

Dear Editor:

Thank you for reading our manuscript and considering it for publication.

I am pleased to resubmit for publication the revised version of manuscript #53248

“Various diagnostic possibilities for zygomatic arch pain: case series and literature review”

The constructive comments of the reviewers have been thoroughly considered and reflected in the revised manuscript.

I have addressed the concerns of the reviewers as outlined below. The answer is described below each reviewer’s comment.

I believe that the content of the manuscript has been expanded thanks to the reviewers’ comments and will be able to benefit the readers. Although zygomatic arch pain may only be a part of the symptoms of a patient with orofacial pain this case report and literature review shows that various underlying causes may appear as the same symptom in the clinic. So cautious and thorough investigations on part of the clinician are necessary to avoid misdiagnosis. The authors believe that this manuscript will be able to provide a comprehensive review to help the clinician when treating an orofacial pain patient presenting with pain concentrated in the zygomatic arch region.

Reviewer 1:

1. Clarify the etiology of case 1: muscle pain & osteoarthritis of joint; case 6: myositis & osteoradionecrosis. What really makes the large differences between the 2 cases?

Re: Thank you for your review.

In both case 1 and case 6, pain in the zygomatic arch region was caused by muscle problems. However, myalgia (muscle pain) and myositis were classified into two separate cases because the original cause of the muscle problem and treatment methods differed.

As in case 1, myofascial pain is a non-inflammatory condition and is mainly caused by muscle overuse, trauma, parafunctional habits and shows a close relationship with psychological state. Treatment of myofascial pain generally includes medication, physical

therapy, and behavioral therapy.

On the other hand, the case of myositis presented in this report was an inflammatory muscle disorder caused by radiation therapy. Inflammation may also be caused by infection, trauma or prolonged muscle tension. Myositis can be divided into infectious and non-infectious subtypes. In non-infectious myositis, persistent muscle pain may cause a change in the central nervous system, and thus is called centrally mediated myalgia which is associated with neurogenic inflammation. In the case of non-infectious myositis, treatment is similar to that of myofascial pain as mentioned above. However, infectious myositis occurs with bacterial or viral infections and is accompanied by typical signs of inflammation, such as swelling, rupture, and fever. In this case, enhanced CT or MR imaging may be necessary to find the site of infection. Also treatment with anti-inflammatory drugs and antibiotics may be called upon, and a multidisciplinary approach may be necessary depending on the source of infection.

For the reader's better understanding and following the reviewer's indication, we combined the two cases into one category under the case title "Masticatory muscle disorders", and then divided into subtitles "Myofascial pain" and "myositis" as below.

Case 1: Masticatory muscle disorders

Case 1.1 Myofascial pain

Case 1.2 Myositis

The cause of case 1.1 was more definitely described in the final diagnosis section as "The main cause of the patient's zygomatic arch pain was diagnosed as myofascial pain of both masseter muscles and osteoarthritis of the left mandibular condyle".

Also discussions concerning the difference between myofascial pain and myositis were added in the Discussion section as below.

"Infection, trauma or persistently elevated muscle tension may cause inflammation. Myositis can be divided into infectious and non-infectious subtypes. In non-infectious myositis, prolonged muscle pain may lead to a change in the central nervous system, thus resulting in centrally mediated myalgia which is associated with neurogenic inflammation. However, infectious myositis occurs with bacterial or viral infections and is accompanied by typical

signs of inflammation, such as swelling, rupture, and fever” and “Treatment of myofascial pain is generally conservative including medication, physical, and behavioral therapy. On the other hand, when the pain is due to myositis caused by radiation therapy as presented in this report treatment with antibiotics may be called upon and a multidisciplinary approach may be necessary depending on the source of infection”.

2. Etiology of both cases 2 & 3 are related to dental problem. What really makes the large differences between the 2 cases?

Re: Thank you for your comment. It is clear that the two cases were due to dental problems causing odontogenic pain, but tooth crack and dental caries, which were the cause in each case, have distinct pain characteristics. The cracked tooth is more frequently accompanied by sharp pain, which lead to the initial misdiagnosis of neuralgia. Dental caries presents a more dull pain similar to muscle pain, making diagnosis difficult.

Different pain patterns may appear depending on the cause of toothache, so there may be difficulties in differential diagnosis. Both cases were included to emphasize the importance of applying various tests to thoroughly rule out all possibilities.

We agree that the reader may more easily understand the flow of this article if the two cases were put into the same category of odontogenic pain and then subdivided into subcategories. The manuscript has been reorganized as below.

Case 2: Odontogenic pain

Case 2.1 Tooth crack

Case 2.1 Dental caries

3. On the other hand, the manuscript has some merits regarding the proposed issue. I encourage the authors to expand, restructure and reorganize their manuscript to upgrade it to a review article to summarize the current state-of-the-art understanding of the topic.

Re: Thank you for your kind review. We agree with your suggestion and have followed your recommendations to further improve this manuscript.

As for etiologies that could cause pain in the zygomatic arch area, we added information on neoplasms and temporal tendinosis, which were not mentioned before but could be found in

the literature, and also on a rare case report of pain in the zygomatic arch region due to cardiac problems. The discussion section has been expanded to include all literature directly related to pain appearing in the zygomatic arch region and corresponding references have been listed as below. We believe that this addition will help provide a broader perspective for the reader that is interested in this specific area of pain.

“Temporal tendinosis has also been cited as a cause of orofacial pain in recent literature so should be considered when the patient complains of pain occurring in the zygomatic arch region[35]. Tendinitis is inflammation located in the tendon, while tendinosis is a degenerative state caused by persistent overuse and lacks signs of inflammation both clinically and histologically[36]. Tendinosis is commonly misdiagnosed as tendinitis. Temporal tendinosis is typically accompanied by chronic pain of the orofacial region and stiffness in the temporalis muscle area that is exacerbated by jaw function. Mouth opening limitation can be observed in certain cases. Temporal tendinosis can be easily overlooked in the differential diagnosis of pain in the zygomatic arch region because of the anatomic complexity of the area. Since palpation shows low sensitivity and specificity in its diagnosis, imaging especially ultrasound should be considered when the presence of temporal tendinosis is questioned[35]”

“Referred pain due to coronary insufficiency may also appear in the mandible, zygomatic arch, and temporal region[37]. A case was reported where facial pain, including the zygomatic arch, was caused by myocardial infarction[38]. A previous review summarized that referred pain due to cardiac origins may appear in the maxilla, mandible, zygomatic arches, submandibular, neck, temporal and teeth regions[39]. The underlying mechanism of such pain referral is complicated and it would be difficult to locate a single transmission route, but cardiac etiology could be another possibility when the cause of orofacial pain is not clinically evident[40]”

“Although relatively rare, various neoplasms of the maxillofacial region could also be another possibility. In osteochondroma affecting the coronoid process, pain was not a common symptom, but approximately 10% of the cases reported facial pain[42]. With peripheral osteoma of the zygomatic arch, some patients complained of pain[43]. When the complaint of pain in the zygomatic arch region is accompanied by swelling, facial asymmetry, and limited mouth opening, appropriate imaging should be performed with the above diagnoses in mind”.

Added reference list

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43. Autorino U, Borbon C, Malandrino MC, Gerbino G, Roccia F. Surgical management of the peripheral osteoma of the zygomatic arch: A case report and literature review. *Case Rep Surg* 2019; 2019: 6370816 [PMID: 31316857 DOI: <https://doi.org/10.1155/2019/6370816>]

Reviewer 2:

This is a report of a few cases of orofacial pain around the zygomatic area. The truth is this article does nothing to improve the existing knowledge of orofacial pain, and zygomatic area is just a small part of the whole maxillofacial region. Having said that, this manuscript does illustrate to the readers how the various causes of orofacial pain could be diagnosed, and for that reason I'd recommend publication of this manuscript in the *World Journal of Clinical Cases*.

Re: Thank you for your kind review.

I believe this manuscript will contribute to the reader's understanding of diseases that may present with zygomatic arch pain, thus providing guidance for the clinician in its diagnosis and treatment.

Thank you once again for reviewing this manuscript and providing helpful comments.

Pain of the zygomatic arch region is common among patients with orofacial pain but the causes vary and could easily result in misdiagnosis. However, we have not yet been able to find a comprehensive review and case report concentrating on this specific region. Therefore, I believe this manuscript will contribute to the reader's understanding of diseases that may cause zygomatic arch pain and aid in its clinical diagnosis and treatment.

Sincerely,

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