A case series of trigeminal nerve injuries caused by periapical lesions of mandibular teeth

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In brief

Outlines a case series of patients presenting to a tertiary care centre, with trigeminal nerve injuries caused by periapical lesion of mandibular teeth.

Discusses the procedure for assessing patients with trigeminal nerve injuries, as well as the key symptoms and functional problems experienced by these patients.

Suggests strategies for managing patients who present with trigeminal nerve injuries due to periapical lesions of mandibular teeth.

Aims Periapical lesions have been implicated in mandibular trigeminal sensory neuropathy. This study aimed to report on a case series of consecutive patients presenting with mandibular division trigeminal nerve injuries (TNI) caused by periapical lesions. Common presenting characteristics and possible strategies for management were also investigated. **Materials and methods** A retrospective study of 22 patients with TNI caused by periapical lesions. Data were extracted from patient records and analysed using Microsoft Excel and SPSS. Factors associated with TNI resolution were assessed using Student's t-Tests and one-way Analysis of Variance (ANOVA), where $P < 0.05$ indicated statistical significance. **Results** Twenty-one patients had inferior alveolar nerve injuries (IANI) and one had a lingual nerve injury (LNI). The most commonly affected teeth were the first molars (11 patients; 50%). TNI symptoms included numbness, pain and/or paraesthesia. IANI resolved completely among five patients within a mean time of 4.7 months (range 1.5–12 months). Patients who showed complete resolution had the affected teeth extracted or primary endodontic treatment with antibiotics. **Conclusions** Patients with TNI caused by periapical lesions can suffer significantly from combined numbness, pain and paraesthesia. Resolution of these injuries may be maximised upon early diagnosis and treatment of the periapical lesion by tooth extraction or primary endodontic treatment.

Introduction

Trigeminal nerve injuries (TNI) are known to be caused by a number of common dental procedures including extraction of teeth, local anaesthetic block administration, implant placement and endodontic procedures.[1] Injuries to the mandibular division of the trigeminal nerve, in comparison to the ophthalmic and maxillary divisions, are more prevalent due to the anatomy of the mandible. The inferior alveolar nerve (IAN) is particularly at risk of injury as it is contained within a bony canal, predisposing it to ischaemic trauma.

Nerve injury as a complication of endodontic treatment has been reported in a number of case series and review articles, however, the overall incidence within the population undergoing endodontic treatment is unknown.[2] Direct neural injury can be caused by over-instrumentation beyond the apex in teeth in close proximity to the IAN canal or mental foramen.[3] Chemical and mechanical injury to the nerve can occur due to extravasation of cytotoxic irrigation or filling materials, particularly in teeth with open apices or large periapical lesions.[4,5]

There are relatively few reports in the literature of injury to the trigeminal nerve resulting from periapical lesion.[4,6–10] Localised periapical lesion adjacent to the IAN canal may result in neural injury both by compression due to localised oedema of the periapical tissues and by release of inflammatory mediators such as interleukin 1, tumour necrosis factor and nitric oxide which all have low pH and therefore neurotoxic activity.[11,12] Bacterial products in the periapical tissues may also cause neural irritation.[12]

Knowles *et al.* reported eight cases of periapical lesion related paraesthesia of the IAN occurring over a seven year study period giving an incidence of 0.96% within the study group.[13] All cases were caused by periapical lesion of a mandibular premolar tooth. There are many other single case reports of mandibular TNI caused by periapical lesion, treated with varying levels of success with antibiotics, endodontic treatment or tooth extraction.[4,9,14,15] However, as there are so few reported cases, no protocol for management of these injuries currently exists and there is little known about the likelihood of resolution of the injury particularly in those with duration of several months. Schultze-Mosgau and Reich suggest that the likelihood of sensory recovery

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after three to six months is low;[16] however, in some case series sensory recovery is reported following surgical intervention up to twelve months following injury.[17]

The aim of this present study was to report a case series of consecutive patients presenting with mandibular division TNIs caused by periapical lesions to identify common presenting characteristics and possible strategies for management of these injuries.

Materials and methods

Background

A multidisciplinary orofacial pain and trigeminal nerve injury service has been running at King's College Hospital (KCH) for over seven years. Weekly clinics run by an oral surgeon, neurologist, neurosurgeon, psychiatrist and psychologist assess and manage patients referred by general dental practitioners, general medical practitioners and other hospital-based dentists and doctors. This article describes a retrospective case series of consecutive patients referred for management of mandibular division trigeminal nerve (V_3) injury caused by periapical lesions.

Assessment and clinical history

All patients referred to the clinic were assessed by the same practitioner (TR). A full medical, social and dental history was taken. A detailed history of the probable causative event (in this case, periapical lesion) was taken to include: duration of symptoms and previous treatment carried out by the referring practitioner (such as extirpation of dental pulp, antibiotic therapy, endodontic treatment or extraction of the tooth).

Clinical examination

Extraoral examination of the patient included chairside cranial nerve examination, assessment of the temporomandibular joints and masticatory muscles, facial and cervical lymph nodes and facial asymmetry. Intraoral examination included a full assessment of the dentition, mucosa and existing restorations. Testing of dental vitality, percussion and response to thermal stimuli was carried out to rule out any other dental pathology. The affected tooth was assessed for the quality of existing restorations, presence of caries and periodontal disease.

Investigations

Periapical radiographs of the affected tooth or an orthopantomogram (OPG) for larger lesions were taken. Further investigations included routine blood tests, magnetic resonance imaging (MRI) of the brain and cone-beam computed tomography scanning (CBCT) if clinically indicated.

Clinical assessment of nerve injury

Examinations took place in a quiet room with the patients at ease. The patients' self-assessment of neurosensory function in terms of reduced function (hypoesthesia, anaesthesia) and neurogenic discomfort (paraesthesia, dysaesthesia, allodynia or pain) were recorded. Interference with daily function was explored by asking specific questions regarding eating, drinking, speaking, sleeping, kissing, brushing teeth, shaving and makeup application.

A series of standardised tests of neurosensory function was carried out on all patients by the same observer (TR) to identify sensory deficit within the mandibular division of the trigeminal nerve. The clinical examination was based on recommendations by Robinson *et al.*,[18] which utilised a similar kit of instruments and each of the following neurosensory qualities:

- Mapping of neuropathic area: college tweezers were applied to the skin on the normal side and traced to the neuropathic area warning the patient that there may be hypersensitivity as well as hyposensitivity. The neuropathic area was mapped out and recorded pictorially or by photograph using pen marks on patient's face
- Subjective function (SF) score: the patient was requested to assess their overall level of sensory function of the affected side using a scale ranging from 0–10 (0 = no perception of touch and 10 = normal perception). All ratings were based on comparison with the uninjured side
- Light touch (LT): a corner of tissue paper was gently pulled over the area to be examined and repeated five times; three positive responses were recorded as positive outcome.
- Sharp blunt discrimination (SBD): the pointed and rounded ends of a dental probe were gently applied to the area with minimal pressure and repeated five times. The patient was asked to identify the stimulus as sharp or blunt. Three positive responses were recorded as positive outcome
- Two point discrimination (TPD): a set of college tweezers was applied gently to the affected area with beaks open and closed (both for five stimulations). The patient was asked to identify whether there were one or two pressure points applied. Some authors prefer specially designed callipers which can be set to a specified distance. Normal TPD in the trigeminal mandibular (V_3) dermatome extra-orally ranges from 2–4 mm on lip vermillion to 6–8 mm on the skin of the chin.

Patient selection

A retrospective analysis of the clinic letters and patient records of all patients referred to the trigeminal nerve injury clinic between January 2007 and January 2015 was undertaken to identify patients with nerve injury caused by periapical lesion.

Diagnostic criteria for nerve injury caused by periapical lesion had to include all of the following:

- Patient reported altered sensation in the mandibular division of the trigeminal nerve (numbness, tingling, pins and needles, itching, burning or pain)
- Abnormal clinical neurosensory tests (reduced or increased sensation to light touch, pinprick, sharp/blunt discrimination and two point discrimination)
- Symptom onset coincided with clinically or radiographically diagnosed periapical lesion of a mandibular tooth on the affected side.

Measures analysed in this study

Patient demographics and clinical presentation:

- Tooth involved
- Presence of caries, periodontal disease and periapical lesion
- Radiographic signs of proximity of lesion to inferior dental canal (superimposition of lesion on inferior dental [ID] canal, loss of cortication of canal, deviation of canal)
- Previous treatment given for management of periapical lesion.

Characteristics of nerve injury:

- Presenting symptoms (hypoaesthesia, paraesthesia, neuropathic pain)
- Results of neurosensory tests
- Functional impairment
- Resolution (complete, partial, none)
- Treatment required for nerve injury.

Data collection and analysis

Data collection was carried out retrospectively from the clinic letters and patient records of all patients referred to the trigeminal nerve injury clinic with trigeminal nerve injury from January 2007 – January 2015 by one of the authors (MD). All data was analysed by another author (ZY)

Fig. 1 Sites of periapical radiographic lesions among the patient case series

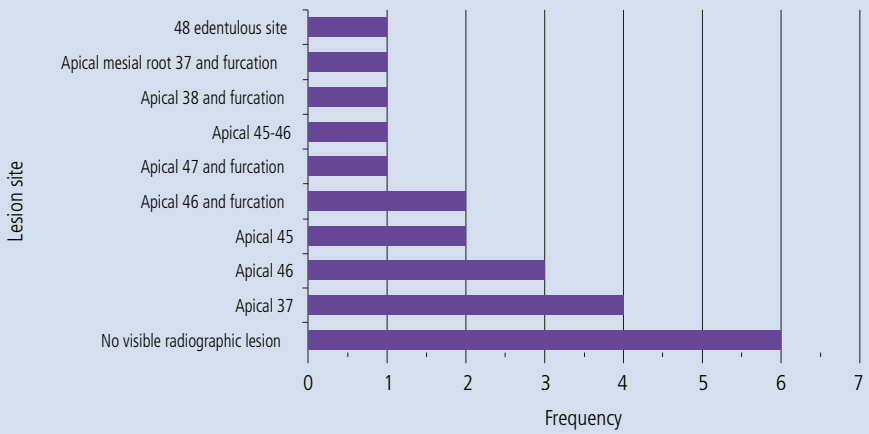


Table 1 Summary of the radiological findings suggestive of close proximity to the inferior alveolar nerve (IAN)

Patient ID	Proximity to ID canal	Loss of cortication	Deviation of canal	Superimposition of canal
IANI 1	In ID canal	Y	N	Y
IANI 2	5.5 mm	N	N	N
IANI 3	N/A	N	N	N
IANI 4	Overlies canal	Y	N	Y
IANI 5	Overlies canal	Y	N	Y
IANI 6	Overlies canal	Y	N	Y
IANI 7	1.2 mm	N	N	N
IANI 8	Overlies canal	Y	N	N
IANI 9	N/A	N/A	N/A	N/A
IANI 10	Previously	Unknown	Unknown	Unknown
IANI 11	N/A	N/A	N/A	N/A
IANI 12	Overlies canal	Y	N	Y
IANI 13	Overlies canal	Y	N	Y
IANI 14	3.4 mm	N	N	N
IANI 15	4 mm	N	N	N
IANI 16	Adjacent to mental foramen	N	N	N
IANI 17	Overlies canal	Y	N	Y
IANI 18	Overlies canal	Y	N	Y
IANI 19	N/A	N	N	N
IANI 20	Overlies canal	Y	N	Y
IANI 21	In contact	Y	N	N
LNI 1	Cortication not visible	Cortication not visible	Cortication not visible	Cortication not visible

using Microsoft Excel 2007 and The Statistical Package for Social Sciences (SPSS) Version 22.0. Factors associated with resolution of the TNIs were assessed using Student's tTests and one-way ANOVA, where P <0.05 indicated statistical significance.

Results

Patient demographics

During the period of study (January 2007 – January 2015), 352 patients were seen in the trigeminal nerve injury clinic. Twenty-two consecutive cases of trigeminal nerve injuries (TNI) caused by periapical lesion (16 females: 6 males) were identified and retrospectively analysed in this study. One of these patients had a lingual nerve injury (LNI) and the remaining 21 had inferior alveolar nerve injuries (IANI). The mean age of these patients was 47 years (range 26–78 years; standard deviation [S.D.] 11.6 years). Ten of these patients did not report any other medical conditions (Fig. 1). Hypertension was the most common reported health problem (N = 3), with other conditions among individual patients including asthma, kidney problems, cancer, deep-vein thrombosis, bladder problems, osteoporosis, arthritis, fibromyalgia, chronic obstructive pulmonary disease, sciatica and anxiety. Three of the patients were smokers.

Clinical presentation

The most commonly affected teeth were the first molars (11 patients; 50%). Six cases related to second molars and three related to the second premolars. The periapical lesion in one case was associated with a lower third molar and another to an edentulous area (third molar region).

Presence of caries

The teeth were carious in eight patients, non-carious in six patients and unknown in seven patients. This was not applicable in one case presentation where the site affected was edentulous.

Endodontic treatment

Primary endodontic treatment was carried out in six cases and extirpation only was carried out in two cases. No endodontic treatment was carried out in nine patients and it was unknown in two patients. Endodontic treatment was not applicable for one patient owing to elected extraction, as the affected tooth had been extracted before them presenting to the King's College Hospital (KCH) clinic.

Periodontal disease

Furcation lesions were present in four of the 22 cases. Whether or not there was presence of periodontal disease was unknown among seven patients. Ten patients did not have any presence of periodontal disease.

Table 2 Summary of the patient demographics, duration of inferior alveolar nerve injuries (IANI's) and lingual nerve injury (LNI), their degree of resolution, the percentage of extra-oral (EO) and intra-oral (IO) dermatomes affected, sites affected and whether or not they were experiencing neuropathic pain

Patient ID	Age	Gender	Duration of NI	Resolution	Neuropathic area (%)		Areas affected	Neuropathic pain
					EO	IO		
IANI 1	78	M	18 months	Partial	40	10	Lip, chin, buccal gingivae	No
IANI 2	45	M	6 weeks	Unknown	Not measured		Lip, chin	No
IANI 3	60	F	2 years	None	40	15	Lip, chin	No
IANI 4	39	F	15 months	None	100		Lip, chin, buccal gingivae	Yes
IANI 5	44	F	8 months	Partial	<5	0	No Data	No
IANI 6	42	F	15 months	None	25	88	Lip, buccal gingivae	Intermittent
IANI 7	48	F	1 year	None	20	16	Lip, chin, buccal gingivae	Yes
IANI 8	42	F	4 months	Complete	80	90	Lip	No
IANI 9	48	F	3 years	None	60	15	Lip, chin, buccal gingivae	Yes
IANI 10	52	M	8 months	None	8	0	Lip, chin	No
IANI 11	47	F	6 months	Partial	5-10	4	Lip, Left quadrant	No
IANI 12	75	F	31 months	None	10	30	Lip, chin	No
IANI 13	38	F	6 months	Partial	5	30	Lip, chin, buccal gingivae	Yes
IANI 14	45	F	18 months	None	45	60	Lip, chin	Yes
IANI 15	40	F	22 months	90%	6		Lip, chin	No
IANI 16	42	M	6 weeks	Complete	90	24	Lip, chin, teeth	No
IANI 17	45	F	1 year	Complete	100	100	Lip, chin, buccal gingivae	Yes
IANI 18	47	F	2 months	Complete	10	0	Lip, chin	No
IANI 19	51	F	14 months	None	40	50	Lip, chin, buccal gingivae	Yes
IANI 20	41	M	4 months	Complete	25	0	Lip, chin	Yes
IANI 21	38	F	3 months	Partial	30		Chin	No
LNI 1	26	M	2 months	Unknown	Not measured		Tongue, lingual gingivae	No

Periapical lesion

Site

The most common sites of lesions were the apical 37 (N = 4) and apical 47 (N = 3; Fig. 1). Other sites included the apical 45 and 45-46 regions (N = 3). No visible radiographic lesions were reported in six patients.

Duration of periapical lesion

The average duration of periapical lesion was 3.5 months, with a range from 1 week to 15 months (S.D. 4.5).

Previous treatment of periapical lesion

The most frequent treatment involved the extraction of the affected teeth (six patients). It was evident that extraction of these teeth was not the cause of the subsequent nerve injuries because these patients were experiencing symptoms of numbness, pain and/or paraesthesia before the teeth were extracted. Primary endodontic treatment followed by extractions was carried out on five patients, and primary endodontic treatment only was carried out on four patients. Four patients did not have any treatment. In one case, extirpation and dressing of the pulp occurred, one patient had a temporary filling placed and in another case the pulp was extirpated and dressed, followed by tooth extraction.

Imaging and size of the lesion

Lesions in 19 of the 22 patients were imaged using plain radiographic imaging, such as long cone periapical (LCPA) radiographs and/or orthopantomographs (OPG) for larger lesions. Although radiographic imaging did not take place in three cases, one of these patients did have a computed tomography (CT) scan which was negative for any lesions, and another had a cone-beam CT (CBCT) scan with magnetic resonance imaging (MRI). This MRI scan was also negative for any lesions. Cone-beam computed tomography (CBCT) was used in five patients in total to determine the extent of larger lesions. Radiographic periapical lesions may not be evident in radiological investigations as early periapical lesions or dental abscesses may not have any radiographic features within the first ten days of infection.[19]

Bony lesions develop later after the initial infection arises in the periapical tissues. The likely initial cause of neuritis, nerve inflammation, is due in part to mediators such as interleukin 1, tumour necrosis factor and nitric oxide which all have low pH and

therefore neurotoxic activity.[11,12] Bacterial products in the periapical tissues may also cause neural irritation,[12] which may or may not be symptomatic. If the infection is not managed in a timely fashion the persistent inflammatory mediators and resultant acidic environment may cause persistent nerve damage and symptomatic neuropathy with or without neuropathic pain.

Lesion size and location

The average periapical lesion size was 9 mm × 6.7 mm (range 3 mm × 4 mm to 14 mm × 9 mm; S.D. 3.2). Ten of these lesions were apical; four were apical and involved the furcation. One was previously apical to lower–left 7 retained roots but subsequently had bony infill. Lesions were not visible radiographically in six patients at the time of their appointment with KCH, since these lesions had previously been identified earlier by their general dental practitioner. Nine of the lesions were superimposed on the ID canal and two were either in contact with the canal or within the ID canal (Table 1). One case was previously associated with the ID canal but had resolved. Other cases were relatively close but not in contact with the ID canal, and one was adjacent to the mental foramen. Loss of cortication was seen in 11 cases. Deviation of the canal was not seen in any case.

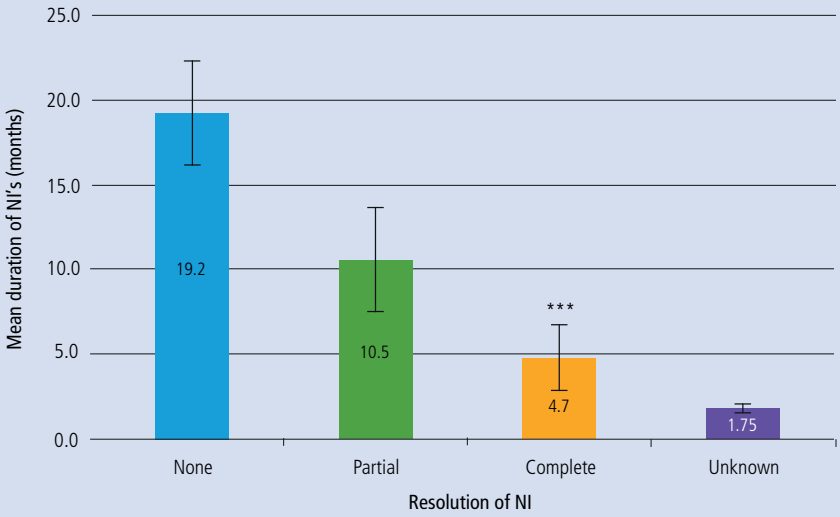
Nerve injuries

Twenty-one patients presented with inferior IANIs. Nerve injury (NI) resolved completely in five patients within a mean time of 4.7 months (range 6 weeks – 1 year). Five patients had partial resolution of their nerve injury, and nine had no resolution of their NI over a maximum follow-up time of three years (Table 2). One additional patient presented with a lingual nerve injury (LNI) caused by a periapical lesion which had been present for two months at the time of presentation. This patient did not attend follow-up appointments, therefore it is unknown whether this injury resolved.

Clinical assessment

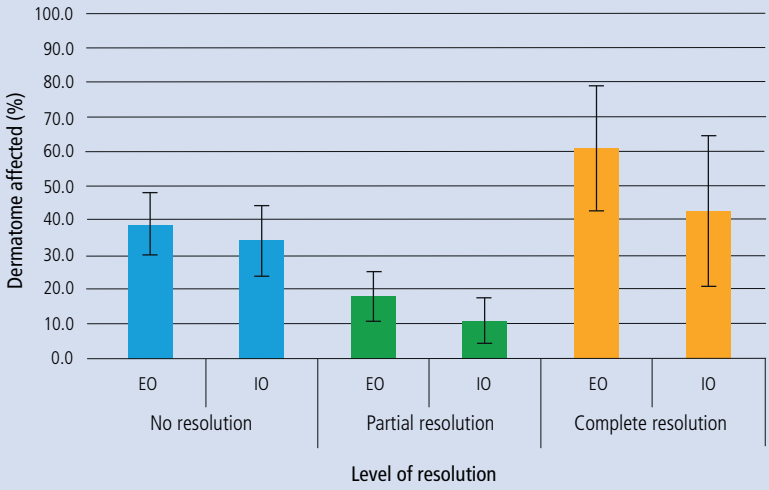
The average subjective function (SF) of patients with IANI was 8.1 (range 2–30; S.D. 6.8). The patient with IANI (Patient ID: IANI 9) who had a SF of greater than 10 indicated allodynia, hyperalgesia and exaggerated response to sharp-blunt discrimination (SBD). Conversely, one of the patients who reported the least SF of 2 (Patient ID: IANI 12) had decreased light touch (LT) and SBD; the other patient who had a SF of 2 reported normal SBD but reduced LT.

Fig. 2 Comparison of the mean duration of the nerve injuries (NIs) with their degree of resolution (error bars = standard error of the mean [SEM])



***Denotes statistically significant difference (P = 0.006) between the mean duration of the TNI among those patients who had no resolution and complete resolution

Fig. 3 Summary of the level of resolution and the mean percentage of extra-oral (EO) and intra-oral (IO) dermatomes affected (error bars = the standard error of the mean [SEM])



*Borderline statistically significant difference between the mean percentage of EO dermatome of those patients who had partial resolution or complete resolution (P = 0.059)

Duration and resolution of the NI

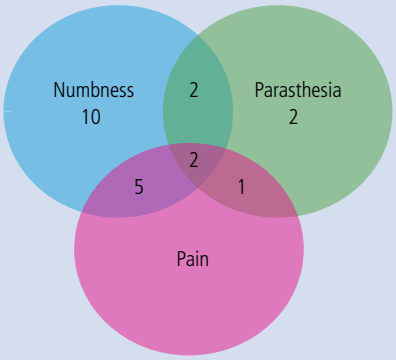
Complete resolution of nerve injury occurred in five patients in an average time of 4.7 months in comparison to those nine patients who did not have any resolution of their injury after an average of 19.2 months (P = 0.006; Fig. 2). Five patients had partial resolution of the nerve injury after a mean follow up period of 10.5 months.

Sites affected and resolution of the NI

The sites affected were predominately the lip and chin (8 patients) or lip, chin and buccal gingivae (8 patients; Table 2). The patient who originally only had symptoms of numbness within the lip (IANI8) had complete resolution of the IANI. It is important to note though that the other

four patients who also had complete resolution of their IANI's did encounter symptoms in the chin and/or buccal gingivae in addition to the lower lip, thus suggesting that the number of sites affected by the IANI did not significantly correlate with the increased chance of resolution of the IANI. This deserves further exploration in a larger cohort of patients. The tongue and lingual gingivae were affected in the patient who had a LNI.

Fig. 4 A summary of the presenting symptoms of patients with nerve injury caused by periapical lesion

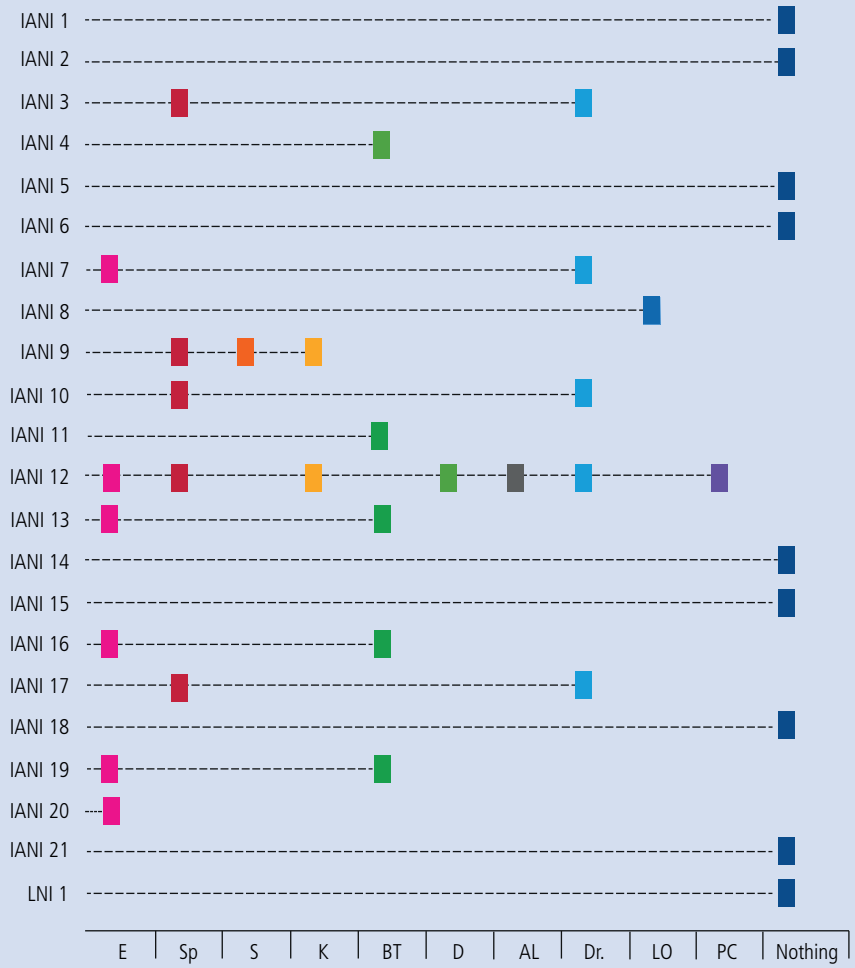


Dermatome affected and resolution of the NI

The patients who reported complete resolution of their NI had originally reported the largest mean extra-oral (EO) and intra-oral (IO) neuropathic areas (61.0% [range 10–100%] and 42.8% [range 0–100%], respectively; Fig. 3) at the initial consultation. In one patient who had 90% resolution of his injury, only 6% of the EO dermatome was affected within the lower lip and chin areas (he presented with an IANI of 22 months duration). The average EO and IO dermatomes among the five patients who had partial resolution were 18% (range from 5–40%), and 11% (range from 0–30%), respectively. Patients who did not have any resolution of their TNI had a mean EO dermatome of 38.7% (range 8–100%) and IO dermatome of 34.3% (range 0–88%)

There was a borderline level of statistical significance between the areas of the EO dermatomes affected among those patients who had partial resolution and those who had complete resolution (P = 0.059). A larger number of patients would need to be assessed to explore this further. There were no statistically significant differences between the EO or IO dermatomes affected among those patients who had complete resolution of their IANI and those who did not have any resolution (P >0.05).

Fig. 5 Functional problems reported by each patient with periapical lesion-related IANI and LNI. Abbreviations: E = Eating; Sp. = Speech; S = Singing; K = Kissing; BT = Brushing teeth; D = Drinking; AL = Applying lipstick; Dr. = Dribbling; LO = Limited opening; PC = Playing clarinet



Symptoms experienced and functional problems

Ten patients with periapical lesion-related IANI in this case series experienced only numbness. A combined experience of numbness and pain was experienced by five patients, two patients had numbness and paraesthesia, and one patient experienced a combination of pain and paraesthesia. Two patients had a mixture of numbness, pain and paraesthesia (Fig. 4). Eight patients were suffering from neuropathic pain (NP), and one patient had intermittent NP (Table 2).

Although nine patients (41%) did not suffer from any functional problems, patients did report problems with eating (27.3%), brushing teeth (18.2%), speech (18.2%), kissing (9.1%), drinking (4.5%), applying lipstick (4.5%) and playing the clarinet (4.5%) (Fig. 5).

Treatment of dental pathology and nerve injury resolution

The dental pathology was treated by extracting the affected teeth alone in 16 (72.7%) cases. One patient had to have endodontic treatment, antibiotics and a tooth extraction. Other treatments included:

- Antibiotics and primary endodontic therapy (one patient)
- Antibiotics and cognitive behavioural therapy (CBT) to manage the symptoms of the nerve injury (one patient)
- Endodontic therapy (two patients).

Since pathology was evident in one case in an edentulous site, this was followed by further assessment for possible metastasis (Table 3).

Patients with complete nerve injury resolution had treatment of their dental pathology in

an average of 1.6 months (range 0.5–3months, SD 1.08) from the diagnosis of the periapical lesion. Those who had partial resolution of their nerve injury had treatment of their dental pathology within an average of 3.8 months (0.25–15 months, SD 5.54) and those with no resolution had treatment with an average of 4.75 months from the diagnosis of periapical lesion (range 0.25–15 months, SD 5.41). These differences were not statistically significant (P >0.05).

Patients with complete return of normal sensation either had the affected tooth extracted (three patients), had a course of antibiotics followed by endodontic treatment (one patient) or antibiotics with CBT (one patient). One of these five patients who showed complete resolution of their IANI was a 42-year-old male. He originally had symptoms of numbness and paraesthesia due to a periapical lesion relating to his 45, for nine days. This resulted in an IANI with symptoms of hyperaesthesia, numbness and paraesthesia affecting 90% of the lower lip, chin and 41–46 teeth. He had problems with eating, brushing teeth and flossing. His periapical lesion was initially treated by a course of metronidazole and root canal treatment (RCT) of the 45. He then also took 15 mg prednisolone immediately on onset of symptoms (initially over five days, which was then reduced over 15 days,), which helped to completely resolve his IANI within six weeks duration. He was then discharged back to his general dental practitioner (GDP).

Another patient who had complete resolution of their IANI was a 45-year-old female. She originally had symptoms relating to her periapical lesion (14 mm by 9 mm), which was associated with the 46, for two weeks. Radiographic imaging indicated that the lesion overlaid the ID canal and there was a loss of cortication, which resulted in numbness and throbbing pain that affected her speech and she kept dribbling. Her lesion and subsequent IANI was treated by endodontic therapy of the 46, followed by extraction. She also took clindamycin for two weeks and had psychiatric support. Her symptoms completely resolved after a year so she was discharged back to her GDP.

The remaining three of the five patients who also had complete resolution of their symptoms only had their affected teeth extracted as treatment. One of these patients (Patient ID IANI 8), who had complete resolution of her IANI by only having their tooth extracted, was 42 years old. She originally had symptoms due to a periapical lesion relating to the furcation and mesial root of her 37 for two weeks. These symptoms included trismus with numbness and paraesthesia within the lower lip, which affected 80% of the extra-oral dermatome and 90% intra-orally. Her affected tooth was extracted and her symptoms resolved within four months. She was then discharged to her GDP.

The other female patient (Patient ID IANI 18) was 47 years old. Symptoms of numbness within her lower lip and chin due to her original periapical lesion of the 37 lasted for two weeks. Once she had her 37 extracted, her IANI resolved within two months. She did not have any functional problems and was discharged to her GDP.

A 41-year-old male (Patient ID IANI 20) who also had complete resolution of his IANI had symptoms relating to a periapical lesion for

Table 3 A summary of the treatments of the dental pathology and trigeminal nerve injuries (TNI), and their resolution. Abbreviations: CBT = Cognitive behavioural therapy; GDP = General dental practitioner; I+D = Irrigation and dressing; RCT = Root canal treatment; XLA = Extraction the tooth under local anaesthesia

Patient ID	Resolution	Duration of periapical infection (months)	Treatment of dental pathology	Treatment for symptoms of nerve injury
IANI 2	Unknown	1.5	XLA 46	None
LNI 1	Unknown	13	Referral to GDP for 46 fill or RCT	None
IANI 3	None	2	XLA 46	None
IANI 4	None	0.25	XLA 37	Pregabalin, Carbamazepine, Nortriptyline
IANI 6	None	15	No dental pathology. Possible metastasis?	None. Investigations included: bone biopsy, positron emission tomography, magnetic resonance imaging negative
IANI 7	None	1	XLA 38	Psychiatric involvement, antidepressants, Versatis (5% lidocaine) patches
IANI 9	None	13	XLA 36	CBT, recommended Pregabalin and beta blocker but refused
IANI 10	None	1.5	XLA 37	None
IANI 12	None	4	XLA 46	CBT
IANI 14	None	4	XLA 45	None
IANI 19	None	2	XLA 37	CBT offered (declined) already under care of psychiatry
IANI 1	Partial	1	XLA 45, 46	None
IANI 5	Partial	15	RCT 46 I+D Abscess	None
IANI 11	Partial	2.5	XLA 36	None
IANI 13	Partial	1.5	Antibiotics, XLA 46 and Exploration, RCT 45	None
IANI 15	90%	0.25	XLA 36	None
IANI 21	Partial	3	XLA 37	None
IANI 8	Complete	2	XLA 37	None
IANI 16	Complete	0.5	Metronidazole, 45 RCT	Prednisolone 15 mg for 5 days reducing over 15 days immediately on onset of symptoms
IANI 17	Complete	0.5	Clindamycin (6 weeks), liaison psychiatry	None
IANI 18	Complete	2	XLA 37	None
IANI 20	Complete	3	XLA 47	None

two months, which included numbness, paraesthesia and electric-shock-like pain within the right lower lip and chin. This radiographic radiolucent lesion of 13.7 mm × 8.2 mm dimensions, overlay the ID canal and there was a loss of cortication. Although the dental pathology was treated by primary endodontic treatment of the 47, this tooth was then extracted. The IANI persisted for four months without any further treatment and the patient was discharged to his GDP.

In cases of permanent nerve injury, the majority (12/17) of patients did not require any symptomatic treatment other than explanation and reassurance. In those with neurogenic discomfort (dysaesthesia, allodynia or neuropathic pain), a combination of therapies was offered including topical Versatis (5% lidocaine) patches to be applied to the affected area, systemic medication including tricyclic antidepressants and anticonvulsants and referral to psychiatry for consideration of CBT to aid in symptom management.

Discussion

This study presents 22 cases of mandibular division TNI caused by periapical lesion seen in a tertiary referral clinic over an eight-year period. The overall incidence of periapical lesion-related TNI in the population is unknown, due to a small number of published reports of this condition. Although this particular cause of nerve injury was infrequently seen in our clinic, the cases may have been referred elsewhere, or managed in primary care.

The most commonly affected teeth in this series were the first molars (11 cases) followed by the second molars (six cases) and second premolars (three cases). To date, the largest published case series reported eight cases of paraesthesia all related to periapical lesion of mandibular premolar teeth.[13] There are many single case reports, however, which report TNI associated with periapical lesion of the mandibular canine, premolars and molars.[15]

The position of the IAN has been estimated in radiological and anatomical studies, which have shown a variable proximity between the IAN and the apices of the mandibular teeth. In a cadaveric study of 40 mandibles, the distance between the IAN and the first molar apices varied between 1–4 mm, whereas the distance was around 1 mm in the second and third molar region.[20] Another cadaveric study of the mandibular premolar region found the position of the IAN to vary from the apices of the premolars to the lower border of the mandible; however, the canal occupied the entire bucco-lingual width of the mandible meaning that the IAN is more susceptible to the effects of an expanding periapical lesion in this region.[13] A recent radiographic study using cone beam computed tomography (CBCT) scanning evaluated the distance of the apices of the first and second premolars and first molar from the mental foramen to be 4.7 mm, 5.7 mm and 6.5 mm respectively. In this study, 4% of root apices were within 3 mm of the mental foramen and there was an anterior loop present in 88% of scans examined.[21] A further study of the distance of the second molar from the IAN canal found that in 54.8% of CBCT scans examined, the distance was ≤3 mm.[22]

The average periapical lesion size in this series was 9 mm × 6.7 mm. Radiographic imaging of the lesions mostly indicated close proximity to the IAN canal or mental foramen. Loss of cortication of the canal was seen in 11 cases. Larger periapical lesions present a greater risk of injury to the IAN both from the neurotoxic products of periapical lesion and from subsequent endodontic treatment, as they reduce the availability of sound bone between the tooth apex and the neurovascular bundle, allowing diffusion of endodontic irrigants and filling materials.[4,7,14]

The patients in this series presented to the nerve injury clinic with a number of symptoms including numbness, paraesthesia and neuropathic pain. Only ten of the 22 patients presented with numbness alone. TNI often presents with neurogenic discomfort, with some studies reporting that up to 70% of patients experience neuropathic pain in combination with numbness and paraesthesia that can interfere with social activities, work and relationships.[23] Indeed, in this study thirteen patients reported significant interference with daily function. Some patients may be misdiagnosed as having pain related to a periapical lesion (inflammatory pain) rather than neuropathic pain (NP), owing to the dentist's familiarity with toothache rather than neuropathic pain conditions. Practitioners should be aware of the possibility of large periapical lesions in close proximity to the IAN or mental foramen causing neurogenic injury. Additional questions should be asked of the patient regarding the presence of other symptoms of neuropathy such as numbness or altered sensation and a chairside examination of trigeminal nerve function may be required.

In this series, only five patients (22.7%) experienced complete resolution of their TNI. The majority of injuries were permanent, although five patients experienced partial resolution of the injury within the average review period of ten months. In those patients with complete resolution, this occurred in an average of 4.7 months following the onset of neuropathy. Other case reports and small case series have reported more favourable results with the majority of nerve injuries resolving following successful endodontic treatment or tooth extraction.[2] This may be due to more prompt diagnosis and treatment of the causative periapical lesion. In our series, patients with complete nerve injury resolution had the dental pathology treated in an average of 1.6 months from the onset of the initial symptoms of the periapical lesion, in comparison to those with no resolution having a delay in treatment of 4.5 months, on average. Although this difference was not statistically significant, this is probably due to the small number of patients in the study. Since KCH is a tertiary care centre, there is usually a delay between the referral from general practice and the patient assessment on our clinic. It is therefore important that general practitioners are aware of the importance of prompt diagnosis and initial management of periapical lesion in primary care.

Due to the small number of published reports of TNIs associated with periapical lesion,[4,6–9] currently no protocol exists on how these patients should be treated for the best chance of resolution of the injury. The majority of patients in our series had the causative tooth extracted and the remainder had primary endodontic treatment carried out in primary care. There was no significant difference in the rates of resolution with tooth removal compared to endodontic treatment. Some authors recommend the use of corticosteroids with high dose non-steroidal anti-inflammatory drugs as immediate management (within one week) of nerve injury to improve sensory recovery.[24] The use of corticosteroids such as dexamethasone has been shown in some animal studies to aid sensory recovery and reduce the incidence of neurogenic discomfort such as dysaesthesia and NP following nerve injury, however, these studies involved deliberate surgical trauma to the mandibular nerve rather than inflammatory injury.[25,26] In addition, the therapeutic value of corticosteroids has not been confirmed in high quality clinical studies.[27] The use of corticosteroids is not advised if the neuropathy has been present for more than a week, in which case high

dose non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen 600–800 mg three times daily, in combination with treatment of the underlying pathology is required.[24]

In patients who experience permanent nerve injury, the sequelae of permanent neurogenic discomfort or NP is often difficult to manage. Neuropathic pain is often refractory to multiple topical and systemic medications, with randomised controlled trials of pharmacotherapy showing that less than half of patients experience significant pain relief.[28,29] A management algorithm proposed by Allegri *et al.* for the management of localised neuropathic pain, favours topical medicaments such as lidocaine plasters, capsaicin patches and botulinum toxin as first line management, with the addition of a systemic medication such as gabapentin, pregabalin, duloxetine, venlafaxine or amitriptyline in non-responders.[28] It is likely that these patients will require long-term pain management on a specialist orofacial pain clinic.

While prompt recognition and management of TNI remains the most effective way to prevent permanent neuropathy, early treatment and prevention of periapical lesion by regular dental care, is the most important way to prevent TNI from occurring in the first place.

Conclusion

Injury to the mandibular division of the trigeminal nerve as a sequelae of dental periapical lesion is rarely reported, however, it is important that dentists are aware of this potentially serious complication of untreated periapical abscesses in mandibular teeth. This has highlighted patients presenting with common characteristics including neuropathic pain, numbness and paraesthesia. Patients presenting with neuropathy affecting the lower lip and chin should be investigated for dental periapical lesion and treatment initiated promptly to give the best chance of sensory recovery. Management strategies should begin with an urgent referral to a specialist endodontist which should be considered if the patient wishes to retain the tooth. Alternatively, extraction of the causative tooth should be carried out immediately and the patient should be regularly reviewed until sensory recovery has taken place. Patients with permanent neuropathy persisting after three months, particularly if neurogenic discomfort is present, should be referred onto tertiary nerve injury and pain management specialists.

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