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REVIEW

Hard palate perforation in cocaine abusers: a systematic review

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Abstract Cocaine abuse has increased in the past decade, with a rise in the reported cases of midpalatine perforations produced as a result. The vasoconstrictive and caustic effect of the drug can produce direct irritation and ischemia of the nasal and palatine mucosa, leading over the long term to the creation of an oronasal perforation secondary to maxillary bone destruction. The present study offers a systematic review of all the clinical cases of necrotic nasopalatine perforations attributed to inhaled cocaine documented in the PubMed literature database. The main clinical characteristics of the disorder and its different management options are examined. Likewise, emphasis is placed on the importance of a correct differential diagnosis with respect to other conditions also characterized by midfacial necrotic destruction. Of the 36 cases included in the study, 21 corresponded to females and 15 to males. Most of the lesions were located in the hard palate (77.7%) with only 5.5% being found in the soft palate. Combined hard and soft palate presentations in turn accounted for 16.6% of the cases. The mean diameter of the perforation was 19.32 ± 16.94 mm (95%CI: 11.81–26.83). The most frequent clinical manifestation was rhinolalia together with the regurgitation of solid food and liquids through the nares. Management consists of a combination of antibiotics, analgesics, prostheses (obturators), and surgical reconstructions of the defect.

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Introduction

In the last decade, drug abuse, including cocaine abuse, has increased considerably—Spain being one of the countries where the increase has been most notorious in relation to population size [1]. This situation in turn has increased the reports of cardiovascular, neurological, respiratory and gastrointestinal complications, and of destructive orofacial lesions [2].

Direct contact of inhaled (snorted) cocaine with the nasal mucosa can cause congestion, epistaxis, erosion, and finally destruction of the nasal septum over the long term. There have been descriptions of damage caused by direct application of the drug to the oral mucosa, including gingival recession, erythema, and even bone sequestration. These lesions can be produced by the potent vasoconstrictive and ischemia-inducing effect of cocaine, as well as by caustic action of the drug upon the mucosa [3, 4]. Likewise, a range of midfacial destructive lesions have been documented as a consequence of cocaine abuse, including perforation of the nasal septum, destruction of the lateral wall of the nasal cavities, and perforation with necrosis of the hard palate. The diagnosis is based on clinical and the radiological findings and requires identification of the lesions in at least two of these locations. There have been few reports in the literature of palatal perforation resulting in an oronasal fistula. The differential diagnosis must be established with traumatisms, neoplasms, infections, and autoimmune processes that affect this zone, along with processes of a reactive nature [5, 6].

The present study offers a systematic review of the literature on necrotic palatine perforations due to cocaine abuse, including a proposal to identify their main clinical characteristics.

Search method

A PubMed search was made of all the articles related to perforation of the palate due to cocaine abuse. The following key words were used (MeSH): *cocaine abuse*/*cocaine adverse effects*, in combination with: *palatal perforation* (27/12 documents), *palatal necrosis* (20/8 documents), *oronasal fistula* (6/1 documents), and *midfacial lesion* (4/0 documents), yielding a total of 78 articles. On crossing palatal perforation necrosis with cocaine, we obtained a total of 251 articles. A selection was made of those that met the inclusion criteria. There were no restrictions regarding the year or journal, though the search was limited to publications in English. The only exception was an article published in a Spanish language journal [7], which nevertheless was also available in English. Another inclusion criteria was the well-documented clinical description of one or more cases of complete perforation of the palate due to prolonged intranasal cocaine abuse. Vilela [8] described a clinical case (involving a 34-year-old woman) which we have not included as a palatine perforation, in which multiple oronasal fistulas were observed in the vestibular fundus and upper gingiva.

The search was completed with a review of the references of the selected articles in order to identify additional studies not found in the initial literature search.

A final total of 27 articles were compiled, describing 36 clinical cases [2, 3, 5, 7, 9–31] (Table 1).

Results

Of the 36 documented cases of palatine perforation in cocaine abusers, 15 corresponded to males (41.66%) and 21 to females (58.33%). In all cases the age of the patients was reported, though in six patients, this information was stated as the joint mean and standard deviation (38.5 ± 6.19 years) [28]. The mean age of the rest of the patients was 38.87 ± 9.83 years (n = 30; range 25–64 years), with a 95% confidence interval (95%CI) of 35.19–42.54 years.

The main complaints for which the patients sought medical help were a nasal tone caused by the defect (rhinolalia) alone in four cases; the regurgitation of food towards the nasal passages when swallowing in six cases and both rhinolalia and regurgitation in 12 cases. Other clinical manifestations were nasopharyngeal infection in eight cases and signs such as sinusitis, facial swelling, nasal crusts, epistaxis, nose congestion, and fever. The reported symptoms also comprised lack of sensitivity sensation, anosmia, pain in the nasal passages, headache, and halitosis (Figs. 1 and 2).

The principal location of the lesion was solely in the hard palate in 28 cases, both in the hard and soft palate in six cases and only in the soft palate in two cases. Destruction of the nasal septum and/or nasal walls was seen in 26 articles.

The major diameter of the palatine perforation was documented in 22 cases, with a mean of 19.32 ± 16.94 mm (95%CI = 11.81–26.83; range 2–70 mm).

Regarding the treatment of these patients, antibiotics were prescribed in nine cases either alone or with surgery (four cases), while an obturating prosthesis was placed in four cases. Surgery involving different techniques was performed in 18 cases, with the placement of an obturator (alone or after surgical failure) in 12 patients.

In 11 cases, antibiotics were initially administered; in six of these cases, such treatment was combined with corticoids, analgesics, or surgical debridement, while in the remaining five cases treatment was completed with the placement of an obturator or with surgical reconstruction of the defect.

Eleven cases received a removable obturating prosthesis—in two cases after the failure of surgical reconstruction.

In 15 patients, surgical repair of the fistula was carried out based on a series of techniques. In two of these individuals, previous obturator placement had been non-satisfactory. Four articles made no mention of the treatment provided.

Discussion

Cocaine hydrochloride is an alkaloid widely used due to its psychoactive properties, acting as a stimulant, affording relief from fatigue, and reducing appetite. Cocaine can be used by placing it in contact with the mucosal membranes (snorted), injected intravenously, or smoked in the form of *crack* [32].

Cocaine is absorbed through the mucosal membrane, giving rise to systemic effects. It acts upon the central nervous system via an indirect sympathomimetic mechanism of action by facilitating catecholamine neurotransmission, increasing the levels of norepinephrine and reducing its reuptake and also increasing the levels of dopamine and serotonin at the synaptic level. The drug induces effects such as tachycardia, mydriasis, and hyperthermia [33]. It enhances alertness and can favor repetitive behavior and generate a sensation of euphoria. At a local level, it induces anesthesia and exerts vasoconstrictive action. The half-life of cocaine is about 1.5 h, while the drug is transformed by

Table 1 Review of cases of cocaine-induced palatine perforation and their main clinical characteristics [2, 3, 5, 7, 9–31]

Author, year	Case	Age (year)	Gender	Location	Size (mm)	Main symptoms	Treatment	Course
Becker G.D. et al. [9]	1	31	F	SP Nasal Nasopharynx	-	Congestion Fever Sinusitis	Antibiotic	-
Kuriloff D.B. et al. [10]	2	29	F	HP Nasal	4	Rhinolalia Congestion Epistaxis	Antibiotic Obturator	-
Mattson-Gates G. et al. [11]	3	28	F	HP	-	Rhinolalia	Surgery	-
Armstrong M. et al. [12]	4	31	F	HP Nasal	7	Rhinolalia Nasal crust Otalgia	Antibiotic Debridement	-
Sastry R.C. et al. [13]	5	37	F	HP Nasal	-	Nasal crust Pain	-	-
Gendeh B.S. et al. [14]	6	44	F	HP Nasal	18	Regurgitation Congestion	Antibiotic Debridement	-
Sittel C. et al. [3]	7	36	M	HP SP Nasal	15	Rhinolalia Regurgitation Congestion Rhinorrhea	Antibiotic Surgery	-
Cottrell D.A. et al. [15]	8	33	F	HP Nasal	15 × 10	Rhinolalia Regurgitation	Obturator	Failure
Villa P.D. et al. [16]	9	38	M	HP	10 × 12	Rhinolalia Regurgitation Sinusitis	Obturator	-
Lancaster J. et al. [17]	10	33	F	HP Nasal Maxillary sinus	-	Rhinolalia Regurgitation Pharyngeal pain Rhinorrhea	Antibiotic Analgesics	Good
Talbott J.F. et al. [18]	11	56	M	HP SP Nasal	-	Infection	Antibiotic Surgery	Good
Gertner E. et al. [19]	12	53	M	HP Nasal Maxillary sinus	-	Regurgitation Pain	Obturator	-
Mari A. et al. [20]	13	37	M	HP Lip filtrum Nasal	15	Severe pain	Obturator	Good
	14	35	F	HP Nasal	-	-	Obturator Surgery	Good
	15	30	F	HP Nasal	30	Rhinolalia	Obturator	Fails to return
Ronda J.M. et al. [7]	16	40	M	HP SP Nasal Right orbit	-	-	-	-
Seyer B.A. et al. [21]	17	50	F	HP Nasal Maxillary sinus	-	Rhinolalia Regurgitation	Antibiotics Debridement	Fails to return
Smith J.C. et al. [5]	18	47	F	HP Nasal	-	Rhinolalia Regurgitation Epistaxis Rhinorrhea	Antibiotics First surgery Second obturator	First failure Second good

Table 1 (continued)

Author, year	Case	Age (year)	Gender	Location	Size (mm)	Main symptoms	Treatment	Course
Monasterio L. et al. [22]	19	64	M	HP Nasal	6 × 7	Rhinolalia Regurgitation	Surgery	Good
Bains W.M. et al. [23]	20	36	M	HP Nasal	2 × 3	Rhinolalia Regurgitation	Obturator	Fails to return
Goodger N.M. et al. [24]	21	43	F	HP	30 × 15	Regurgitation	First obturator	First failure
				Nasal		Sensitivity loss	Second surgery	Second fails to return
Jewers W.M. et al. [25]	22	31	M	HP	8 × 11	Rhinolalia	First surgery	First failure
				Nasal		Xerostomia	Second obturator	Second good
Padilla-Rosas M. et al. [26]	23	48	F	HP Nasal	15 × 17	Rhinolalia Regurgitation	Obturator	Fails to return
				Maxillary sinus				
Simsek S. et al. [27]	24	34	M	HP Nasal	-	Congestion Infection	Antibiotics Corticoids	-
				Maxillary sinus			Obturator	
	25	30	M	HP Nasal	-	Infection	Antibiotics Corticoids	-
Cintra H.L. et al. [2]	26	25	F	HP SP	40 × 70	Regurgitation Sinusitis	Surgery	Good
						Epistaxis		
						Velopharyngeal dysfunction		
	27	42	F	HP	40 × 60	Regurgitation Sinusitis	Surgery	Good
						Epistaxis		
Di Cosola M. et al. [28]	28	-	M	HP	30	Rhinolalia Regurgitation	Surgery	Failure
						Epistaxis		
						Sinusitis		
	29	-	M	HP	20	Rhinolalia Regurgitation	Surgery	Failure
						Epistaxis		
						Sinusitis		
	30	-	F	HP	5	Rhinolalia Regurgitation	Surgery	Good
						Epistaxis		
						Sinusitis		
	31	-	F	HP	20	Rhinolalia Regurgitation	Surgery	Good
						Epistaxis		
						Sinusitis		
	32	-	F	SP	10	Rhinolalia Regurgitation	Surgery	Good
						Epistaxis		
						Sinusitis		
						Velopalatine dysfunction		
	33	-	F	HP SP	20	Rhinolalia Regurgitation	Surgery	Good
						Epistaxis		
						Sinusitis		

Table 1 (continued)

Author, year	Case	Age (year)	Gender	Location	Size (mm)	Main symptoms	Treatment	Course
						Velopalatine dysfunction		
Lypka M.D. et al. [29]	34	25	M	HP Nasal	-	Regurgitation Epistaxis Sinusitis	-	Fails to return
Cohen M. et al. [30]	35	54	M	HP Nasal	6 × 6	Rhinolalia Regurgitation Velopalatine dysfunction	-	Fails to return
Brusati R.et al. [31]	36	46	F	HP SP Nasal Anterior cranial base Left orbit	-	Direct communication: brain–mouth Encephalocele Meningitis	Surgery	Improves

SP soft palate, *HP* hard palate

liver enzymes to produce metabolites which are eliminated in urine. Increased serum magnesium levels have been recorded in cocaine abusers [34].

Consideration must be given to the fact that the intranasal inhalation of cocaine is a toxic habit that has increased in the last few decades. As a direct result of this tendency, a range of alterations in different locations of the gastrointestinal and respiratory mucosas have been reported, such as irritation and dryness of the oral and nasal mucosa, destruction of the nasal septum and lateral walls of the nasal passages [35, 36] and less frequently, midline perforation or destruction of the palate—giving rise to an oronasal fistula or perforation [11, 17, 18, 21]. Destructive lesions leading to perforations of the palate can have a number of causes which must be known in order to establish a correct differential diagnosis.

In the present study, we documented 36 cases of palatine perforation in cocaine abusers reported in 27 articles found in the literature [2, 3, 5, 7, 9–31]. No particular gender predilection was observed, though females represented a little over half of the total cases (58.33%). It has been suggested that this is because women are more susceptible to such complications in the same way as this happens in

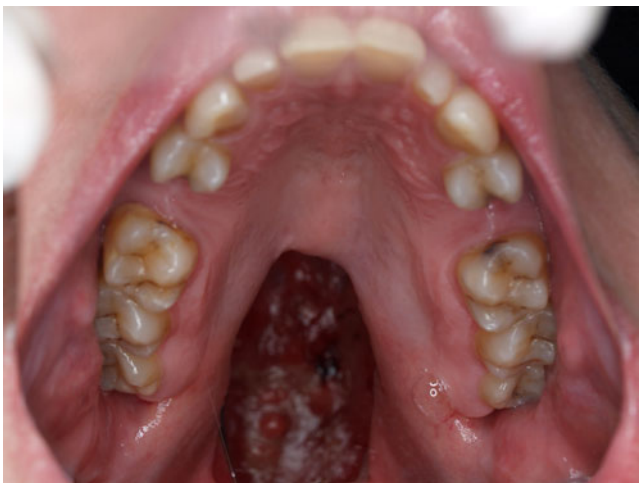

Fig. 1 *Occlusal view* of palatal perforation, including hard and soft palate

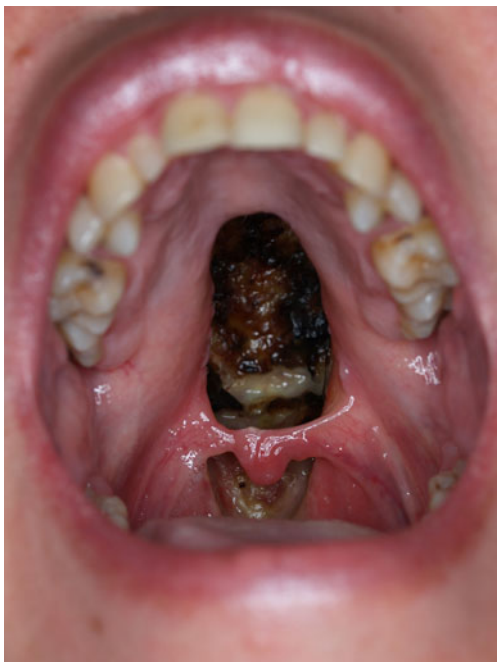

Fig. 2 *Frontal view* of palatal perforation with nasopharyngeal infection

other connective tissue disorders [17, 24]. Another hypothesis is that women reach lower blood drug concentrations, have less sensitivity to cocaine than men, and therefore consume more of the drug [2]. However, we consider that the observed gender difference was not large enough to require an explanation.

Regarding the age, most of the patients were young adults with an average age close to 40 years and a history of addiction to cocaine. Clinically, the main complaints for which the patients sought medical help were a nasal tone caused by the defect (rhinolalia) and the regurgitation of food towards the nasal passages when swallowing. Other clinical manifestations were infections and oral swelling (sinusitis), pain in the nasal passages with congestion, a lack of sensitivity in the area, anosmia, halitosis, or headache secondary to destruction of the nares or to infections resulting from such destruction.

The average diameter of the perforation was considerable, reaching almost 2 cm. However, there were cases in which destruction was very extensive and advanced, while in other cases the perforation measured only a few millimeters in diameter.

The differential diagnosis must be established with traumatisms, neoplasms, infections, and autoimmune processes that affect this zone, along with processes of a reactive nature [3, 14].

Traumatism may be mechanical, thermal, or electric. Different chemical agents can also be involved—not only cocaine but also other opioids. Likewise, surgery for head and neck tumors can also result in communication between cavities such as the mouth and nasal passages or maxillary sinus [37].

The tumors involved comprise malignancies ranging from melanoma to primary squamous cell carcinoma (though a palatine location of the latter is rare), metastases, neoplasms in the surrounding areas such as the maxillary sinus or the nares, lymphoreticular system neoplasms, and minor salivary gland tumors [38–40]. Although very infrequent, the infectious processes that may be found in this location include tuberculous granulomatous lesions, syphilitic gumma, rhinoscleroma, actinomycosis, leishmaniasis, aspergillosis, coccidiomycosis, mucormycosis, histoplasmosis, blastomycosis, and leprosy [41, 42]. Mention must be made of lupus erythematosus, sarcoidosis, chronic inflammatory Bowel disease with oral manifestations, and Wegener granulomatosis [43], as they represent important autoimmune processes. Finally, attention must be also given to reactive lesions such as necrotizing sialometaplasia due to palatine ischemia, which may give rise to extensive necrosis in this area [20].

Advances in molecular genetics and immunocytochemistry have shown that most necrotizing lesions in the middle third facial region are caused by sinonasal tract lymphomas [5].

In order to establish a correct differential diagnosis, complementary tests are needed in the form of computed tomography, lesion biopsy, blood tests, and toxicological tests.

It is common for such tests to detect increased levels of antineutrophil cytoplasmic antibodies (c-ANCA)—thus suggesting the possibility of Wegener granulomatosis (with a sensitivity of 90%) [5, 7]. This diagnosis in addition must be confirmed by the evidence of a granulomatous infiltrate in the lung biopsy.

In our review, six of the 14 articles mentioning the test results obtained were positive for c-ANCA, and one of them (case 12) was negative for c-ANCA but positive for p-ANCA [19].

Seller et al. [21] reported a false-positive rate of 4–6% for c-ANCA in patients presenting only vasculitis but not the rest of the diagnostic criteria for Wegener granulomatosis. Such a false-positive result is compatible with many disorders such as infections due to *Mycobacterium* or cytomegalovirus, immunoblastic lymphoma, renal cell carcinoma, or squamous cell carcinoma of the esophagus and lung [21]. A certain genetic susceptibility may also be implicated [27].

The importance of an early and correct diagnosis of Wegener granulomatosis is based on the fact that the 2-year survival rate in the absence of treatment is a mere 10% [5]. In contrast, the remission rate among patients treated early with prednisone and cyclophosphamide is 90% [7].

Another aspect to be taken into account is the histopathological evaluation of the lesion tissue. In this context, we often observe necrosis and inflammation (confirmed in 19 of the 21 reviewed cases), while less common findings are the presence of eosinophils, infections due to *Actinomyces* or *S. aureus*, epithelial hyperplasia, or squamous cell metaplasia of the minor salivary glands (case 23).

In the case of cocaine-induced lesions, a number of pathogenic mechanisms have been suggested, such as local ischemia secondary to the vasoconstrictive effect of the drug, which would act upon the hard and soft tissues over a prolonged period of time [44]. Likewise, possible direct trauma could result from the local anesthetic effect of cocaine, combined with the mucosal irritation caused by the contaminants contained in the adulterated drug. On the other hand, possible overinfection of the initial lesion has been observed, with the formation of fistulas [8, 18], among cocaine abusers presenting a degree of depressed immune function.

The management of these patients is complicated by their scant cooperativeness. In effect, eight of the 23 subjects for which follow-up was documented failed to return, and three of them resumed cocaine abuse—thereby facilitating treatment failure.

From the management perspective, the ideal treatment for these cocaine-induced perforations would be recon-

structive surgery [24, 28]. In the same way as in oncological surgery, failures are frequent, like flap or graft necrosis secondary, in most of the cases, for the persistence of cocaine abuse [25].

Some authors [20, 23, 28] point to the need to confirm the cessation of cocaine abuse based on toxicological tests, ensuring full rehabilitation for 6 months or even 1 year before surgery, in order to avoid treatment failure. Accordingly, conservative management is advised, based on analgesia, antibiotic treatment, surgical debridement, saline solution lavage, and even obturator placement during the rehabilitation period [16, 23].

A number of surgical techniques have been described, mostly comprising the use of local mucoperiosteal flaps or tongue flaps (due to their intense vascularization) in the case of minor perforations, larger fistulas tend to be managed with distant nonpedicled flaps (generally from the forearm) [28].

A solution in cases of surgical failure is to prepare an obturating prosthesis (as occurred in 11 patients), either directly or sometimes after treatment failure. The obturator is adjusted in the same way as an acrylic plug to the dimensions of the defect, ensuring complete sealing and thus, facilitating correct oral functions [45]. However, once again, if the patient continues to consume cocaine, necrosis at the margins of the defect would cause the latter to grow—resulting in defective fitting of the obturator. As a result, continuous modifications of the acrylic material would be required.

Some authors describe serious inconveniences with obturator use, such as a loss of taste sensation and a lack of retention and stability—particularly in edentulous jaws [28]. However, obturators are a good alternative in cases of failed surgical reconstruction and offer relief from the symptoms of the oronasal fistula.

Few of the reviewed articles mention the duration of cocaine abuse, though the available data suggest that both the duration of abuse and the dose and frequency of inhalation varies greatly—from cases of only 1 year of abuse (case 23) [26] to as long as 23 years (case 35) [30]. Of note is the frequency of cocaine abuse associated to tobacco smoking—a situation which undoubtedly also contributes to tissue necrosis.

Conflict of interest The authors declare that they have no conflict of interest.

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