

SELF-CURE ACRYLIC RESIN SUSPECTED AS A CAUSATIVE AGENT FOR MANDIBULAR INTRA-OSSEOUS CARCINOMA: A CASE REPORT

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ABSTRACT

Primary Intraosseous Carcinoma (PIOC) is regarded as a rare malignant neoplasm of the jaws which shows locally aggressive behavior with poor prognosis. Through knowledge of the various features of PIOC such as clinical, radiographic and histopathologic, not only allows for accurate and early diagnosis of the lesion but also helps in an early and appropriate treatment with better prognosis. This article reports a case presenting with typical features of PIOC due to suspected use of cold cure acrylic resin which was allowed to polymerize inside the oral cavity in contact with soft and hard tissues. Lack of awareness about the cytotoxic and genotoxic potential of MMA needs to be highlighted so that intra-oral curing of MMA should be avoided.

INTRODUCTION

Primary Intraosseous Carcinoma (PIOC) is a rare tumour which has been infrequently reported in the literature. PIOC of the jaw has been defined by WHO as a “squamous cell carcinoma arising within the jaw, having no initial connection with the oral mucosa and presumably developing from residues of the odontogenic epithelium.” [1].

PIOC was also subclassified further into a) carcinoma arising *de novo*, b) carcinomas arising from ameloblastoma, c) carcinomas arising from the odontogenic cyst. There are different considerations regarding its origin. The source of cells for the origin of PIOC may come from the reduced enamel epithelium (REE), the epithelial rests of Malassez and cell rests of Serres lying inside gingiva or within the bone, which can

be initiated *de novo* or by some cytotoxic chemicals which are mainly used in dentistry [2,3].

In daily dental practice, acrylic based resins are frequently used for denture bases and denture liners, temporary crowns and even orthodontic appliances [4]. In the oral cavity, functional efficiency and properties of applied acrylic resins depend upon the methodology and conditions applied for curing/polymerization of acrylic and also extrinsic factors of environment in which material is placed [5,6]. Interactions of acrylic resin present in oral cavity with multiple factors such as saliva, oral microflora and mastication leads to release of residual monomer (RM) in the oral cavity. This residual monomer is often associated with inflammatory, allergic reactions and even irritation of oral mucosa [7,8].

This article reports a case presenting with typical features of PIOC due to suspected use of cold cure acrylic resin which was allowed to polymerize inside the oral cavity in contact with soft and hard tissues. The discussion

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highlights how residual methylmethacrylate monomer can act as cytotoxic agent, so that dentists become aware that residual monomer which leaches out from cold cure acrylic used intraorally can lead to development of PIOC.

CASE REPORT

A 50-year-old Indian male patient reported to a general dental practitioner in New Delhi, India, with chief complaint of chronic low intensity pain in the anterior mandible since 9-10 months, and was referred to us. Past dental history revealed that the patient had mobile mandibular anterior teeth that were splinted together by placing cold cure acrylic (chemically cured / self-cure acrylic) intraorally and allowing it to cure in the mouth directly, by a quack somewhere on the outskirts of Delhi. This happened 1 year prior to the onset of pain. Three months prior to the patient reporting to us, all anterior teeth that were splinted with cold cure acrylic were spontaneously exfoliated. Mucosa healed but occasional nagging pain continued to be present. On intraoral examination, one small ulcer (less than 1cm) was seen on the lingual aspect of mandibular ridge in the region of 42; this ulcer was non-indurated, not everted, with moderate inflammation surrounding it, and was painful on palpation. Otherwise the ridge appeared to be healthy. There was no initial clinical suspicion of malignancy when examining the oral mucosa or overlying skin. On extraoral examination, right submandibular lymph nodes were palpable but not fixed.

An orthopantomogram (Figure1) showed a destructive diffuse radiolucent lesion within the anterior mandible, with ill-defined irregular borders extended from 33 to 43 (FDI). Multiple fragile soft tissue bits were curetted surgically from the lesion site after raising a mucosal flap. The specimens were preserved in 10% formalin. The flap tended to be fragile and easily tearable. Healing was uneventful and uncomplicated, amoxicillin with clavulanic acid was used as antibiotic, sutures

removed after 7 days. The small ulcer noticed at initial examination also healed.

Microscopic examination of hematoxylin-and-eosin (H&E) stained sections showed neoplastic squamous epithelial proliferation in form of cords and islands with presence of keratin pearls and areas of necrosis. The malignant epithelial cells showed prominent features such as cellular and nuclear pleomorphism along with hyperchromatism. The superficial epithelium, where visualised, did not appear to have undergone neoplastic change. Serial sections were obtained to rule out ameloblastoma or odontogenic keratocyst (Figure 2a,2b,2c,2d). Hence, histopathological diagnosis of PIOC of the mandible was made. The patient was referred to AIIMS, Delhi, India for further treatment.

DISCUSSION

Pindborg coined the term PIOC in 1971. [9] PIOC was subclassified into carcinoma arising *de novo*, carcinomas arising from ameloblastoma and carcinomas arising from odontogenic cyst. Later intraosseous mucoepidermoid carcinomas were added as a fourth type of PIOC. PIOC has been classified by WHO as odontogenic carcinoma [1].

Mustoe's and Waldron classification [3] for PIOC is widely accepted and frequently cited according to which PIOC may originate from different sources as follows:

- Type 1: PIOC ex-odontogenic cyst
- Type 2A: Malignant ameloblastoma
- Type 2B: Ameloblastic carcinoma arising *de novo*, ex-ameloblastoma or ex-odontogenic cyst
- Type 3: PIOC arising *de novo*:
 - (a) Keratinizing type
 - (b) Non-keratinizing type
- Type 4: Intraosseous mucoepidermoid carcinoma

Figure 1. Orthopantomogram showing diffuse radiolucent lesion within anterior mandible with ill-defined irregular borders extending from 33 to 43 (FDI)



Figure 2a. H&E section of epithelium (10X), Figure 2b. H&E section of epithelium (40X), Figure 2c. H&E section of scc islands (10X), Figure 2d. H&E section of scc islands (40X)

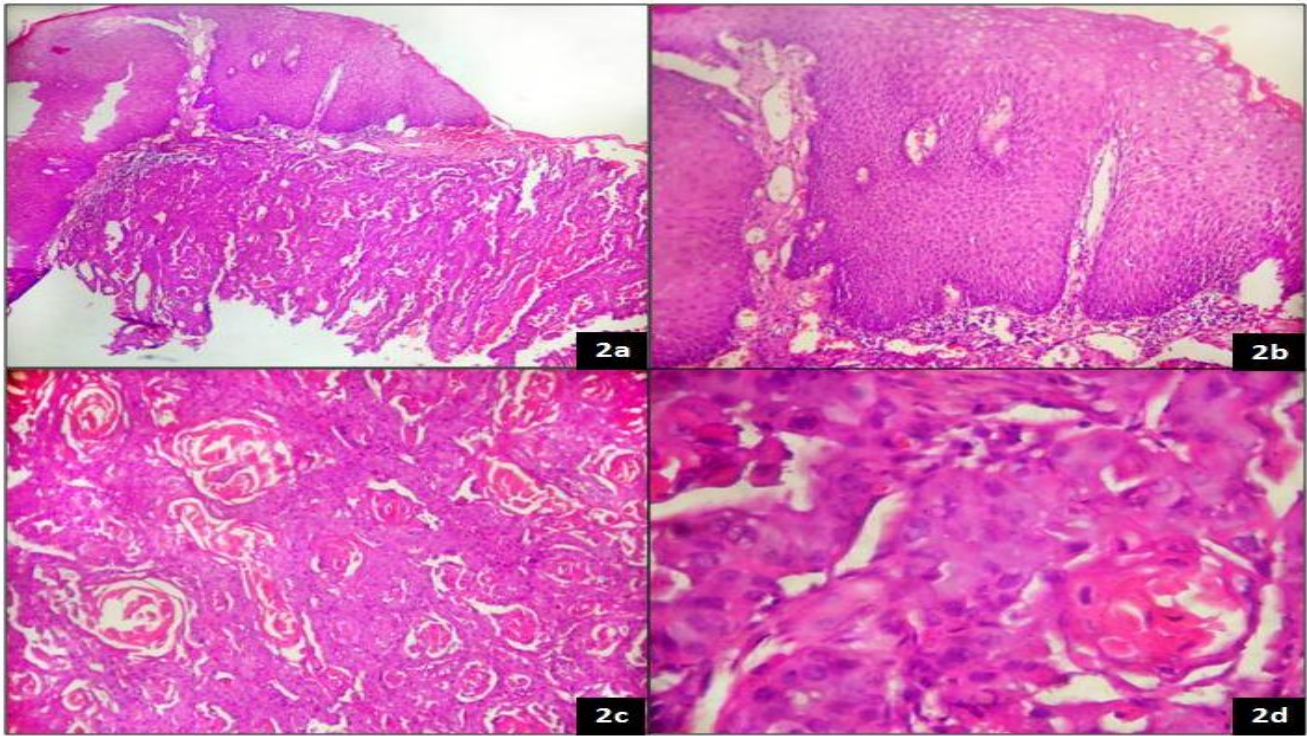


Figure 3 a,b. Lower Removable partial denture splinted to adjacent teeth using cold cure acrylic done by road side dental quack



According to WHO classification, PIOC can develop from odontogenic epithelium or pre-existing odontogenic cyst [1]. According to Lucas, PIOC could arise from odontogenic rests or from epithelium entrapped within deeper structures during fusion of various facial processes [10]. The source of epithelium is necessary for PIOC to develop. The source of epithelium may be derived from remnants of Hertwig's epithelial root sheath, cell rest of Serra's, remnants of enamel organ, odontogenic tumors/cyst and even epithelium entrapped between fusion of facial processes(3). These epithelial remnants proliferate and transform into odontogenic

carcinoma, a process that may be potentially triggered by an inflammatory process [11].

The data analysis of the world literature of PIOC reveals that the mean age of the patients of PIOC is 52.3 years, with the age ranging from 4 years to 81 years. 65% of the patients were in the sixth or seventh decades of life (2). It is most commonly located in the mandible with a predilection for the posterior region of mandible. In maxilla lesions are mostly located in anterior region and often cross midline [12, 13]. The tumour affects men more often than women, with a male: female ratio ranging from 1.5 - 3.5:1 [14].

Common symptoms of patients with PIOC range from pain and swelling to complete absence of subjective symptoms in early phases; lesions may be coincidentally discovered on routine dental radiographs. There is progressive swelling of jaws and loosening of teeth. Accelerated growth with swelling, trismus, sensory disturbances such as paraesthesia and numbness can also occur due to compression of inferior alveolar nerve in advanced cases [15]. Spread to regional lymph nodes has been recorded in several cases. Three specific criteria may be present to define a lesion in the jaws as PIOC (15, 16): 1) Histological confirmation of squamous cell carcinoma, 2) Absence of ulcer on the overlying mucosa, and 3) Absence of a distant primary tumor at the time of diagnosis and at least 6 months during the follow-up period. Acrylic is used widely for complete and partial denture fabrication in dental practice, though the use of autopolymerised acrylic resins is absolutely not recommended for long-term insertion in the mouth. Unqualified practitioners of dentistry (quacks) often insert cold cure acrylic resin and allow it polymerize intraorally, to splint mobile teeth and provide immediate 'dentures' and crowns at low cost for economically weak patients (Figure 3a,3b). Such a procedure is not advocated due to the presence of higher level of residual free monomer in the autopolymerised or chemically cured acrylic resins [17].

Acrylic resin is composed of polymethyl methacrylate (PMMA) along with activator & initiator depending upon type of polymerization. Polymerization of a PMMA-based dental resin is an addition reaction that requires the activation of an initiator, such as benzoyl peroxide, which can then be decomposed by many different means, such as heat (heat polymerization) or microwave polymerization or by addition of a chemical activator, such as dimethyl-p-toluidine, at moderate temperatures (autopolymerization), or light-activated polymerization [17-18]. The process of polymerization (also known as curing process) converts methyl methacrylate (MMA) to PMMA. During this process, all the monomers are not converted into PMMA and some unreacted monomers are left which are called residual monomers (RM) [18].

The concentration of the monomers varies depending on the methods and the conditions of polymerization [19]. RM which is left in the polymer might leach into surrounding media such as water as well as human or artificial saliva [5]. Various degrees of in vivo allergic responses and in vitro cytotoxicity reactions are caused by leached RM (6-8). Leaching of the residual monomer may influence biocompatibility of denture material. Also, the possible toxic substances pre-leached include formaldehyde, methacrylic acid, plasticisers, organic additives, benzoic acid, and biphenyl and phenyl benzoate [20]. The exposure of the tissues to the resin materials in general occurs both directly and indirectly.

Direct tissue-material contact exposure occurs in tissues, such as oral mucosa, skin, opened dental pulp and blood cells. Indirect resin-tissue contact occurs when the tissue is exposed to components which are released from the acrylic resins into the local environment, such as chemicals released into the saliva [21]. Products of acrylic based resins biodegradation have been suspected of being a contributing factor for local chemical irritation, sensibilization, pain, mucosal inflammation or ulceration, labial edema, oral diseases such as a burning mouth syndrome and denture stomatitis, even systemic allergic reactions due to acrylic resin. [22]. The review of the studies available in English literature shows that heat-polymerized resins showed lower cytotoxic effects as compared to autopolymerizing denture base acrylic resins (self-cure acrylic resins) and light-polymerized or dual-polymerized reline resins. Bayraktar et al [23]. Revealed that auto polymerized resins eluted considerably more substances compared to the heat and microwave-polymerized resins which are in accordance with findings of Cimpan et al [24]. Who also studied the effect of microwave heating on the residual monomer level of an auto polymerized resin used in the repair of prostheses. The cytotoxic effects of chemically-activated, heat-activated, and microwave-activated acrylic resins on gingival fibroblasts were also reported by Sheridan et al [25]. who observed that, among the tested materials, the greatest cytotoxic effect was produced by chemically activated acrylic resins.

Many studies are available in literature focusing on the cytotoxicity of leached MMA. Different test systems have been employed to assess the cytotoxicity of RM but all the studies indicate changes in cell structures such as integrity of cell membrane and various cell functions like enzyme activities or synthesis of macromolecules. The adverse effect of MMA is thought to be caused by two ways:

- a) Direct toxicity from residual or released MMA
- b) Oxidative stress caused by free radicals released during process of polymerization [26]

Schweikl H et al [27] and Lee DH et al [28] in 2006 conducted studies which have shown that RMs reduce the levels of the glutathione radical (GSH). GSH protects cell structures from damage caused by reactive oxygen species (ROS), which consequently contributes significantly to toxicity as a corresponding increase in ROS levels can activate pathways which lead to apoptosis or programmed cell death of cells. Arossi et al in 2009 [29] indicated that monomers of acrylic resins induce toxic genetic events and that mitotic recombination is the main mechanism of action for genetic changes.

In the present case report use of chemically cured acrylic resin for splinting anterior mobile teeth by quack might have caused release of large amount of residual monomer which exerted its cytotoxic and genotoxic effect leading to intra-osseous carcinoma of the mandible.



CONCLUSION

It is common practice of road side dental quacks to use autopolymerised acrylic resin intraorally as material for filling teeth, material to splint teeth and even to

convert removable partial denture to fixed in oral cavity. But lack of awareness about the cytotoxic and genotoxic potential of MMA needs to be highlighted so that intra use of MMA should be avoided.

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