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Hereditary Angioedema and Orbital Cellulitis: Similarities with Dis-Similarities

Dae Wook Lee*

Takeda Pharmaceutical Ltd, Asia-Pacific Region, Singapore

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***Corresponding author:** Dae Wook Lee, Takeda Pharmaceutical Ltd, Medical Affairs, Asia-Pacific Region, Singapore.

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Introduction

Hereditary Angioedema (HAE) is a rare, autosomal dominant disorder [1-4]. The disease is a potentially debilitating life-threatening rare genetic disorder, requiring an acute and prophylactic treatments on emerging condition [2-4]. The prevalence accounts for approximately 1:10,000 to 1:50,000 [4,5] and this was estimated approximately 6,000 patients in United States [4,6]. The associated symptoms of HAE includes recurrent acute episodes of attacks in swelling of various body parts, including face, feet, hands, abdomen, and also airway involvements may also last in several days, which the episodes are not usually associated with urticaria or pruritis [1-3]. The pathophysiology on HAE is occurred by the mutation of C1-INH in Chromosome 11, which in term characterized to abnormal levels and/or function on C1-inhibitor (C1-INH) resembling by a result of common heterogeneity as spontaneous mutation [7,8]. This is due to the excessive generation of Bradykinin in combined results of contact and fibrinolytic pathways impacting via pro-inflammatory kallikrein-kinin system, leading to the enhance the vascular permeability by mimicked vasoactive peptide Bradykinin to extravasation of plasma to localized cutaneous or mucosal edema [1,9,10]. Based on C1-INH levels/functions and C4 levels, HAE subtypes from I-III are classified for their disease state [2]. Although the severe form on laryngeal involvement in edema will carry the risk on asphyxiation [1,3] HAE could potentially and frequently misdiagnosed to other allergic conditions due to the rarity and multiple origins of symptoms which could be associated with other conditions, as a result diagnosis of HAE is often mis-diagnosed and under-diagnosed which also lead to unnecessary delays on diagnosis, surgery or treatments [3,11]. The current studies on both retrospective and prospective including the surveys in both perspectives of physicians and the patient have shown the substantial and multi-faceted burden on HAE as debilitating condition, which HAE could induce the major impact on overall quality of life on patients with consequential burden on socio-economic complexity in their most daily aspects [3,12]. One of the recent references from Lumry et al reported that the average annual healthcare burden for individual patient in 2017 for their economic consumption on overall direct and indirect cost was foreseen approximately over $65,000 [12]. In contrary, orbital cellulitis (OC) is an inflammatory condition which manifests infectious inflammation of tissues inside on bony orbit posterior to the orbital septum [13]. OC affects approximately 1.6:100,000 in pediatric patients and account by 0.1:100,000 in overall population [14]. The classic definition of their segmentation on orbital complication of acute sinusitis reports the grouping of orbital conditions from I-V including orbital cellulitis (group II), whereas simplified version from Jain and Rubin described from I-III with OC (group II) including possibility of intracranial complications [15].

The clinical symptoms of OC with most common presentation as swelling and erythema of eyelid, conjunctival chemosis, lacrimal discharge, and pain associated particularly with eye movement, which in severe also causes drooping of eyelid as ptosis [16-18]. Unlike symmetric facial presentation of HAE mimicking symptoms and signs, OC commonly presents as unilateral manifestation. However untreated OC have potentially a severe life-threatening complication and visual deterioration, which more serious complications including optic neuropathy, brain abscess, permanent loss of vision and meningitis by extensive inflammation especially more vulnerable sub-population as pediatric patients [19], hence their accurate diagnosis and proactive treatment is key to define the goal on symptom remission [16]. The original of microbiological organisms to infection could be either single or multiple sources that are usually defined by nasal and throat swab or

ocular lachrymal secretions including materials obtained from sinus aspirates and orbital abscess in culture is generally an identifiable investigation to perform for the diagnosis and consideration of their choice based on medical treatment of anti-biotics regime [16,20]. For additional diagnostic imagining tool such as orbital CT scan proves their effective confirmation which are helpful on monitoring of OC especially when orbital abscess with their location and estimated diameters [13]. The treatment for OC emerges with accelerated diagnosis and migrating medical treatment as essential cascade to prevent further extension on orbital complications [13]. Hence their focused anti-biotic treatment regimen ranged their intravenous duration as 1-2 weeks with up to four weeks of oral therapy based on the identified source of causative micro-organism including Third generation Cephalosporin, Metronidazole, and flucloxacillin, etc [16,21]. In hereditary Angioedema, the treatment objective is according to the most recent international WAO/EAACI guideline 2017 to enhance and support the diagnosis and management of HAE worldwide with individualized treatment plan [22]. The treatment includes effective on-demand regimen additionally with home care and self-administration including their family screening to manage incidental HAE attacks such as C1-esterase inhibitors or bradykinin B2 receptor antagonist as icatibant [23-25]. Moreover, the plan on prophylaxis require a regular assessment for efficacy and safety on therapy dosage and interval which could be reflected by their individual clinical response [22]. Prophylactic agents as C1-esterase inhibitors and recent plasma kallikrein inhibitor are commonly used, which in particular multi-national HELP research group recently reported in phase III randomized clinical trial that plasma kallikrein inhibitor showed a significant reduction in the number of attack episodes in compared with placebo in 26 weeks of administration in HAE type I or II [26]. In overall, both HAE and OC have a rare modality of swelling in facial compartments requiring an acute and proactive treatments on their clinical manifestation with paucity of current evidences, however their in-depth understanding on pathophysiolgy and orientation of etiology induces more emphasis of precise acknowledgement of rare disease state including their characteristic and general awareness for managing a prompt diagnosis in their earlier stage to address the acute and long-term symptom management [27-29].

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