

Malacoplakia of the tongue: a case report and clinicopathologic review of 6 cases

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Abstract

Background: Extra-urogenital tract malacoplakia is uncommon, with tongue malacoplakia being exceptionally rare. The nonspecific clinical presentation and variable histologic patterns can make recognition of this lesion and separation from other lesions challenging. There are only a few reported cases in the English literature.

Materials and methods: Five case reports of tongue malacoplakia were compiled from the literature (MedLine 1960–2008) and integrated with this case report.

Results: The patients included 4 males and 2 females, ranging in age from 9 to 98 years (mean, 64 years). Patients presented with difficulty swallowing, foreign body sensation, a mass lesion, or referred pain (neck or ear). Symptoms were present from a few days up to 18 months. The base of the tongue was the most frequent site, although midline tongue and half of the tongue were also affected. Radiographic studies demonstrated a mass, with a single lesion showing positron emission tomography positivity. Two patients had previous cancers (prostate and colorectal; larynx). This case report was a farm hand for horses, with gram-negative rods, suggestive of *Rhodococcus equi* identified. The lesions were 1 to 2 cm in greatest dimension. Histologically, there is pseudoepitheliomatous hyperplasia or ulceration with a heavy acute and chronic inflammatory infiltrate. The subepithelial spaces are completely filled with eosinophilic histiocytes, most of which contain granular material in their cytoplasm. Well-formed, blue, calcific bodies are noted, a few showing a “targetoid appearance” and concentric lamination. These Michaelis-Gutmann bodies are positive with von Kossa, iron, and periodic acid-Schiff stains. These findings support a diagnosis of malacoplakia. The differential diagnosis includes granular cell tumor, poorly differentiated carcinoma, and Langerhans histiocytosis. Patients are managed with antibiotic therapy and excision.

Conclusions: Tongue malacoplakia is rare, often presenting as a mass lesion. Histologic recognition of this abnormal phagocytic disorder will prevent potentially disfiguring surgery.

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1. Introduction

Malacoplakia is a rare granulomatous disease initially described by Michaelis and Gutmann in 1902 [1], then

further clarified in 1903 by Von Hasemann, who named it by combining the words “malacos” meaning soft and “placos” meaning plaques [2]. This disease is usually identified in the genitourinary tract and in the gastrointestinal tract. The disease is rare in the head and neck, with only 5 previously reported cases in the tongue specifically [3-7]. The initial presenting symptoms are often nonspecific, making it important to render the correct diagnosis, because the disease is associated with a high mortality when identified within vital organs [8-11]. This case report is presented in the context of a literature review (Table 1).

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Table 1
Review of literature combined with current case [3-7]

Characteristic	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Reference	Love et al [3]	Seifert et al [4]	Carbone et al [5]	Gillett et al [6]	Lewis et al [7]	Current case
Sex	M	M	F	F	M	M
Age (y)	9	68	57	98	82	70
Symptoms	Referred otalgia; difficulty swallowing and speaking	Difficulty swallowing and speaking (ringing voice)	Painless mass	Left neck mass	Positive PET scan during routine cancer follow-up	Foreign body sensation in back of throat
Duration (mo)	0.25	18	n/r	2	n/r	3
Anatomic site	Right half of tongue and FOM	Left BOT	Median, dorsum tongue; right FOM	Left BOT	Left vallecula, left BOT	Right BOT
Physical examination	Swollen right tongue and FOM; fetid breath	Brown, coarse material; r/o carcinoma	Mucosal covered nodules	Neck ulcer with induration and BOT mass	“Whitish exudate”	Pink, nodular, submucosal mass
Radiology	CT with swelling of tongue	Ultrasound showed mass	n/r	n/r	PET positive	n/r
Medical history	Episode 1 mo prior	n/r	n/r	n/r	Colorectal and prostatic carcinoma	Larynx SCC; farm hand for horses
Size	Multiple small fragments	1 cm	1	n/r	2 cm	1.5 cm
Treatment	Tobramycin and methylprednisolone	Refused	Excision	Excision (methicillin-resistant <i>Staphylococcus aureus</i>)	n/r	Excision; antibiotic therapy
Follow-up	NED, 7 mo	n/r	120 mo	n/r	n/r	NED, 21 mo

M, male; F, female; y, years; FOM, floor of mouth; BOT, base of tongue; NED, no evidence of disease; n/r, not reported; CT, computed tomography; SCC, squamous cell carcinoma; r/o, rule out.

2. Case presentation

A 70-year-old white man presented with a 3-month history of a foreign body sensation along the back of his throat. He also experienced the sensation of food getting caught in the back of his throat. He was unable to relieve the sensation despite throat clearing or drinking fluids. The patient denied recent weight loss, fever, chills, or pain. The patient worked as a ranch hand, boarding horses and working in the equestrian industry for the past several years. He denied urinary tract or gastrointestinal symptoms. Five years before, the patient had been treated with laryngectomy and bilateral selective neck dissections for a larynx squamous cell carcinoma. He declined postoperative radiation therapy because the lymph nodes were negative for metastatic carcinoma.

Physical examination showed an intact tracheostomy. Fiberoptic nasopharyngoscopy revealed a tan-pink, nodular, pedunculated 1.5-cm mass at the right base of tongue. An exudate was not identified. The lesion, including the small stalk, was completely removed with minimal bleeding.

By histology, the squamous mucosa was intact, demonstrating pseudoepitheliomatous hyperplasia (Fig. 1). The subepithelial spaces were completely filled with eosinophilic large, granular or foamy histiocytes, with a low nuclear to cytoplasm ratio. A heavy mixed inflammatory infiltrate was noted throughout, including eosinophils and plasma cells. Within this milieu, a number of well-formed blue, calcific bodies were noted, both within the cytoplasm of the cells and in the stroma. A few of them were targetoid and concentrically laminated (Fig. 2). They were strongly black (positive) with both a von Kossa (calcium stain) and a Prussian blue (iron stain; Fig. 3). These bodies were interpreting to be Michaelis-Gutmann bodies, a finding

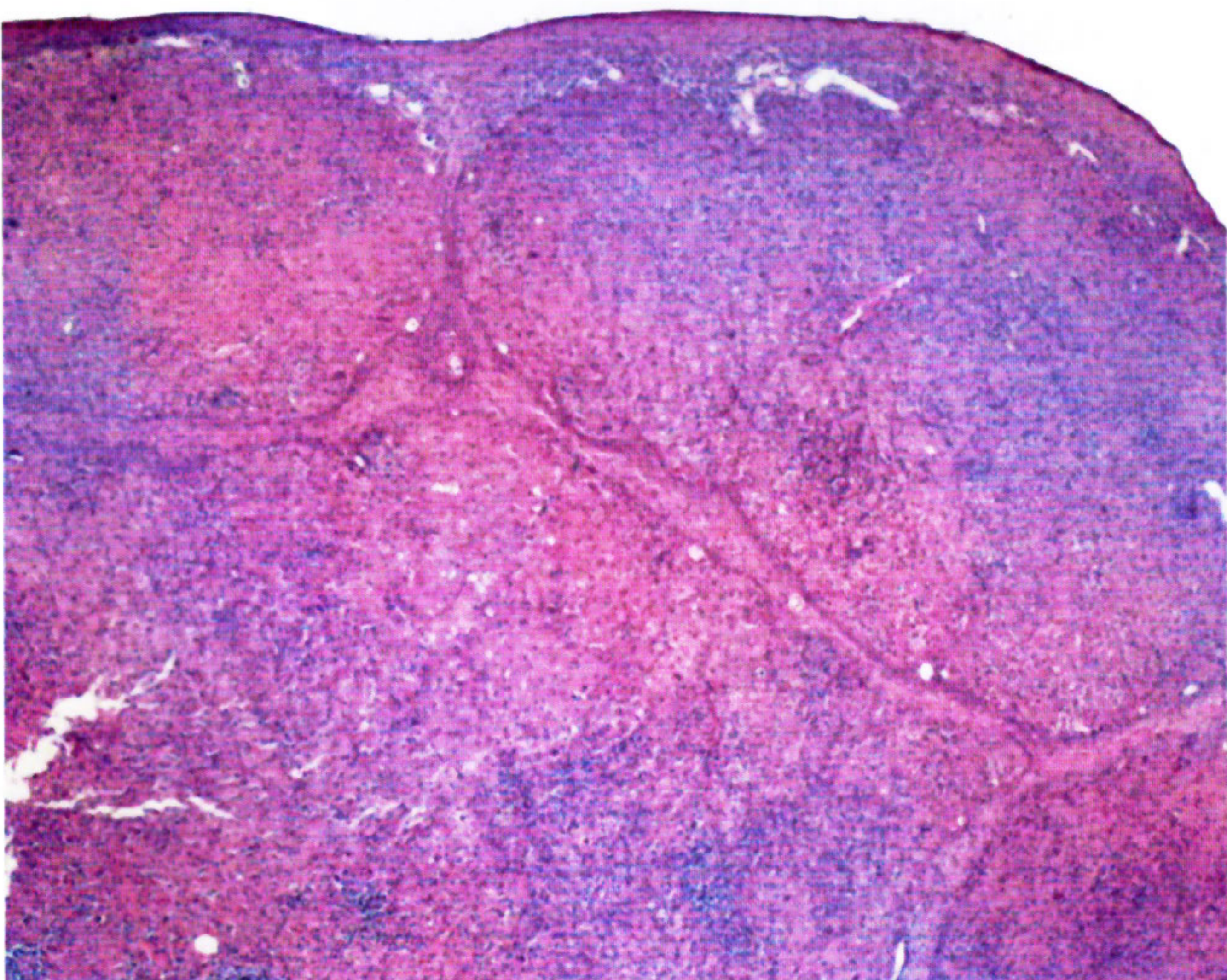


Fig. 1. The surface epithelium is intact with a pseudoepitheliomatous hyperplasia. There is a heavy histiocytic and inflammatory cell infiltrate. The eosinophilic macrophages (von Hasemann cells) dominate.

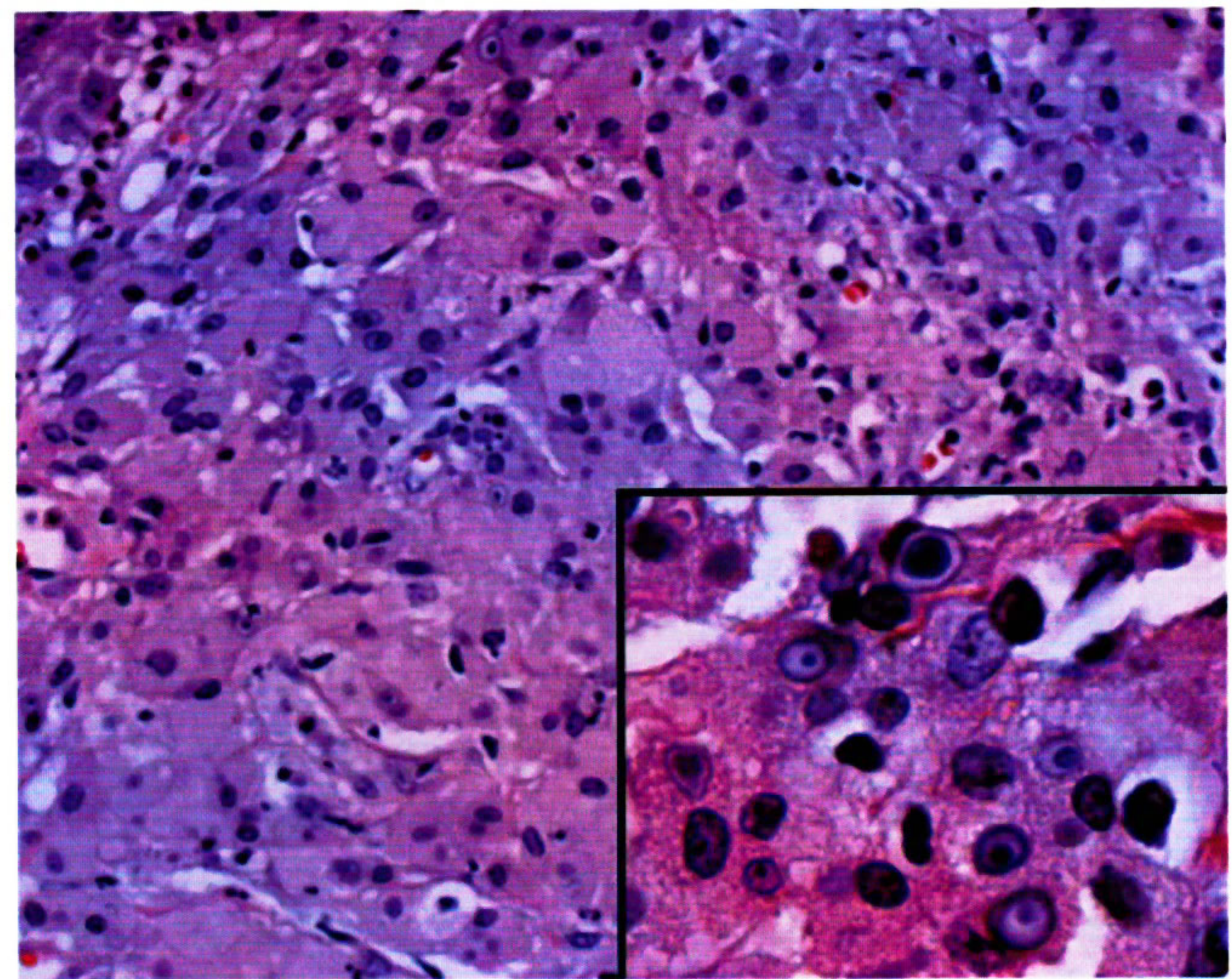


Fig. 2. The histiocytes are filled with granular to finely vacuolated eosinophilic cytoplasm with small blue calcospherites. The inset shows the characteristic Michaelis-Gutmann bodies with a central targetoid pattern.

pathognomonic for malacoplakia. Periodic acid-Schiff (PAS) stain identified organisms in the cytoplasm of the histiocytes. S-100 protein, keratin, CD1a, and CD20 were nonreactive, whereas the histiocytes were strongly positive with CD68. These findings are diagnostic of malacoplakia.

During his postoperative care, gram-positive coccobacilli were identified on culture. Initially, they were interpreted to represent diphtheroids, but after further evaluation, the organisms were best classified as *Rhodococcus equi*, identified in a background of significant contaminating oral flora. Multiagent antibiotics including ciprofloxacin, diflucan, and flagyl resulted in no further

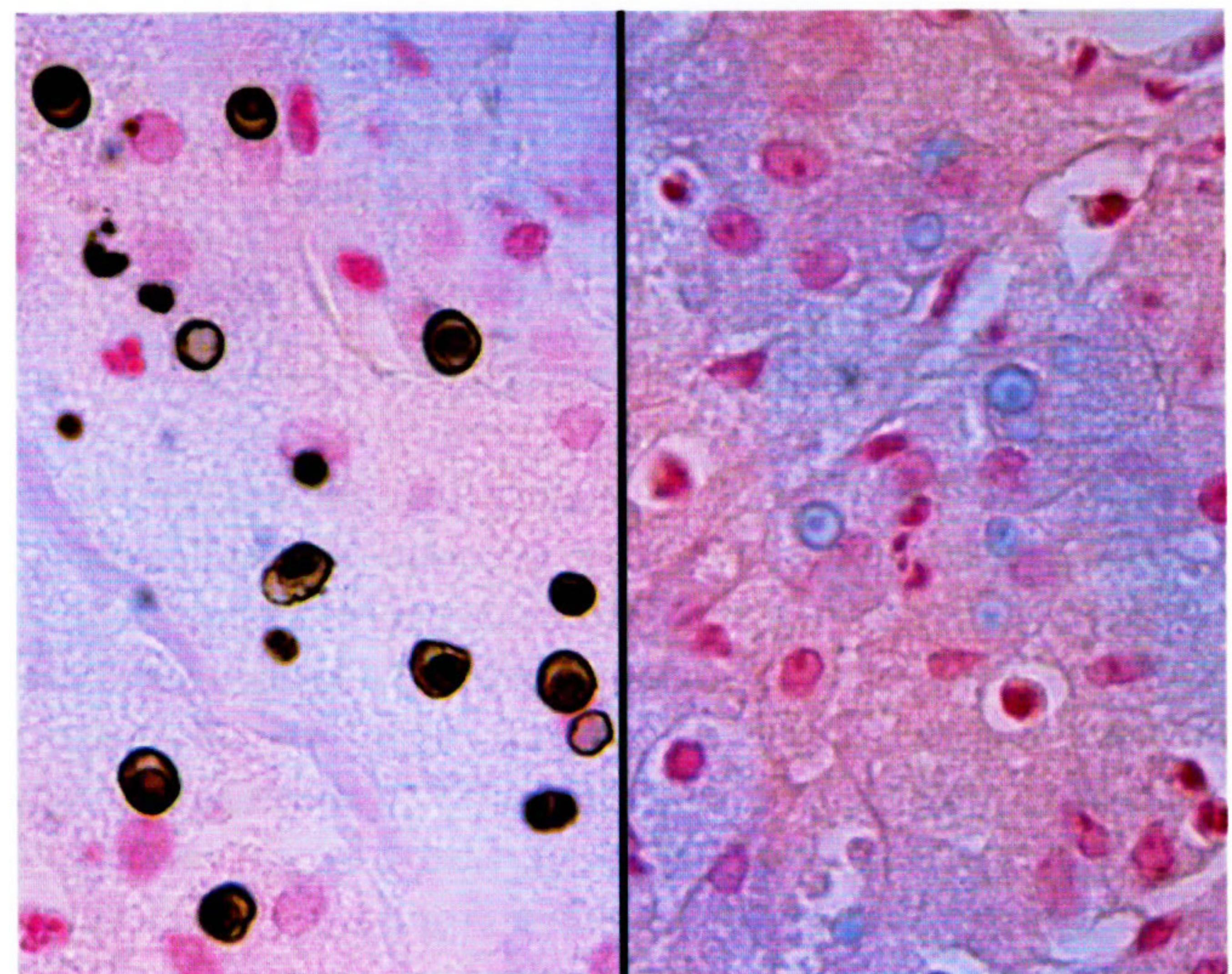


Fig. 3. The Michaelis-Gutmann bodies can be highlighted with (left) a von Kossa calcium stain or with (right) a Prussian blue iron stain.

oral lesion. He is alive, without evidence of disease at last follow-up (21 months).

3. Epidemiology

Malacoplakia usually develops in a postoperative site or areas in which there has been inflammation or infection, usually in the genitourinary and gastrointestinal tracts. This disorder is a distinctive, chronic inflammatory reaction. It is characterized by an infiltrate composed of lymphocytes plasma cells, acute inflammatory cells, and large granular or foamy histiocytes. The latter are associated with Michaelis-Gutmann bodies. The bodies are lysozymes that form concentrically layered calcospherites. The disorder usually develops as a wound complication (such as bacterial infection, hematoma, suture abscess, or dehiscence), with an infectious agent considered etiologic. The pathogenesis is not well delineated, but it is postulated that there is a deficiency in cellular immunity and a failure of intracellular bactericidal and phagolysosomal function [8-11,13,15]. This results in the inability of the macrophage to destroy the phagocytized bacteria, with Michaelis-Gutmann bodies formed when organic and inorganic material (calcium and iron) is deposited on residual bacterial glycolipid, a small localized granuloma to the ingested foreign body—the bacteria [12].

Escherichia coli is the most common organism identified in malacoplakia. However, *R equi*, a primarily zoonotic infectious agent, can cause malacoplakia, especially in patients who are immunocompromised [13]. Our patient worked with horses, with possible exposure to manure-contaminated soil (inhaled or direct contact) [14-16]. Immunocompromise is frequent in malacoplakia and includes organ transplantation, malignancy, diabetes mellitus, AIDS, malnutrition, and immunosuppressive medicines (chemotherapy and steroids) [12,13]. Our patient had a history of larynx squamous cell carcinoma, which would suggest a diminished immune capacity. Furthermore, with a tracheostomy, or “open wound,” this may have been the site of inoculation during his work.

4. Clinical presentation and associations

Men are affected more commonly than women (2:1) with tongue malacoplakia, distinctly opposite to genitourinary disease, where women are affected much more commonly than men [8-11]. Most patients with tongue lesions are older at presentation (mean, 64 years), with rare exception. Presenting symptoms include difficulty swallowing, trouble speaking, foreign body sensation, and a mass, with and without pain. The symptoms range from a few days up to 18 months. The physical examination showed a mass. Radiographically, the lesions appeared as masses, with the one reported case showing positron emission tomography

(PET) positivity [7]. Two of the patients had a history of previous malignancies: one patient had a colorectal carcinoma and prostate carcinoma [7], whereas our patient had a larynx squamous cell carcinoma. There are reported cases of adenocarcinoma of the colorectal region associated with malacoplakia [12,17,18], but the malacoplakia seems to be at the advancing edge and in the draining lymph nodes when associated with tumor, rather than more diffuse as it is in other conditions (such as ulcerative colitis or diverticular disease). It is unclear whether the malacoplakia represents a local response to the tumor or a local alteration in the gastrointestinal flora adjacent to the tumor [19].

5. Pathologic features

The lesions all appeared as tumors, ranging in size from a few millimeters up to 2 cm. The masses are yellow-brown, soft plaques characterized by a central navel or ulcer, and an intense peripheral hyperemia.

The diagnosis is based on sheets of granular, eosinophilic histiocytes without atypia, inflammatory cells, and the sine qua non of malacoplakia, Michaelis-Gutmann bodies. Drs Carl Gutmann and Leonor Michaelis first described these rounded, lamellar calcium and iron-laden targetoid inclusions in histiocytes (eponymically called Hansemann macrophages) within a urinary tract infection in 1902 [1].

R equi is an intracellular bacterium, often surviving in macrophages. The organism is gram-positive, and can exist as a coccus, bacillus, or intermediate form depending on conditions. The name “rhodo” is due to its ability to form a red-salmon pigment. The organism resembles diphtheroids and used to be grouped with *Corynebacterium* (family *Nocardiaceae*, order *Actinomycetales*). The typical histologic pattern shows a granulomatous reaction with a predominance of macrophages. The macrophages have granular cytoplasm that is filled with PAS-positive coccobacilli. In fact, it is in this setting that malacoplakia can be mimicked because Michaelis-Gutmann bodies are also PAS-positive. However, the strong von Kossa (calcium) and Prussian blue (iron) reactions with the Michaelis-Gutmann bodies help to make the separation. Interestingly, *R equi* seems to avoid being killed within macrophages by interfering with phagosome-lysosome fusion [20]. Therefore, it is possible that both mechanisms may come to play in the human setting.

6. Differential diagnosis

Differential diagnoses include granular cell tumor, xanthogranulomatous inflammation, Langerhans cell histiocytosis, carcinoma, atypical mycobacterial infection, and lymphoma. Pseudoepitheliomatous hyperplasia can be seen in granular cell tumor, fungal infections, and malacoplakia. The lack of pleomorphism helps to eliminate carcinoma from consideration. The neoplastic cells of a granular cell tumor

are S-100 protein immunoreactive. Xanthogranulomatous inflammation is more common in the genitourinary tract and has a specific histiocytic infiltrate. Langerhans histiocytes have nuclei that are coffee-bean shaped with a groove in the nucleus. These cells are set in a background rich in eosinophils and the histiocytes are immunoreactive with CD1a, among other markers. Lymphoma will show a monotypic, atypical lymphoid infiltrate. Atypical mycobacteria can be accentuated with acid-fast stains, but *R equi* may also show weak reactivity. Culture or fluorostain techniques would help to yield a specific diagnosis.

7. Treatment

The treatment depends on the extent of the disease and the anatomic site of involvement. In asymptomatic patients, an excellent prognosis can be achieved with antibiotics directed against the suspected infectious organism, but in severe involvement, aggressive management is necessary. Treatment may require combination antibiotic therapy of prolonged duration, sometimes in combination with surgical therapy. All of the patients reported had excisional biopsy or excision in addition to many receiving antibiotic therapy. Specific therapy depends on the underlying bacterium. High concentration in macrophages and the ability to penetrate cell membranes are an important consideration in choosing antibacterial agents [12]. In the case of suspected *R equi*, it is important to note that in general, the organism is susceptible to erythromycin, rifampin, vancomycin, imipenem, and ciprofloxacin but is usually resistant to penicillin G and ampicillin.

8. Conclusions

The mass lesion clinical presentation in the tongue of malacoplakia makes the separation of this lesion from other tumors of the head and neck important. Awareness of this rare entity in an uncommon site will help make the diagnosis. The presence of Michaelis-Gutmann bodies in a sea of eosinophilic granular histiocytes should help to confirm the diagnosis histologically. Appropriate antibiotic therapy combined with surgery should be curative.

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