

Pathogenesis of temporomandibular joint ankylosis: A perspective

Sir,

The following write-up is to string the known facts in one thread to explain all the etiologies of temporomandibular joint (TMJ) ankylosis.

While being the most common etiology, a very minor percentage of condylar trauma patients progress to ankylosis; others regain normal function despite conservative/no treatment. Besides, computed tomography scans of TMJ ankylosis show hyperdense bone beyond the anatomical boundaries of the joint, in the mandibular ramus, and at the cranial base. Likely, there are differences in response to injury between ankylosis cases and others.

A significant percentage (21.9%) of ankylosis patients have procoagulant states of blood, pointing to hitherto unknown links between processes, leading to TMJ ankylosis.^[1] The prevalence of hypercoagulability in ankylosis patients goes quite above the figures for general population. Following trauma, the extent of hypoxia at the fracture site plays an important role in determining the amount of callus formation and course of healing. Hypoxia induces *HIF-1α* and its downstream gene *VEGF*. Posttrauma expression of TGF-β superfamily genes, importantly many BMPs, initiate angiogenesis; osteoblast precursor cells accompany these newly forming endosteal blood vessels and penetrate hematoma from the adjacent medullary cavity.^[2] In a procoagulant/hypofibrinolytic state, conceivably, clotting process may involve more of medullary capillaries and the hypoxia would be enhanced. The scaffold of hematoma stays longer *in situ*, allowing the newly forming blood vessels to spread. Just enough immobilization at this vascularization phase can then lead to callus formation [Figure 1]. In addition, protein C has anti-inflammatory properties; hence, in deficiency states, children might have more and prolonged duration of swelling and pain posttrauma, thereby reducing their use of joints and causing indirect immobilization.

Hypoxia induces multiple effects on different cell types [Figure 2]. It causes a reversible state of quiescence in osteoblasts and promotes osteoclastic activity. However, osteoblasts survive and start osteogenesis once hypoxia

reverse.^[3] Hypoxia also facilitates recruitment and osteogenic differentiation of multipotent mesenchymal stromal cells using *HIF-1α* and *RUNX-2* genes.^[4] However, some reports suggest that on the contrary, hypoxia rather promotes chondrogenesis.^[5] This incongruity among experiments may be due to laboratory conditions such as different levels and duration of hypoxia to treat different cell types. In a real scenario, if prolonged hypoxia causes suppression of osteogenesis and promotion of chondrogenesis, it can explain the radiolucent zone in ankylosis and its longer course to ossification. It is plausible that the internal milieu and external mechanical factors together govern the pathogenesis.

During varicella infection and childhood sepsis (other known causes behind ankylosis), protein S levels are reduced. In many cases, there is physiologic protein C deficiency in the perinatal period; increasing risk of ankylosis even with minor trauma by forceps delivery. *In vitro* studies have suggested protective effects of activated protein C in rheumatoid arthritis. In deficiency states, there could be excessive destruction during an active inflammatory period followed by surge in bone deposition. Activated protein C in a hypoxic wound can also play its tweaking role on type of differentiation the mesenchymal stem cells undergo. Hence, research on effects of different levels of hypoxia and activated protein C (APC) on stem cells is the way forward.

Financial support and sponsorship

Nil.

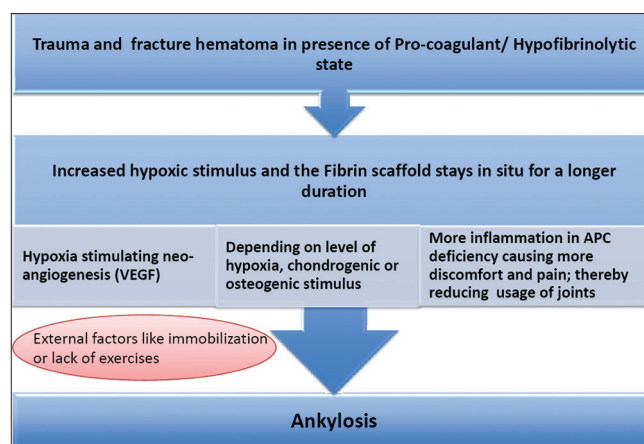


Figure 1: Proposed pathway of ankylosis in procoagulant state

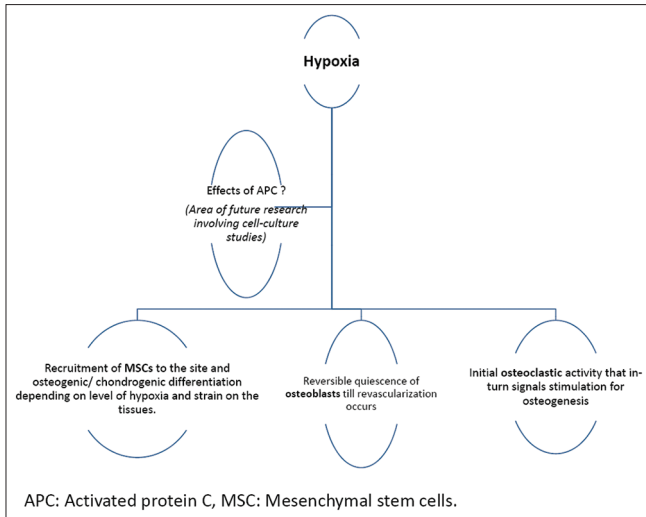


Figure 2: Effects of hypoxia on mesenchymal stem cells, osteoblasts, and osteoclasts

Conflicts of interest

There are no conflicts of interest.

KRUSHNA V. BHATT, AJAY ROYCHOUDHURY, ONGKILA BHUTIA

Department of Oral and Maxillofacial Surgery, All India Institute of Medical Sciences, New Delhi, India
E-mail: bhatt_krushna@yahoo.com

Received: 27 December 2018, **Revised:** 17 February 2019, **Accepted:** 28 May 2019, **Published:** 18 June 2020


REFERENCES

1. Bhatt KV, Roychoudhury A, Bhutia O, Saxena R, Subbiah V,

Chattopadhyay P, *et al.* Study of risk factors for developing post-traumatic temporomandibular joint ankylosis. *Eu J Oral Maxillofac Surg* 2019;3:12-6.

2. Ferretti C, Bryant R, Becker P, Lawrence C. Temporomandibular joint morphology following post-traumatic ankylosis in 26 patients. *Int J Oral Maxillofac Surg* 2005;34:376-81.
3. Utting JC, Robins SP, Brandao-Burch A, Orriss IR, Behar J, Arnett TR. Hypoxia inhibits the growth, differentiation and bone-forming capacity of rat osteoblasts. *Exp Cell Res* 2006;312:1693-702.
4. Wagegg M, Gaber T, Lohanatha FL, Hahne M, Strehl C, Fangradt M, *et al.* Hypoxia promotes osteogenesis but suppresses adipogenesis of human mesenchymal stromal cells in a hypoxia-inducible factor-1 dependent manner. *PLoS One* 2012;7:e46483.
5. Huang J, Deng F, Wang L, Xiang XR, Zhou WW, Hu N, *et al.* Hypoxia induces osteogenesis-related activities and expression of Core binding factor α 1 in mesenchymal stem cells. *Tohoku J Exp Med* 2011;224:7-12.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Access this article online	
Website: www.njms.in	Quick Response Code 
DOI: 10.4103/njms.NJMS_91_18	

How to cite this article: Bhatt KV, Roychoudhury A, Bhutia O. Pathogenesis of temporomandibular joint ankylosis: A perspective. *Natl J Maxillofac Surg* 2020;11:154-5.

© 2020 National Journal of Maxillofacial Surgery | Published by Wolters Kluwer -Medknow