REVIEW ARTICLE

Emboli cutis medicamentosa after root canal treatment: a review

Beena J Dev[1], Devendra Chaudhary[2], Shweta Sharma[3], Harmeet Singh[3]

Abstract

Calcium hydroxide used in RCT when pushed beyond apex through pressure syringe system causes tissue necrosis and other hazardous effects of adjacent supporting structures. Similar conditions were also observed in the injection of various drugs including NSAIDS, corticosteroids, antibacterial agent, chlorphineramine maleate etc. In 1924 first case with similar symptoms was reported after the injection of bismuth for syphilis in the gluteal area by Freudenthal and named it as Nicolau syndrome (Emboli cutis medicamentosa). The aim of the review article is to bring out the thorough knowledge in understanding and managing the adverse effects and consequences of Nicolau syndrome in root canal treatment.

Keywords:

Calcium hydroxide, Emboli cutis medicamentosa, Nicolau syndrome, Skin necrosis.

INTRODUCTION

Calcium hydroxide has been used successfully in root canal therapy for many years.

However, it can cause Nicolaus syndrome, if it is inadvertently displaced into surrounding vital structures, resulting in thrombosis if displaced into blood vessel, damaging connective tissue, and causing skin necrosis[1].

The case of the adverse reaction to intra canal medicament calcium hydroxide was published in 2000.

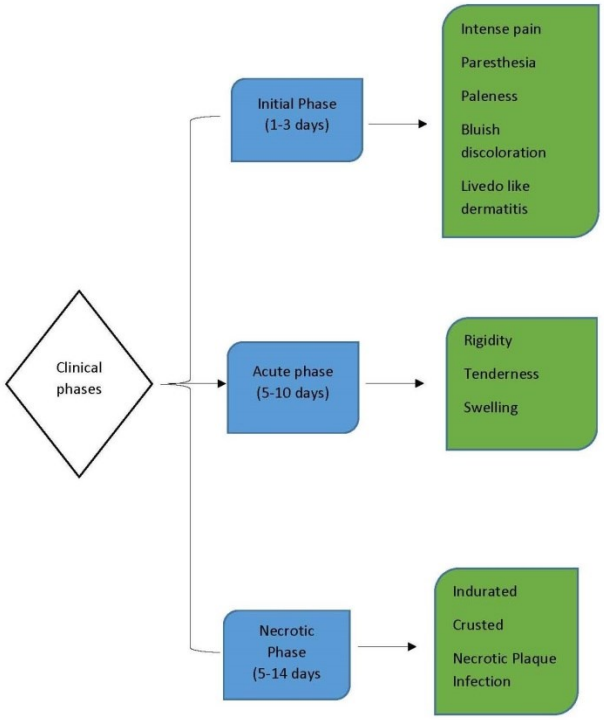
Although it has been considered as a safe agent[2], a few reports dealt with the negative side effects of CaOH2 including bone necrosis and continuing inflammatory response in repaired mechanical perforations, the neurotoxic effect of root canal sealers, cytotoxicity on cell cultures, damaged epithelium with or without a cellular atypia when applied on hamster cheek pouches and cellular damage following early CaOH2 dressing of avulsed teeth[3]. Some authors have reported deleterious effects if the material is extruded under a high pressure during endodontic treatment[4].

1 Post graduate student
2. Principal & Head of the Department
3. Professor
Department of Conservative Dentistry and Endodontics,
Corresponding Author:
Beena J Dev, post graduate student
Ph. 9747446130, Email:drbeenajdev@gamil.com,
Department of Conservative Dentistry and Endodontics,
Maharaja Ganga Singh Dental College & Research Centre,
Sri Ganganagar, Rajasthan.

Calcium hydroxide paste can result in necrosis and degenerative changes in animal models by intense inflammatory responses. Its pH is around 12; it has very low solubility at body temperature and will remain in the tissue for considerable time and therefore cannot be considered biocompatible[4].

CLINICAL FEATURES

Clinical features of NS are presented by three typical phases[7],



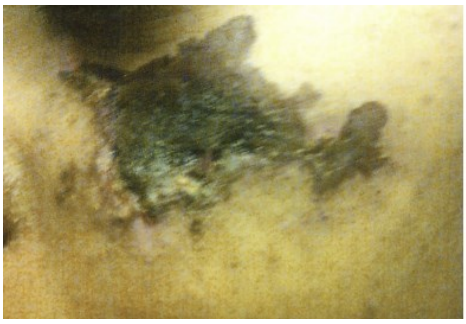


Fig.1 Skin necrosis in the left infraorbital area after 2 weeks following endodontic treatment of tooth 14[1]

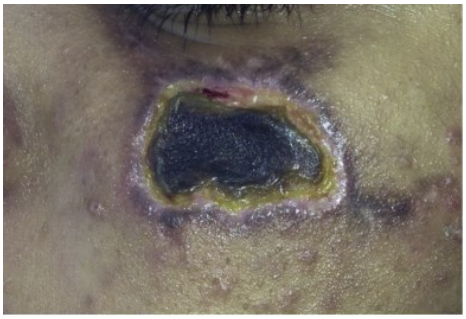


Fig.2 The appearance of the skin after endodontic treatment[1]

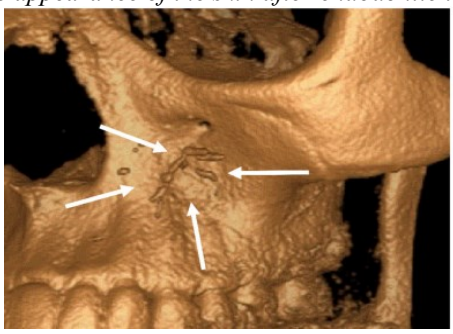


Fig.3 Three-dimensional construction of the cone-beam computed tomographic scan showing a contrast material in the route of the infraorbital artery[1]

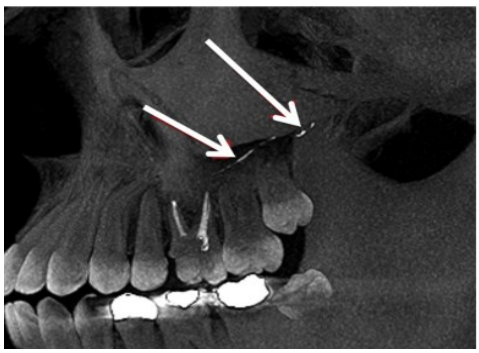


Fig.4 CBCT image showing the presence of opaque material in the root of the posterior superior alveolar artery[1].

PATHOGENESIS

Pathogenesis of Nicolau syndrome is not clear but a vascular origin is the most reasonable hypothesis. Acute vasospasm, inflammation of arteries and thromboembolic occlusion of arteriole are the key mechanisms[5]. The leakage of around artery and neural space has been suggested as cause of intense pain. Moreover, sympathetic nerve stimulation and vasospasm lead to ischemic change and skin necrosis. Unintended intravascular injection of drugs also has been proposed as causing inflammation or thromboembolic occlusion of the arterioles. These may cause arterial intimal necrosis, destruct the arterial membrane and induced subsequently cutaneous necrosis[6].

NICOLAU SYNDROME AFTER ENDODONTIC TREATMENT

The reaction inadvertent calcium hydroxide extrusion into the soft tissue or blood vessels can vary from a simple inflammatory reaction to serious damage. In some cases where the canal bleed profusely during the root canal therapy, the bleeding might be explained by the proximity of the apices of the root to vascular structure. Immediately after the injection of intra canal calcium hydroxide, pain and ischemia in skin extra orally occur[7].

BRIEF REVIEW OF REPORTED CASE

- De Bruyne et al. reported gingival necrosis after extrusion of Ca $(OH)_2$ paste (La Maison Dentaire, Balzers, Switzerland) through a root perforation of maxillary central incisor[3].

  They treated the necrotic gingival zone with rinses of hydrogen peroxide 3% and chlorhexidine 2% and daily application (BID) of chlorhexidine di gluconate 10 mg/g gel and concluded that as long as Ca $(OH)_2$ does not come into direct contact with surrounding soft tissues, problems either do not occur or are of a mild transient nature[4].

- Sharma et al. described two severe cases of iatrogenic extrusion of $Ca(OH)_2$ Nordiska Dental, Angelholm, Sweden) on upper and lower molar tooth causing extensive necrosis in the scalp, skin, and mucosa in the first case and infraorbital nerve paraesthesia and palatal mucosal necrosis in second case[8]. Both patients reported severe pain immediately after $Ca(OH)_2$

  Injection. A computerized tomography (CT) scan with 3-dimensional (3-D) reconstruction in second case confirmed the intravascular distribution of the material. Authors explained that an exposure of Ca $(OH)_2$ to blood resulted in crystalline precipitation and the consequent ischemic tissue necrosis. Their patient underwent thrombolytic, steroid and antibiotic therapies to maintain tissue reperfusion, limit inflammatory responses, and prevent infections, respectively[4].

- Lindgren et al. reported a case of $Ca(OH)_2$ (Calasepts, Nordiska Dental, Angelholm, Sweden) injection into the root of a lower second molar, the inferior alveolar and farther maxillary and external carotid artery, causing necrosis of the ear lobe and superficial necrosis of the cheek skin[9]. When the paste was applied with a syringe in the distal canal, the patient experienced severe local pain. Angiogram showed a number of vascular occlusions in the right external carotid artery branches[4].

- Bramante et al. reported a case of $Ca(OH)_2$ therapy for root resorption control in a maxillary lateral incisor[10]. Three days after $Ca(OH)_2$ placement (Biodinâmica, Ibiporã, PR, Brazil), an irregular zone of necrosis was observed on buccal mucosa. Careful curettage was performed around the region for removal of necrotic tissue and extruded $Ca(OH)_2$; healing was observed at a 15-day follow-up[4].

- Ahlgren et al. showed paraesthesia and changes in surrounding bone after a mishap with $Ca(OH)_2$ extrusion (Calasept Nordiska Dental, Angelholm, Sweden) through the apex of a mandibular premolar tooth[11]. They surgically excavated the excessive paste from the spongious bone and after six months, patient was symptom free[4].

Four cases of seven patients reported moderate to severe pain immediately after $Ca(OH)_2$ injection. Blurred vision occurred in two cases, anesthesia or paresthesia in four, swelling in three, facial palsy or weakness in two, and mucosal ulceration in six cases. In two cases, angiogram or computerized tomography scanning revealed vascular obstruction. In five of the above cases, pressure syringe system was the culprit; however, two cases did not use a pressure syringe system for the application of $Ca(OH)_2$ [4]

HISTOPATHOLOGY

The tissue sections were stained with H & E and examined by light microscopy for histopathological changes. Histopathological analysis revealed areas of degenerative changes and necrosis in the tissues in direct contact with the injected paste. Granulomatous tissues containing numerous giant cells and macrophages with engulfed particles in their cytoplasm were also observed in contact with the extruded material. The aggregation of macrophages and giant cells around $Ca(OH)_2$ particles in the absence of other inflammatory cells such as neutrophils, lymphocytes, and plasma cells suggests that the paste induced a typical foreign body reaction[4].

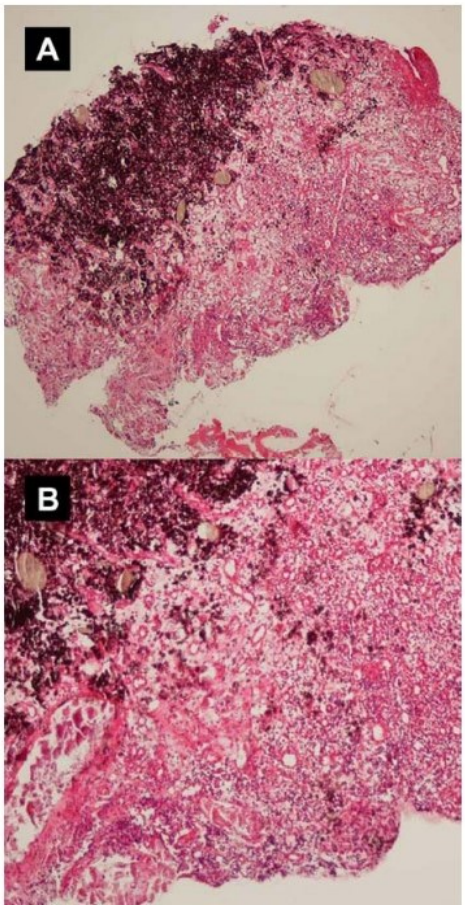


Fig. 5 Photomicrographs of biopsy specimen showing foreign material surrounded by necrotic tissues

DIAGNOSIS

Clinical Diagnosis of Nicolau Syndrome is done mainly by:

- Skin biopsy shows necrotic changes caused by ischemia[12].
- Ultra-sonography of the skin
- Magnetic resonance imaging help in delineating the extent of damage[13].

TREATMENT

There is no consensus of treatment of Nicolau syndrome so far. However we suggest the treatment of Nicolau syndrome step by step as the three phases. Phasic treatments depend on the extent of the necrotic lesion and ranges from medication to surgical debridement[6].

Initial phase: Because of severe pain, conservative pain control with analgesics and dressings is usually recommended.

And differential diagnosis is most important in the initial phase. Ice pack application increases the acute focal vasospasm and can aggravate the disaster14, 15. Until cellulitis of affected site is ruled out, systemic antibiotics are suggested. After any signs of cellulitis ruled out such as fever, elevated white blood cell count, C-reactive protein and erythrocyte sedimentation rate, prophylactic antibiotics might be useful6.

Acute phase: Hypothesis of vascular origin and inflammatory sequelae is most reasonable. For this reason systemic steroid and anticoagulant agent are usually used[16, 17]. Hyperbaric oxygen treatment was given to patient with the assumption of micro arterial thrombi as well as heparin and pentoxyphilline[18]. Subcutaneous injection of heparin 5000 to 10000 U b.i.d.[17] and intravenous infusion of betamethasone diphosphate 24 mg/d induce improving symptom within 2d. Patient responses rapidly to methylprednisolone 1g IV q.d. or dexamethasone 32 mg intravenous injection for three days and pentoxifylline 400 mg PO t.i.d.. Warm intermittent compression is also recommended[6].Necrotic phase: The patients with NS undergo surgical debridement of the affected skin, subcutaneous tissue and muscle in case of clinical and radiographic evidence of tissue necrosis6. And after the ulcerative necrotic lesion was filled with healthy granulation, split-thickness skin graft or reconstructive surgery were performed. Finally the wound healed well and uneventfully with atrophic skin scar or wound contraction19.

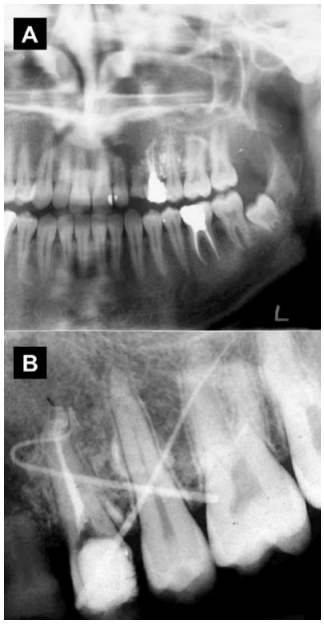


Fig.6a Radiographs showing radiopaque CaOH2 paste surrounding root of the premolars[4] Fig.6b, Radiograph showing the tracing of gingival detachment by gutta-percha[4]

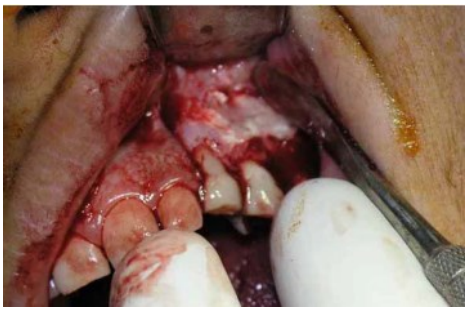


Fig.7 Discolored cortex due to an ischemia and decreased blood supply[4].

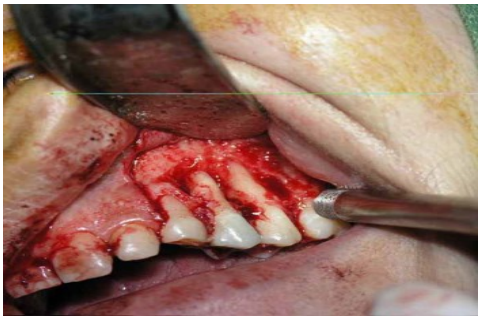


Fig.8 Removal of foreign material and necrotic tissues around the roots[4].

CONCLUSION

Nicolau syndrome is rarely occurring side effect of injectable drugs. Post signs and symptoms of injectable drugs should be considered as wake-up call in nicolau syndrome, so that the complications can be treated at the earliest. Proper and efficient health care is mandatory from the licensed professionals for the awareness.

REFERENCE

1. Fatima Al-sheeb BDS et al: Nicolau syndrome after Endodontic Treatment: A Case Report. Journal of Endodontics 2022 Feb.
2. Lindgren P, Eriksson KF, Ringberg A: Severe facial ischemia after endodontic treatment. J Oral Maxillofac Surg. 2002; 60(5):576-9.
3. De Bruyne MA, De Moor RJ, Raes FM: Necrosis of the gingiva caused by calcium hydroxide: a case report. Int Endod J. 2000; 33(1):67-71.
4. Arash Shahravan et al: Oveextension of Nonsetting Calcium Hydroxide in Endodontic Treatment: Literature Review and Case Report. Iranian Endodontic Journal 2012;7(2):102-108
5. Luton K, Garcia C, Poletti E, Koester G: Nicolau Syndrome: three cases and review. Int J Dermatol 2006.
6. Kwang-Kyoun Kim et al: Nicolau syndrome A Literature Review. World J Dermatol 2015; 4(2): 103-107.

7. Dr.Ruchi paharia : Nicolau syndrome saraswati dental college and hospital 26 may 2023.
8. 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.
9. Lindgren P, Eriksson KF, Ringberg A: Severe facial ischemia after endodontic treatment. J Oral Maxillofac Surg. 2002
10. Bramante CM, Luna-Cruz SM, Sipert CR, Bernadineli N, Garcia RB, Moraes IG, Vasconcelos BC:Alveolar mucosa necrosis induced by utilisation of calcium hydroxide as root canal dressing. int dent journal. 2008
11. 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
12. J Cutan Aesthet surg : nicolau syndrome: an iatrogenic cutaneous necrosis. Journal of cutaneous and esthetic surgery 2009 july.
13. Geukens J, Rabe E, Bieber T: Emboli cutis medicamentosa of the foot after sclerotherapy. Eur J Dermatol 1999.
14. Cherasse A, Kahn MF, Mistrih R, Maillard H, Strauss J, Tavernier C. Nicolau's syndrome after local glucocorticoid injection. Joint Bone Spine 2003; 70: 390-392 [PMID: 14563471 DOI: 10.1016/S1297-319X(03)00137-4]
15. Stricker BH, van Kasteren BJ. Diclofenac-induced isolated myonecrosis and the Nicolau syndrome. Ann Intern Med 1992; 117: 1058 [PMID: 1443979]
16. Hamilton B, Fowler P, Galloway H, Popovic N. Nicolau syndrome in an athlete following intra-muscular diclofenac injection. Acta Orthop Belg 2008; 74: 860-864 [PMID: 19205337]
17. Luton K, Garcia C, Poletti E, Koester G. Nicolau Syndrome: three cases and review. Int J Dermatol 2006; 45: 1326-1328 [PMID: 17076716 DOI: 10.1111/j.1365-4632.2006.02674.x]
18. Ocak S, Ekici B, Cam H, Taştan Y. Nicolau syndrome after intramuscular benzathine penicillin treatment. Pediatr Infect Dis J 2006; 25: 749 [PMID: 16874179]
19. Nischal K, Basavaraj H, Swaroop M, Agrawal D, Sathyanarayana B, Umashankar N. Nicolau syndrome: an iatrogenic cutaneous necrosis. J Cutan Aesthet Surg 2009; 2: 92-95 [PMID: 20808597]