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# Inflamed benign tumors of the parotid gland: Diagnostic pitfalls from a potentially misleading entity

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**ABSTRACT:** *Background.* The purpose of this study was to evaluate our experience in the diagnostic approach to inflamed benign tumors of the parotid gland at a single tertiary center.

*Methods.* A retrospective evaluation was carried out for all patients with signs of inflammation in the parotid gland on the ground of a benign parotid tumor, as confirmed by permanent histology.

*Results.* Sixteen patients were detected for our study. Histopathologic examination confirmed cystadenolymphoma in 11 cases (with metaplastic changes in 2 cases), 2 pleomorphic adenomas, 2 monomorphic adenomas, and 1 oncocytic cystadenoma. Diverse clinical signs (inflam-

mation signs, facial palsy), ultrasound and MRI findings (poorly defined lesion margins), and the presence of squamous metaplastic changes on cytology often raised the suspicion of parotid malignancy or abscess.

*Conclusion.* In most cases, a high suspicion index combined with close monitoring of the patient may allow prompt and successful diagnosis and therapy. © 2014 Wiley Periodicals, Inc. *Head Neck* 37: 23–29, 2015

**KEY WORDS:** parotid gland, benign tumor, inflammation, squamous metaplasia, cystadenolymphoma

## INTRODUCTION

The first report on “inflamed” benign tumors of the parotid gland in the literature comes from 1970, when Patey and Thackray<sup>1</sup> presented 2 cases of acute inflammatory swelling progressing to abscess formation, which developed from parotid adenolymphomas. Since then, there has been little data on this entity.

The purpose of the present study was to evaluate the experience in the diagnostic approach to inflamed benign tumors at a single tertiary center specialized in salivary gland disease treatment. An additional purpose of this study was to obtain relevant information on the possible diagnostic pitfalls arising from the clinical, sonographic, and histopathologic characteristics that inflamed benign tumors have in common with other conditions. This could be of practical importance for improving patient counseling and optimizing the diagnostic and therapeutic approach, as well as possibly minimizing the need for urgent decision-making or unnecessary surgical treatment.

## MATERIALS AND METHODS

This retrospective case series study was conducted at a tertiary referral center specialized in diagnosis and man-

agement of salivary gland diseases (Department of Otorhinolaryngology, Head and Neck Surgery, University of Erlangen – Nuremberg, Erlangen, Germany). The records of all patients presenting with clinical symptoms and imaging findings compatible with an inflamed benign tumor between 2004 and 2012 were evaluated. Included were all patients with clinical signs of inflammation on the ground of a benign tumor of the parotid gland proven on definitive histology. Patients with insufficient data as well as histologic findings other than a benign tumor of the parotid gland were excluded from this study. Approval was obtained from the institutional review board of our hospital.

Over a period of 8 years, 1650 patients with parotid tumors underwent surgery at our center. Twenty-three patients with relevant clinical symptoms and typical ultrasound findings were identified. Chronic nonspecific inflammation was found in histology in 4 cases and a malignant tumor (adenocarcinoma, not otherwise specified) was diagnosed in 1 case. In addition, the tumor proved to be an intraparotid lymph node in 2 patients. Consequently, 16 patients met the inclusion criteria for our study (0.9% of the overall population of the patients with parotid tumors; Table 1).

## RESULTS

Affected patients were 12 women and 4 men (ratio, 3:1). The mean age was 61 years (range, 13–81 years).

A rapid progression in tumor size was detected in 7 cases (43.7%). A slight facial palsy was detected in

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TABLE 1. Clinical, ultrasound, and histologic characteristics of the 16 patients of the study group.

Case	Age/sex	Clinical findings	Sonographic findings	Findings on permanent histology
1	74/F	Severe pain with tenderness on palpation for 6 d; acute onset.	Blurred tumor margins.	Cystadenolymphoma with regressive changes and moderate lymphocytic infiltrates.
2	81/F	Rapid progression in size; severe pain with tenderness on palpation; diagnostic needle aspiration biopsy.	Blurred tumor margins; parotid lymphadenitis; and hypoechoic parenchyma.	Cystadenolymphoma with regressive changes; slight lymphocytic infiltration; and squamous and goblet cells metaplasia (metaplastic cystadenolymphoma).
3	13/F	Rapid progression in size; severe pain.	Blurred tumor margins, hypoechoic parenchyma.	Pleomorphic adenoma with subtotal infarction and necrosis; excessive confluent foam cell reaction.
4	71/F	Rapid progression in size; severe pain.	Blurred tumor margins; strong perfusion (Doppler).	Pleomorphic adenoma with central hemorrhage and regressive changes; parotid parenchyma with moderate lymphocytic infiltration.
5	57/F	Acute swelling of the parotid gland for 2 d; drainage of suspected abscess drainage – no pus.	Blurred tumor margins.	Cystadenolymphoma with regressive changes.
6	54/F	Severe pain with tenderness on palpation; onset 1 mo previously.	Clearly defined margins at onset; blurred tumor margins 1 mo later; progression in size; hypoechoic parenchyma; parotid lymphadenitis.	Cystadenolymphoma; parotid lymphadenitis; ductal ectasia; moderate lymphocyte infiltrates
7	76/M	Redness, swelling, and severe pain with tenderness on palpation.	Blurred tumor margins.	Cystadenolymphoma with a major xanthogranulomatous inflammatory reaction.
8	80/F	Severe increasing pain with tenderness on palpation, longstanding “lump” suddenly rapidly progressive.	Clearly defined tumor margins; obvious progression in tumor size (compared to previous examination); strong perfusion.	Monomorphic adenoma (basal cell adenoma, trabecular type), focal microhemorrhages with pseudo-cystic acinar cells.
9	70/F	Pain and swelling of acute onset.	Blurred tumor margins.	Oncocytic monomorphic adenoma with focal apoptotic and degenerative changes, foam cell reaction.
10	55/M	Redness, swelling, and severe pain with tenderness on palpation.	Blurred tumor margins.	Cystadenolymphoma.
11	57/F	Rapid progression in size, severe pain.	Blurred tumor margins; hypoechoic parenchyma.	Cystadenolymphoma with moderate lymphocyte infiltrates.
12	62/M	Redness, swelling, pain, diagnostic needle aspiration without pus.	Clearly defined tumor margins; hypoechoic parenchyma, central perfusion (“hilum signs”).	Cystadenolymphoma with metaplastic changes, excessive foam cell reaction, focal granuloma formation.
13	37/F	Rapid progression in size, severe pain with tenderness on palpation, facial palsy.	Blurred tumor margins.	Cystadenolymphoma with regressive changes, signs of hemorrhage and cholesterol deposition, foreign body reaction, and focal necrosis.
14	61/F	Redness, swelling, and pain for 7 d.	Clearly defined tumor margins, hypoechoic parenchyma, small size, central perfusion (“hilum signs”).	Oncocytic cystadenoma.
15	70/M	Redness, swelling, and pain.	Clearly defined tumor margins, small size, central perfusion (“hilum signs”).	Cystadenolymphoma, moderate lymphocyte infiltrates.
16	87/F	Rapid progression in size, and severe pain with tenderness on palpation.	Blurred margins, hypoechoic parenchyma.	Cystadenolymphoma with metaplastic changes.

1 study case (6.2%; Table 1). On sonography, blurred tumor margins were described in 13 of 16 cases (81.3%; Figure 1). In 3 other cases, central tumor perfusion in color duplex ultrasound was described (18.7%; Figure 2). Considering the low sensitivity of MRI in the differentiation between benign and malignant parotid tumors, this imaging modality was performed in only 4 of our study

patients. In 3 cases, the lesions detected were not clearly circumscribed. Although in 2 cases, the characteristics of the lesions on MRI were indicative of cystadenolymphomas (hypointense signal in the T1 sequence, slightly hyperintense signal in the T2 sequence; Figure 3), blurred tumor margins and poorly defined lesion borders suggested an underlying malignancy. Fine-needle aspiration

FIGURE 1. Diverse ultrasound findings in our study cases. The blurred tumor margins and the poorly defined borders of the lesion with adjacent structures (white arrows) raised the suspicion of malignancy or abscess. GLP, parotid gland; MASS, masseter muscle; MSCM, sternocleidomastoid muscle; MD, digastric muscle. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

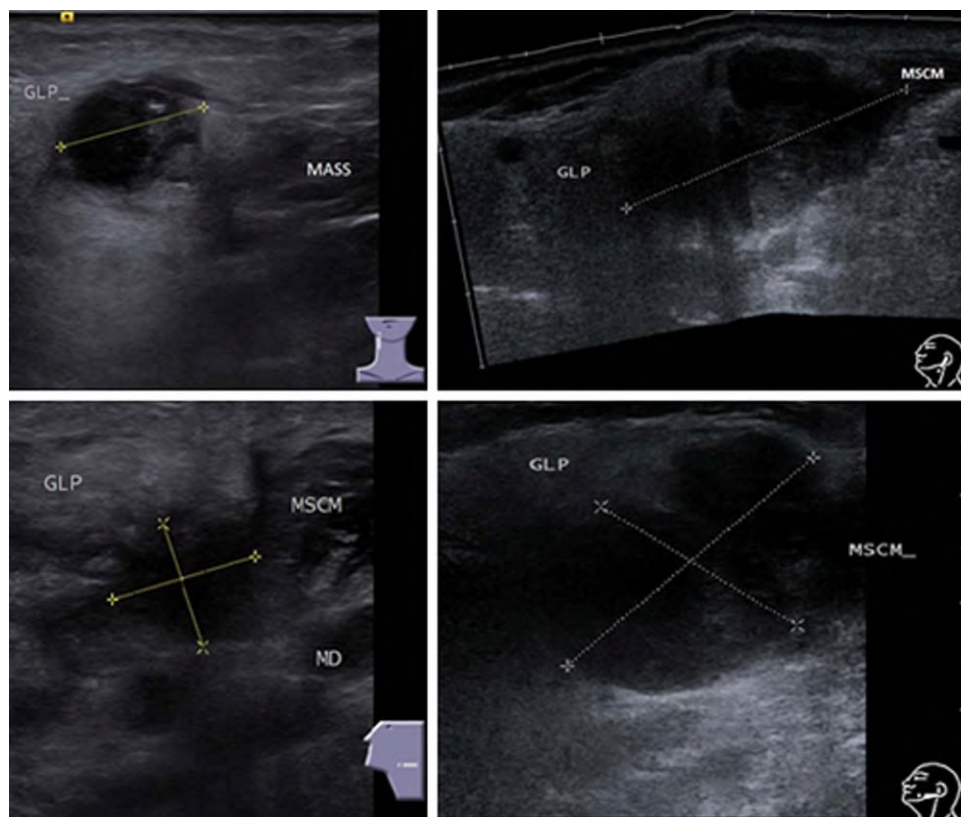
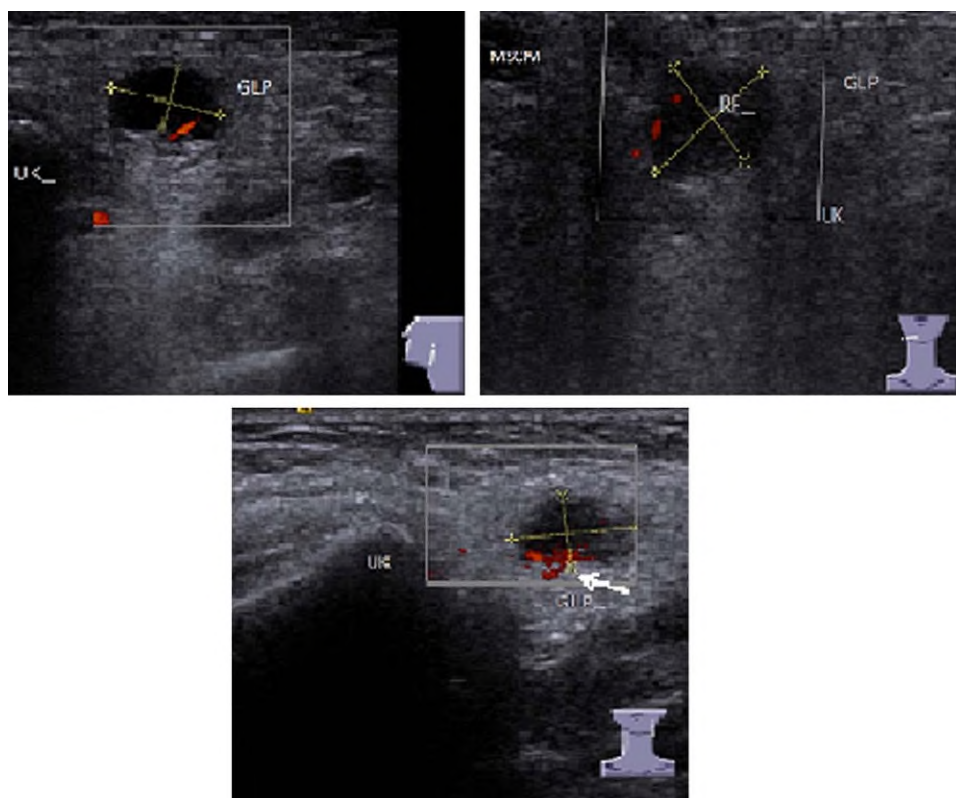


FIGURE 2. The very small size of the lesion in combination with central perfusion ("hilum signs," white arrow) led to the misdiagnosis of an intraparotid lymph node. GLP, parotid gland; UK, mandible. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]





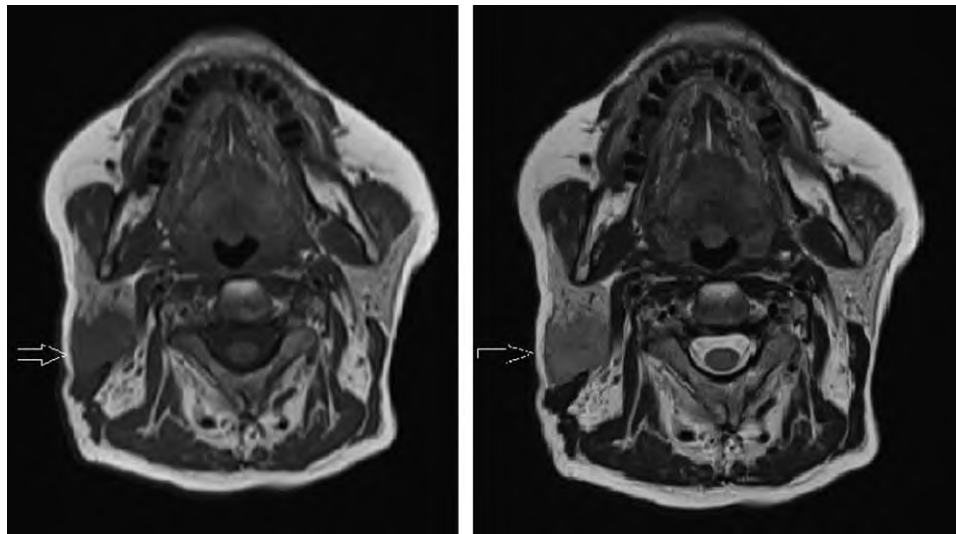


FIGURE 3. MRI finding of a study case. The poorly defined borders of the lesion raised the suspicion of malignancy. Left: Low signal in the T1-weighted sequence. Right: Slightly high signal intensity in the T2-weighted sequence.

(FNA) was performed in 4 cases, revealing uncommon findings (atypical squamous cells, epithelioid cells) in 2 cases. Permanent histologic examination revealed cystadenolymphoma (“Warthin tumor”) in 11 cases (with metaplastic changes in 3 cases), 2 pleomorphic adenomas, 2 monomorphic adenomas, and 1 oncocytic cystadenoma (Table 1). The cut surface of 2 cystadenolymphoma cases was described as hemorrhagic with extensive necrosis, cystic changes, and areas of whitish tissue reflecting fibrosis and metaplastic tissue. In some tumors, necrosis and metaplastic changes dominated the histological picture and diagnostic areas were seen only focally (Figure 4). Inflammation varied from necrotizing and purulent to chronic inflammation rich in foamy macrophages, mononuclear cells, and fibroblasts resulting in a xanthogranulomatous pattern.

## DISCUSSION

The main problem in the review of the literature on inflamed benign tumors is caused by the different definitions and names used by different authors for this disease: to the clinical otolaryngologist, an “infected” benign tumor of the parotid gland (a confirmed cystadenolymphoma in all cases described previously)<sup>2,3</sup> represents a condition with easily recognizable symptoms. Diagnostic suspicion is strengthened by ultrasound findings and confirmed by histopathologic examination.<sup>1–5</sup> From the clinical point of view, the term “inflamed” is preferred instead of “infected,” as signs of inflammation seem to dominate the clinical picture in the parotid gland. However, the presence of extensive necrosis led pathologists to use histology-based terms such as “infected” or “infected” for those parotid cystadenolymphomas with histopathologic inflammatory changes in their lymphoid stroma and featuring extensive necrosis.<sup>6,7</sup>

Analyzing 275 cases, Seifert et al<sup>7</sup> divided parotid cystadenolymphomas into 4 histopathologic subtypes according to the proportion of epithelial and stromal components (types 1–3) and the presence of goblet or

squamous cell metaplasia in the epithelium (type 4). Because it has been proposed that metaplastic changes in cystadenolymphomas can be induced by various factors (including radiation in the maxillofacial region,<sup>7</sup> trauma from FNA,<sup>8–11</sup> and spontaneous extravasation of oncocytic/mucinous secretions or cyst contents),<sup>12</sup> or

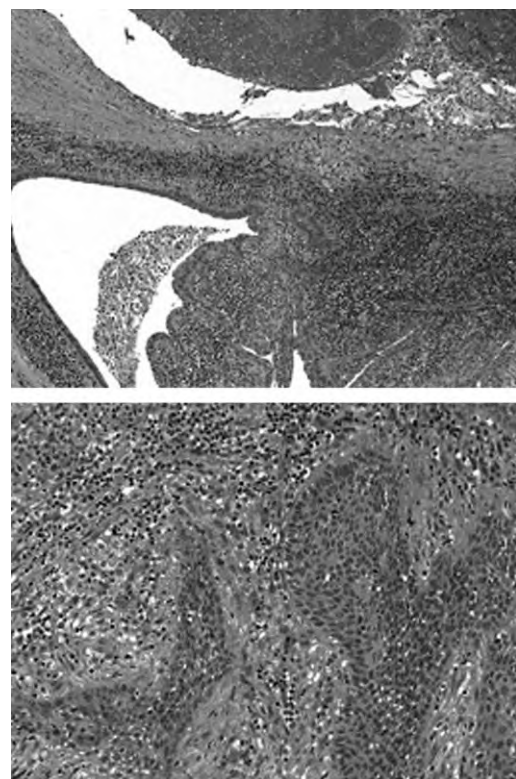


FIGURE 4. Above: Residual cysts lined by oncocytic epithelium are seen at lower left and necrosis at upper right. Below: Florid squamous metaplasia could easily be mistaken for squamous cell carcinoma by the unwary.

may arise from localized infarction with necrosis in the tumor,<sup>12,13</sup> or an (even subclinical) infection,<sup>1,8</sup> many authors tend to use the terms “infarcted” or “infected” as synonyms for the “metaplastic” subtype,<sup>6</sup> thereby worsening the confusion.

A review of the relevant literature reveals remarkable efforts to explain the pathogenesis of this entity. Rössle et al<sup>5</sup> favored the primary infarction of a Warthin tumor, leading to a massive release of intraluminal preformed crystals, which subsequently induces inflammation of the foreign body reaction type in the surrounding parenchyma, corresponding to the clinical simulation of acute parotitis or parotid abscess. According to this scenario, the parotid tumor seems to be the cause of the clinical condition, with the residual parenchyma “suffering from the consequences.” Patey and Thackray<sup>1</sup> attributed the disease to exogenous bacterial contamination, suggesting the blood stream as the route of infection.

A thorough search of our archives identified only 16 inflamed benign tumors over a period of 8 years. On the one hand, our study population consisted of selected patient cases with certain clinical, imaging, and histopathologic characteristics and, of course, a few patients may have been lost in the selection procedure. On the other hand, this extremely low incidence reflects the strict diagnostic (clinical and sonographic) criteria for inflamed benign tumors in our department. Unfortunately, it was not possible to perform a statistical analysis of our data because of the small number of cases ( $n = 16$ ).

According to the existing literature, a malignancy must always be considered in patients with a parotid mass and a peripheral facial nerve paralysis.<sup>14–16</sup> Facial nerve paralysis associated with histologically confirmed parotid malignancy is one of the criteria for T4a classification in the TNM staging,<sup>17</sup> negatively affecting the prognosis in these cases to a significant extent.<sup>18</sup> In our salivary gland registry, 26 of 203 cases of malignant parotid gland tumors (12.8%) presented with a facial palsy. Interestingly, there are several case reports of inflamed benign tumors with a temporary facial palsy during the course of disease.<sup>3,4,6,19,20</sup> A slight palsy occurred in 1 of our study cases and resolved completely on conservative treatment. In agreement with the relevant reports, facial palsy could possibly be explained by a mechanism of inflammation-induced paralysis. Remarkably, Chilla and Droese<sup>3</sup> noted that the facial palsy in their case gradually resolved after parotidectomy. In 3 additional cases, an abscess-forming process in the parotid gland was suspected because of the severe symptoms (pain, swelling, and redness) and local clinical findings. In only 1 case did a diagnostic needle-aspiration biopsy of the parotid mass detect pus and provide temporary relief of the local symptoms. In the second case, a needle biopsy was performed, obtaining chocolate brown aspirate but no pus. The inflammatory process was located deeper in the tissues of the third case so that surgical exploration in the acute phase was done with the patient under general anesthesia, encountering a relatively solid tumor mass but failing to find any signs of abscess formation. Interestingly, clinical symptoms of local tenderness, pain, or redness were shown by 51 of 203 cases of malignant parotid gland tumors (25.1%) in our registry.

In the sonography of the parotid gland, benign tumors normally present with regular contours, well-defined margins, and a homogeneous hypoechoic texture. In contrast, most malignant lesions are poorly demarcated, irregular, heterogeneous, and diffusely perfused.<sup>21–24</sup> In our salivary gland tumor registry, 120 of 203 cases of malignant tumors (59.1%) of the last 8 years were poorly demarcated with irregular margins in sonography. In our study sample, diverse (and in many cases contradictory) ultrasound findings led to serious problems in the differential diagnosis: blurred tumor margins and irregularity of the lesion often led to a high suspicion of malignancy (Figure 1). In 3 cases, the poorly defined contours of the lesion (combined with signs of severe local inflammation) resulted in the misdiagnosis of parotid abscess. Finally, small inflamed benign tumors with central perfusion were wrongly diagnosed on ultrasound as enlarged (“infected”) intraparenchymal lymph nodes (Figure 2). Bilateral or multifocal parotid lesions in such cases may suggest the possibility of a cystadenolymphoma rather than a malignant tumor.<sup>25</sup>

Differential diagnosis of salivary gland tumors with MRI still remains a major challenge for clinicians and radiologists.<sup>26</sup> According to the relevant literature, benign and malignant parotid tumors seem to exhibit a considerable overlap with regard to tumor properties, such as margins, shapes, and borders.<sup>27,28</sup> Modern MRI technologies, such as dynamic contrast-enhanced MRI, diffusion-weighted MRI, and proton MR spectroscopy have shown promising results in this field.<sup>29–31</sup> In our center, MRI is performed only in the case of deep parotid gland lesions or in cases in which ultrasound is not sufficient as a diagnostic procedure. Interestingly, the problem of poorly defined lesion margins remained unsolved in 3 of 4 cases that underwent this imaging modality, pointing to an additional potential source of diagnostic errors.

Apart from clinical and imaging findings, a third potential pitfall in the diagnostic approach to inflamed benign tumors may be found in cytological examination by FNA. The widespread use of FNA biopsy for salivary gland lesions is undoubtedly testimony to its usefulness and acceptance as a diagnostic technique.<sup>32</sup> In many centers, it is the first procedure used to establish a diagnosis before any surgical intervention. Nevertheless, cytology findings may be of questionable reliability, as both false-negative and false-positive results are possible even when the biopsy is carried out under ultrasound guidance.<sup>21,33,34</sup> For these reasons, FNA is performed exclusively in selected cases in our department.

As mentioned above, metaplastic cystadenolymphomas are characterized by several layers of squamous epithelium, isolated goblet cells, and often by regressive changes with only a few foci of oncocyctic cells<sup>7</sup> (Figure 3). This could be the reason for several differential diagnostic problems: squamous cells can be also found in aspirates from mucoepidermoid or squamous cell carcinoma. The presence of intermediate and mucous cells indicates mucoepidermoid carcinoma, whereas high-grade nuclear features and a total absence of oncocytes favor squamous cell carcinoma.<sup>32</sup> In principle, invasive and atypical tumor cells should raise the suspicion of malignancy.<sup>8</sup> Cysts (epidermal or lymphoepithelial) of the parotid gland,<sup>35</sup> from chronic inflammatory and obstructive duct lesions,<sup>32</sup> may

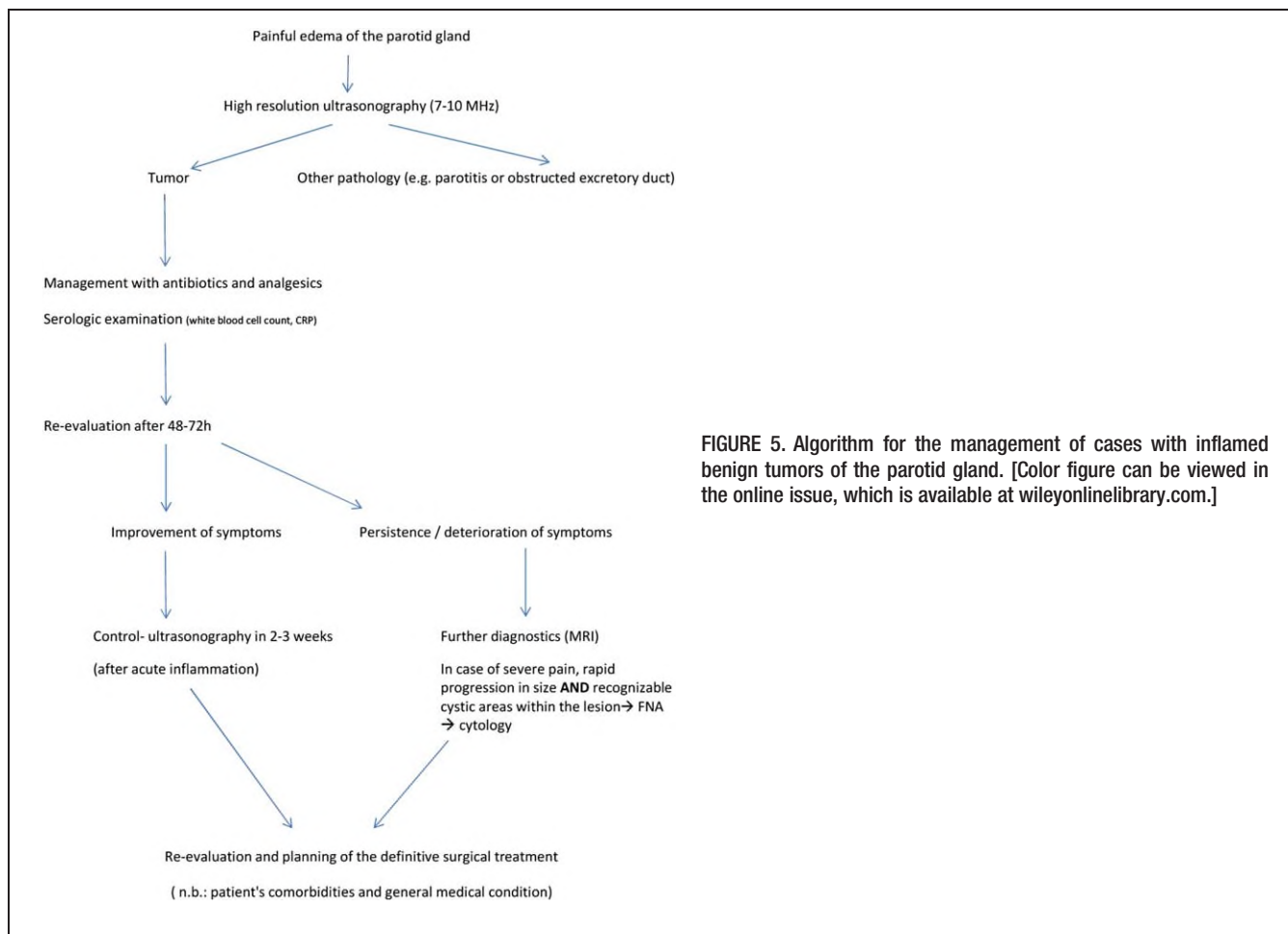


FIGURE 5. Algorithm for the management of cases with inflamed benign tumors of the parotid gland. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

accumulate fluid and show squamous metaplasia, thus widening the differential diagnosis and enhancing the possibility of diagnostic confusion.

Interestingly, in 7 cases of the initial patient group (7 of 23), an unexpected diagnosis was shown on permanent histology. This information led to some useful, clinically relevant, conclusions. First, clinical signs of local inflammation, even in combination with clearly defined margins on ultrasound, do not definitely rule out a covert parotid malignancy, emphasizing the need for prompt histopathologic diagnosis. In our initial sample, an adenocarcinoma (not otherwise specified) with aggressive behavior and unfavorable prognosis imitated the sonographic features of a benign tumor (clearly defined margins, regular contour) and “hid” behind an acute painful parotid swelling with local redness. Second, a well-defined lesion seen in the parotid gland on ultrasound does not always turn out to be a tumor but could be associated with localized chronic inflammation (Table 1). In such cases, only a high index of suspicion, taking the clinical and imaging findings into account, will allow prompt and successful management without immediate radical surgery. Further examination with MRI could be eventually helpful in these cases.

Considering the scarcity of literature reports and the lack of therapeutic guidelines for this rare entity, based on our findings, we put forward an algorithm on how to approach

such cases (Figure 5). First, we would recommend a conservative initial treatment with antibiotics and analgesics in all cases. In our view, FNA should not be proposed routinely because of the aforementioned debatable reliability. In cases with severe pain, rapid progression in size, and recognizable cystic areas within the lesion, ultrasound-guided aspiration could be performed for attenuation of symptoms, after which the aspirate material could be sent in for cytology. According to our experience, “close monitoring” of the clinical status, laboratory parameters, and imaging (eg, ultrasound or MRI in selected cases) findings, plus avoidance of surgery in the acute inflammation phase, are 2 important aspects in the approach to such cases. Of course, the role of surgery for purposes of biopsy, especially in still unclear cases, cannot be ignored. Considering that most of our patients were over the age of 65, one should be aware of the patient’s comorbidities and general medical condition, which could frequently determine whether or not they can even withstand surgery. The data point to the need for close monitoring of patient status and timely decision-making.

In conclusion, our study reports the first cases in which an inflamed benign tumor proved to be a benign tumor other than a cystadenolymphoma, accounting for more than a quarter of our cases. Critical analysis of our cases revealed possible pitfalls in the differential diagnosis

because of diverse, overlapping clinical, imaging, and histologic findings. Signs of inflammation and (rarely) facial palsy, poorly defined lesion contours on ultrasound, and the presence of squamous metaplastic changes on cytology offer ideal circumstances for diagnostic errors.

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