Dent*. 2012;2012:904963.

36. Sharma S, Hackett R, Webb R, Macpherson D, Wilson A. Severe tissue necrosis following intra-arterial injection of endodontic calcium hydroxide: a case series. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;105(5):666-669.

37. Ahlgren FK, Johannessen AC, Hellem S. Displaced calcium hydroxide paste causing inferior alveolar nerve paraesthesia: report of a case. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2003;96(6):734-737.

38. Fava LR. Calcium hydroxide paste in the maxillary sinus: a case report. *Int Endod J*. 1993;26(5):306-310.

39. Blanscet ML, Tordik PA, Goodell GG. An agar diffusion comparison of the antimicrobial effect of calcium hydroxide at five different concentrations with three different vehicles. *J Endod*. 2008;34(10):1246-1248.

40. Alacam T, Gorgul G, Omurlu H. Evaluation of diagnostic radiopaque contrast materials used with calcium hydroxide. *J Endod*. 1990;16(8):365-368.

41. Shearwood-Porter N, Browne M, Sinclair I. Micromechanical characterisation of failure in acrylic bone cement: the effect of barium sulphate agglomerates. *J Mech Behav Biomed Mater*. 2012;13:85-92.

42. Beruto DT, Botter R. Liquid-like H_2O adsorption layers to catalyze the $Ca(OH)_2/CO_2$ solid–gas reaction and to form a non-protective solid product layer at 20°C. *Journal of the European Ceramic Society*. 2000;20(4):497-503.

43. Jensen OM, Hansen PF. Water-entrained cement-based materials: I. Principles and theoretical background. *Cement and Concrete Research*. 2001;31(4):647-654.

44. De Moor RJ, De Witte AM. Periapical lesions accidentally filled with calcium hydroxide. *Int Endod J*. 2002;35(11):946-958.

45. Formosa LM, Mallia B, Bull T, Camilleri J. The microstructure and surface morphology of radiopaque tricalcium silicate cement exposed to different curing conditions. *Dent Mater*. 2012;28(5):584-595.

46. Viapiana R, Guerreiro-Tanomaru JM, Hungaro-Duarte MA, Tanomaru-Filho M, Camilleri J. Chemical characterization and bioactivity of epoxy resin and Portland cement-based sealers with niobium and zirconium oxide radiopacifiers. *Dent Mater*. 2014;30(9):1005-1020.