



Deposited via The University of Sheffield.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/id/eprint/186119/>

Version: Published Version

Article:

Mahmood, H., Hoare, J. and Atkins, S. (2022) Chemical neurotoxicity to the inferior alveolar nerve — a rare sequela of endodontic treatment. *Oral Surgery*, 15 (4). pp. 663-668. ISSN: 1752-2471

<https://doi.org/10.1111/ors.12741>

Reuse

This article is distributed under the terms of the Creative Commons Attribution (CC BY) licence. This licence allows you to distribute, remix, tweak, and build upon the work, even commercially, as long as you credit the authors for the original work. More information and the full terms of the licence here:

<https://creativecommons.org/licenses/>

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

CASE REPORT

Chemical neurotoxicity to the inferior alveolar nerve—A rare sequela of endodontic treatment

Hanya Mahmood¹  | Johnathan Hoare² | Simon Atkins¹

¹Academic Unit of Oral & Maxillofacial Surgery, School of Clinical Dentistry, University of Sheffield, Sheffield, UK

²Speciality Dentist in Restorative Dentistry, Charles Clifford Dental Hospital, Sheffield, UK

Correspondence

Hanya Mahmood, Academic Unit of Oral & Maxillofacial Surgery, School of Clinical Dentistry, University of Sheffield, 19 Claremont Crescent, S10 2TA, Sheffield, UK. Email: h.mahmood@sheffield.ac.uk

Abstract

Aim: Damage to the inferior alveolar nerve (IAN) during endodontic procedures is a rare complication. However, over-instrumentation and over-filling during root canal treatment can cause injury through direct trauma, pressure or neurotoxicity from intra-canal irrigants or root canal filling materials, particularly where the roots of mandibular molars or premolars are in close proximity to the IAN. This report describes the clinical presentation and management of a severe chemical injury to the right IAN following the endodontic treatment. We also provide practical considerations to help minimise such complications.

Methods: A 27-year-old female developed immediate onset numbness and tingling to the right mental region following endodontic treatment of tooth 47. Radiographic examination confirmed widespread extrusion of root canal sealer within the marrow spaces of the right mandibular body extending centrally within the mandibular canal and perforating the lingual cortex.

Results: Urgent surgical exploration and decompression of the right IAN were undertaken, which revealed an avascular and fibrotic nerve with virtually no normal neuronal structure. There was evidence of foreign material both in contact with the epineurium and within the nerve trunk, much of which could not be eliminated. This severe chemical insult to the nerve resulted in irreversible anaesthesia in the right IAN distribution.

Conclusion: This case highlights the diligence that is required when performing root canal treatment in high-risk mandibular molar teeth, particularly in relation to confining materials within the canal space, accurate canal measurements and comprehensive radiographic evaluation both pre- and post-operatively. Urgent specialist referral for the elimination of foreign material is essential to maximise the potential for nerve regeneration.

KEYWORDS

anaesthesia, endodontics, inferior alveolar nerve injury, neurotoxicity, oral surgery, paraesthesia

INTRODUCTION

Although damage to the inferior alveolar nerve (IAN) during endodontic procedures is a rare complication, it can result in

permanent anaesthesia, and debilitating neuropathic pain.^{1,2} In cases where the roots of mandibular molars or premolars are in close proximity to the IAN, over-instrumentation and over-filling during endodontic treatment may result in nerve

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2022 The Authors. *Oral Surgery* published by British Association of Oral Surgeons and John Wiley & Sons Ltd.

injury via direct trauma, pressure or neurotoxicity from intra-canal irrigants or root canal filling materials.³⁻⁵

All endodontic sealer materials exhibit some level of toxicity⁶ but small material extrusions are generally well tolerated by the periradicular tissues.^{7,8} However, extrusion of sealer materials into the mandibular canal may result in significant neurosensory deficit as a result of neurotoxicity and compression.¹ This can result in symptoms of paraesthesia, dysaesthesia, hyperaesthesia, hypoaesthesia and anaesthesia in the region supplied by the IAN.^{1,2,9} The prognosis is influenced by the time elapsed from nerve injury to elimination of the foreign material and nerve decompression.¹⁰

This report describes an extreme case of right IAN injury following root canal treatment of a mandibular right second molar (47). The clinical presentation and surgical management have been described in accordance with the Preferred Reporting Items for Case reports in Endodontics (2020) guidelines.¹¹ We also provide practical considerations to help prevent and minimise such complications.

BACKGROUND

Patient history

A 27-year-old female was referred to the Sheffield Trigeminal Nerve Injury clinic as a tertiary referral from a specialist Oral Surgeon in primary care. The patient's primary complaint was a history of persistent numbness and tingling to the right mental region which had developed immediately following endodontic treatment of tooth 47, completed 2 months previously by her General Dental Practitioner. Approximately 6 weeks after completion of the endodontic treatment, the patient presented to the referring Oral Surgeon, who proceeded to extract tooth 47 due to symptoms of pain and infection. However, the numbness had not diminished after extraction, and the patient reported recurrent biting and trauma of the lip, although there was no neuropathic pain. She was otherwise medically fit and well, did not take any routine medications and had no known drug allergies. She was a non-smoker and had a low alcohol intake.

Clinical examination

A full clinical assessment was undertaken at the nerve injury clinic. There was no facial asymmetry or cervical lymphadenopathy, and the temporomandibular joint was normal on examination. Neurosensory testing of the fifth cranial nerve revealed an inability to detect light touch (using a von Frey filament) and sharp pinprick testing (using a dental probe) to the right lower lip and chin, suggesting significant anaesthesia (Table 1). Two-point discrimination testing was conducted using a two-pronged instrument with blunt ends which allowed measurements between the two prongs to assess innervation density. Findings revealed significantly reduced tactility in the right mental region until the width between two distinct points was measured at 18 mm apart, in comparison to 2–4 mm on the unaffected side. Intra-oral soft tissues were healthy, and the socket of tooth 47 appeared to have full mucosal healing. Sensation to the lingual nerve was normal and there were no other neurological deficits in sensory or motor function identified.

Radiographic investigations

Periapical radiographs provided by the referring Oral Surgeon demonstrated the presence of radiopaque material at the root apices of the endodontically treated tooth 47 (Figure 1, left) which can also be seen after extraction in the region of the mandibular canal (Figure 1, right). A cone-beam computed tomography scan (Figure 2) confirmed widespread extrusion of root canal filling material/sealer within the marrow spaces of the right mandibular body extending centrally within the mandibular canal and perforating the lingual cortex of the mandible. There was evidence of bony destruction and periosteal reaction in keeping with chronic infection.

Surgical decompression and exploration

Surgical exploration of the right IAN under general anaesthetic was urgently arranged and took place within 2 weeks of initial clinic attendance. Corticotomy of the buccal cortical plate was undertaken, and under an operating microscope,

TABLE 1 Outcome of neurosensory testing of the fifth cranial nerve at initial presentation to Sheffield trigeminal nerve injury clinic

Neurosensory test	Site: Lower lip	Detection and thresholds	Site: Chin	Detection and thresholds
Light touch	Injured side	0% detection	Injured side	0% detection
	Unaffected side	100% detection	Unaffected side	100% detection
Sharp pin-prick	Injured side	0% detection	Injured side	0% detection
	Unaffected side	100% detection	Unaffected side	100% detection
Two-point discrimination	Injured side	>14 mm	Injured side	>18 mm
	Unaffected side	2–4 mm	Unaffected side	2–4 mm



FIGURE 1 Periapical radiographs showing apical radiolucency with superimposed radiopaque sealer material extruded through apices of endodontically treated tooth 47 (left) and present in socket 47 and after extraction (right)



FIGURE 2 Cone beam computed tomography demonstrating remnants of radiopaque sealer material from the previous endodontically treated and extracted tooth 47, with associated radiolucency indicative of chronic infection

the IAN canal was explored. The right IAN was avascular and fibrotic with virtually no normal neuronal structure remaining. A fibrous neuroma was present with evidence of foreign material not only in contact with the epineurium but also within the nerve trunk (Figures 3 and 4). As such, a significant proportion of sealant could not be eliminated from within the neuronal structure. Necrotic tissue was gently debrided away from the nerve and sent for histopathological analysis. A sample of pus was taken from the apical aspect of the socket and sent for microbiological culture and sensitivity (MC&S).

The patient was admitted for an overnight stay in the hospital and received post-operative doses of intravenous dexamethasone and co-amoxiclav. There was minimal swelling and bruising at the site of surgery 1 day postoperatively and the pain was controlled. The patient was discharged with a 5-day course of 625 mg oral co-amoxiclav, 1 g oral paracetamol, 400 mg oral ibuprofen and 60 mg oral codeine phosphate.



FIGURE 3 Intraoperative clinical photo demonstrating suppuration (blue arrow) in the socket of tooth 47

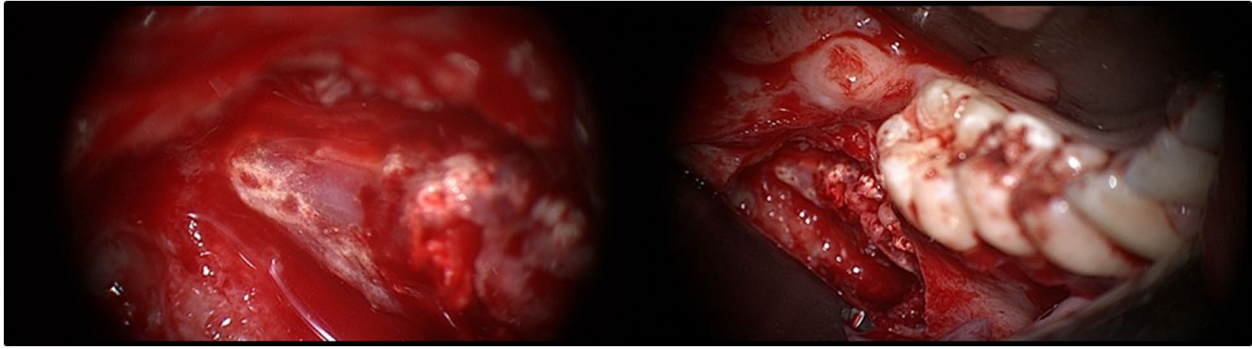


FIGURE 4 Intraoperative clinical photos showing widespread fibrosis and necrotic nerve tissue in the apical region of extracted tooth 47 (left) and evidence of foreign material on the external surface and within the nerve epineurium (right)

Outcome

MC&S did not identify the growth of any organisms. Histological examination of the specimen demonstrated fibrotic nerve tissue with prominent inflammation and deposition of exogenous material within bony fragments of woven and reactive bone. Although the patient was unable to attend a formal follow-up after the procedure, a post-operative telephone call suggested no improvement in symptoms of anaesthesia in the right mental region. As a significant amount of the endodontic sealer material could not be eliminated from within the neuronal structure, it would not be expected for the nerve to recover long-term.

DISCUSSION

Iatrogenic damage to the IAN secondary to endodontic treatment is rare. However, damage to the nerve can occur as a result of mechanical, thermal, or chemical trauma from overextension and/or overfilling of the root canals in mandibular molar teeth.^{5,12} The incidence of this complication is influenced by various factors including the root canal configuration, trajectory of the IAN with respect to the apices, technique-related parameters and the choice of root canal filing system or sealer cement used.¹³

Successful endodontic outcomes are achieved by thorough chemo-mechanical debridement and obturation of the canal space. Commonly used endodontic medicaments have strong alkalinity (sodium hypochlorite pH 11–12, calcium hydroxide pH 10–14) that have the potential to cause cellular necrosis of tissues that are in direct contact.¹⁴ Experimental animal studies have shown evidence of Wallerian degeneration, which is the interruption of nerve cell bodies that leads to cell death when calcium hydroxide has been expressed into the mandibular canal.¹⁴ One study has shown greater material extrusion with bioceramic sealers in comparison to resin-based sealers ($p < 0.05$) with no significant difference in post-operative pain between the two materials ($p > 0.05$) following endodontic treatment of single-rooted maxillary teeth.¹⁵ With the increasing potential for use of single cone obturation techniques with bioceramic sealers that involve

increased sealer volume, there is a greater concern for the risk of material extrusion.

To reduce the incidence of IAN injury, clinicians must ensure that important precautions are undertaken. Preoperative imaging should allow assessment of the proximity of the apices with the mandibular canal borders in addition to other features that increase risks, such as immature root apices and complex root canal configuration. This is especially the case when treating mandibular second molars as they pose an increased risk of injury to the IAN. One study demonstrated that more than 50% of mandibular second molars ($n = 272$) had an intimate relationship between the roots and mandibular canal.¹⁶ Cone-beam CT imaging assists greatly in evaluating the three-dimensional position of the mandibular canal to allow planning and delivery of medicaments in close proximity.¹⁷

Irrigants and obturation materials should be confined within the prepared canal space through the use of accurate root canal measurements, and an awareness that the toxicity of intra-canal medicaments is highest when newly placed. Careful consideration should be given to the selection of a sealant with the least neurotoxic effect. Experimental models have shown eugenol to be a highly neurotoxic material^{18,19} and zinc oxide eugenol and AH26 have also been shown to display neurotoxic effects.¹⁰ The application of intra-canal dressings using syringes or rotary paste fillers should also be avoided to minimise the risk of material displacement beyond the apices into the mandibular canal area.¹⁰ Finally, a post-operative radiograph showing at least 2–3 mm of the periapical region should be undertaken to assess the quality of the root canal filling and to identify signs of material extrusion that warrant urgent specialist referral.²⁰

There are several mechanisms in which IAN injury can occur following endodontic treatment, these being: (1) mechanical trauma caused by over-instrumentation into the canal; (2) compression of the canal from the extruded material during condensation; (3) chemical neurotoxicity caused by penetration of intracanal irrigants and/or sealer into the nerve. In this case, the root-filling was not seemingly overextended, and mechanical trauma caused by over-instrumentation has not been shown to damage the

nerve to this extent. It is also unlikely that intra-canal irrigants have penetrated the canal, given the absence of extreme patient for the patient. It is therefore most likely that the anaesthesia and paraesthesia were caused by degeneration of the nerve due to compression from the extruded sealer material, in addition to chemical neurotoxicity from the material used.

Irreversible nerve damage can be minimised by early nerve decompression and debridement of the foreign material.^{21–24} Although the prognosis for anaesthesia and paraesthesia following endodontic treatment is poorer if the extruded material cannot be eliminated entirely from the mandibular canal.¹⁰ In this case, the time elapse from nerve injury to surgical decompression was almost 8 weeks, significantly reducing the prognosis for nerve recovery. Surgical management is less effective in cases of nerve injury in which there is widespread material overfill and time delays, emphasising the importance of urgent referral to a surgeon skilled in microsurgery and trigeminal nerve repairs.²⁵ Furthermore, it is recommended that steroid therapy is prescribed (step down 5-day course of Prednisone Oral 50–40–30–20–10 mg) at the earliest identification of a traumatic IAN injury.²⁶ This is supported by various experimental studies which have shown steroids play an important role in reducing neuroinflammation, which can lead to accelerated functional recovery of nerves after trauma.^{27,28} In severe cases, such as the one described, further treatment may involve a nerve graft.²⁹

CONCLUSION

Whilst the prevalence of IAN injuries secondary to endodontics is low, with only a limited number of published case reports, it is important for clinicians to be able to recognise which teeth pose a greater risk and how to expedite management should such a complication arise. This case highlights the diligence that is required when performing root canal treatment, especially in cases where root apices have an intimate relationship with the mandibular canal. Radiographic imaging is essential to identify high-risk cases, provide accurate root canal measurements and verify the quality of root fillings. In cases where material extrusion is observed, we recommend urgent referral to an oral surgeon to expedite surgical decompression with consideration for early steroid therapy. This will help to maximise the potential for nerve regeneration and optimise patient outcomes.

CONFLICT OF INTEREST

None declared.

ETHICS STATEMENT

Not applicable. We have obtained permission from the patient for the publication of all images included in this article.

ORCID

Hanya Mahmood  <https://orcid.org/0000-0001-7159-0368>

REFERENCES

1. Morse DR. Infection-related mental and inferior alveolar nerve paraesthesia: literature review and presentation of two cases. *J Endod.* 1997;23(7):457–60.
2. Gallas-Torreira MM, Reboiras-López MD, García-García A, Gándara-Rey J. Mandibular nerve paresthesia caused by endodontic treatment. *Medicina oral: organo oficial de la Sociedad Española de Medicina Oral y de la Academia Iberoamericana de Patología y Medicina Bucal.* 2003;8(4):299.
3. López-López J, Estrugo-Devesa A, Jané-Salas E, Segura-Egea JJ. Inferior alveolar nerve injury resulting from overextension of an endodontic sealer: non-surgical management using the GABA analogue pregabalin. *Int Endod J.* 2012;45(1):98–104.
4. Knowles KI, Jergenson MA, Howard JH. Paresthesia associated with endodontic treatment of mandibular premolars. *J Endod.* 2003;29(11):768–70.
5. Fanibunda K, Whitworth J, Steele J. The management of thermomechanically compacted gutta percha extrusion in the inferior dental canal. *Br Dent J.* 1998;184(7):330–2.
6. Hargreaves KM, Berman LH. *Elsevier Health Sciences: Cohen's pathways of the pulp expert consult*; 2015.
7. Ørstavik D, Ford TP, editors. *Essential endodontology: prevention and treatment of apical periodontitis.* Oxford, UK: Blackwell Munksgaard; 2008.
8. Fristad I, Molven O, Halse A. Nonsurgically retreated root filled teeth—radiographic findings after 20–27 years. *Int Endod J.* 2004;37(1):12–8.
9. Ørstavik D, Brodin P, Aas E. Paraesthesia following endodontic treatment: survey of the literature and report of a case. *Int Endod J.* 1983;16(4):167–72.
10. Escoda-Francoli J, Canalda-Sahli C, Soler A, Figueiredo R, Gay-Escoda C. Inferior alveolar nerve damage because of overextended endodontic material: a problem of sealer cement biocompatibility? *J Endod.* 2007;33(12):1484–9.
11. Nagendrababu V, Chong BS, McCabe P, Shah PK, Priya E, Jayaraman J, et al. PRICE 2020 guidelines for reporting case reports in Endodontics: a consensus-based development. *Int Endod J.* 2020;53(5):619–26.
12. Neaverth E. Disabling complications following inadvertent overextension of a root canal filling material. *J Endod.* 1989;15:135–9.
13. Renton T. Prevention of iatrogenic inferior alveolar nerve injuries in relation to dental procedures. *Dent Update.* 2010;37(6):350–63.
14. Nakamura C, Tomida M, Hasegawa H, et al. Injury and the recovery reaction due to the penetration of material into the Mandibular Canal. In *Pathological basis of root canal restoration: using calcium hydroxide paste.* Tokyo, Japan: IDP; 2012. p. 39–51.
15. Fonseca B, Coelho MS, da Silveira Bueno CE, et al. Assessment of extrusion and postoperative pain of a bioceramic and resin-based root canal sealer. *European Journal of Dentistry.* 2019;13(03):343–8.
16. Chong BS, Quinn A, Pawar RR, Makdissi J, Sidhu SK. The anatomical relationship between the roots of mandibular second molars and the inferior alveolar nerve. *Int Endod J.* 2015;48(6):549–55.
17. Gluskin AH, Lai G, Peters CI, Peters OA. The double-edged sword of calcium hydroxide in endodontics: precautions and preventive strategies for extrusion injuries into neurovascular anatomy. *J Am Dent Assoc.* 2020;151:317–26.
18. Ozeki M. The effects of eugenol on the nerve and muscle in crayfish. *Comp Biochem Physiol.* 1975;50:183–91.
19. Trowbridge HO. Effects of eugenol on nerve excitability. *J Dent Res.* 1977;56:115A.
20. European Society of Endodontology. Quality guidelines for endodontic treatment: consensus report of the European Society of Endodontology. *Int Endod J.* 2006;39(12):921–30.
21. Boiesen J, Brodin P. Neurotoxic effect of two root canal sealers with calcium hydroxide on rat phrenic nerve in vitro. *Endod Dent Traumatol.* 1991;7:242–5.
22. Grötz K, Al-Nawas B, de Aguiar E, et al. Treatment of injuries to the inferior alveolar nerve after endodontic procedures. *Clin Oral Investig.* 1998;2:73–6.

23. Ahlgren F, Johannessen A, 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;96:734–7.
24. Giuliani M, Lajolo C, Deli G, Silveri C. Inferior alveolar nerve paresthesia caused by endodontic pathosis: a case report and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2001;92:670–4.
25. Pogrel MA. Damage to the inferior alveolar nerve as the result of root canal therapy. *J Am Dent Assoc.* 2007;138(1):65–9.
26. Renton T. Trigeminal nerve injuries. *Aust Endod J.* 2018;44(2):159–69.
27. Sun H, Yang T, Li Q, Zhu Z, Wang L, Bai G, et al. Dexamethasone and vitamin B12 synergistically promote peripheral nerve regeneration in rats by upregulating the expression of brain-derived neurotrophic factor. *Arch Med Sci.* 2012;8(5):924–30.
28. Günay AY, Ünverengil G, Ak G. Investigation of three drugs with Neuroregenerative effects on inferior alveolar nerve injury in rats. Istanbul: Research Square; 2021.
29. Zuniga JR. Sensory outcomes after reconstruction of lingual and inferior alveolar nerve discontinuities using processed nerve allograft—a case series. *J Oral Maxillofac Surg.* 2015;73(4):734–44.

How to cite this article: Mahmood H, Hoare J, Atkins S. Chemical neurotoxicity to the inferior alveolar nerve—A rare sequela of endodontic treatment. *Oral Surg.* 2022;00:1–6. <https://doi.org/10.1111/ors.12741>