Meige's Syndrome

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The terms "Meige's syndrome" and "Meige syndrome" are often used by neurologists and other clinicians to describe the combination of blepharospasm and involuntary movements of the lower facial and/or masticatory (jaw) muscles. Application of Meige's syndrome and other eponyms to the various forms of dystonia is problematic for a multitude of reasons. First of all, Meige, a physician, did not suffer from the syndrome which bears his name. Along this line, the possessive form of eponyms has been discouraged by the Council of Science Editors and the father of Online Mendelian Inheritance in Man®, the late Dr. Victor McKusick. Second, Meige was not the first person to describe the combination of blepharospasm and dystonia of other cranial muscles. Lastly, Meige's or Meige syndrome could be confused with Meigs syndrome which is defined as the triad of a benign ovarian tumor, ascites (fluid in the abdominal cavity) and a pleural effusion (fluid in the chest cavity).

Historical Perspective: Dr. Horatio Wood, a Philadelphia neurologist, first drew attention to blepharospasm and other cranial dystonias in 1887. Wood briefly mentioned facial and oromandibular dystonia in his textbook on disorders of the nervous system. He stated, "The contraction is tonic, causing a complete closure of the eye, and consequent blindness. This is accompanied by innumerable bizarre grimaces, due to the efforts of the antagonistic muscles to overcome the force which is closing the lids." Clearly, his second sentence was incorrect.

In 1910, Henri Meige, a French neurologist, described approximately ten (he did not provide an exact number!) patients with involuntary closure of the eyelids. Blepharospasm was associated with involuntary contractions of the jaw muscles in only one of these patients. Over 60 years later, an American neurologist, George Paulson, described three patients with blepharospasm and oromandibular dystonia and emphasized the probability of a common pathophysiological basis.

In 1976, David Marsden, an English neurologist based in London, called attention to a work of art, *De Gaper*, by Pieter Brueg(h)el the Elder, a Renaissance painter, in an article on blepharospasm and oromandibular dystonia. Brueg(h)el the Elder was not a physician and his painting of a yawning man has nothing to do with dystonia. Pieter Brueghel the Elder dropped the 'h' from his name in 1559, one year after painting the "Head of a Yawning Man." Brueghel the Younger was also a painter, further confounding historically exact usage of this eponym.

Careful inspection of the relevant medical literature over the past 30 years indicates that "Brueghel" and "Meige" syndromes remain poorly delineated. One author, Dr. Gordon Gilbert, suggested that the essential sign of Brueghel syndrome is "a widely and dystonically opened jaw." In reality, however, jaw-opening dystonia may occur in the setting of multifocal or generalized dystonia and is often associated with blepharospasm; application of Brueughel syndrome to these cases would be unnecessarily complicated and confusing. Marsden, in the title of his 1976 article on the subject, actually defined blepharospasm-oromandibular dystonia syndrome as Brueghel's syndrome and he did, in fact, use the possessive eponym.

Anatomically-Based Classification of Dystonia by Distribution: In 1984, an *Ad Hoc* Committee of the Dystonia Medical Research Foundation developed a widely-accepted definition of dystonia and classification of dystonic movements. Dystonia is characterized by sustained muscle contractions, usually producing twisting and repetitive movements or abnormal postures. Almost all dystonic movements share a directional quality that is typically

sustained, sometimes for only an instant. Dystonia is often precipitated by action. In focal dystonia, a single body part is affected. Common types of focal dystonia are blepharospasm, laryngeal dystonia, writer's cramp, and cervical dystonia (also called spasmodic torticollis). The term "segmental dystonia" is used to describe involvement of two or more contiguous regions of the body. Furthermore, the segmental dystonias were subdivided into regional categories: cranial, axial, brachial, and crural. With this classification scheme, segmental "cranial" dystonia was used to indicate involvement of any combination of musculature in the head and neck region. In reality, however, the neck and mandible are not parts of the cranium. Therefore, the combination of blepharospasm, masticatory dystonia, and cervical dystonia, for example, is more precisely classified as segmental "craniocervical" dystonia rather than segmental "cranial" dystonia.

In most patients, use of the term "**segmental craniocervical dystonia**" may be more accurate than "segmental cranial dystonia" for several additional reasons. First, involuntary contractions of the platysma muscle can be seen in an important percentage of patients with blepharospasm. The platysma is innervated by the facial nerve, the same nerve which innervates the orbicularis oculi muscles in the eyelids. The platysma is a broad, thin, superficial muscle that extends from the upper chest, shoulder and clavicle upwards to the chin, mandible and lower face. Second, the pharyngeal or swallowing muscles, which can be affected in dystonia, encompass both the cranial and cervical regions. Similarly, several muscles involved in jaw-opening originate in the cervical region. Based on these considerations, "segmental craniocervical dystonia" would cover virtually all past clinical utilization of the terms "Meige syndrome" and "Breughel syndrome."

Clinical Features of Segmental Craniocervical Dystonia: Patients with blepharospasm may also have lower facial dystonia, masticatory (jaw muscles) dystonia, lingual (tongue) dystonia, pharyngeal (swallowing) dystonia, laryngeal (voice box) dystonia, or cervical (neck) dystonia. Involvement of the lower facial and masticatory muscles is fairly common in patients with blepharospasm. Involuntary lower facial and masticatory movements may include lip pursing, chewing, jaw thrusting, jaw opening, and jaw closing/clenching. In some patients, the lower facial and jaw movements may be rhythmic or tremor-like. In addition, the involuntary lower facial and jaw movements seen in patients with blepharospasm may not result in sustained postures and, as such, may not be compatible with the definition of dystonia. Instead, these involuntary movements are oftentimes described as dyskinesias, a poorly-defined term which may include several forms of involuntary movements (e.g., chorea, athetosis, and myoclonus), each of which carries a more precise meaning.

Most of the time, dystonia begins focally. Over time, however, dystonia may spread to involve other muscles of the body. Most commonly, dystonia spreads to contiguous muscles. For example, when blepharospasm does spread, it typically spreads to the lower face and/or masticatory muscles. Rarely, dystonia may spread to more distant muscles in the arms and legs. Although the probability of spread is highest within the first 3 years after dystonia onset, spread may occur a decade or more later. In patients with blepharospasm, older age-of-onset and female gender may increase the risk of spread. Overall, patients with initial onset of dystonia in the eyelids (i.e., blepharospasm) have at least a 50% lifetime probability of spread.

Segmental craniocervical dystonia should be diagnosed by a clinician with extensive experience in movement disorders. Although usually idiopathic, segmental craniocervical dystonia may be associated with neurodegenerative disorders such as progressive supranuclear palsy or caused by medications which block dopamine receptors in the brain such as antiemetics (e.g., metoclopramide) and antipsychotics (e.g., haloperidol). Oftentimes, a brain MRI scan and blood tests are ordered to exclude the possibility of secondary causes such as Wilson's disease or a stroke. In most cases, all diagnostic studies will prove to be normal. The

term "idiopathic" does preclude a distinct genetic etiology or genetic contributions, however, since blepharospasm and segmental craniocervical dystonia clearly have a hereditary component. In this regard, some studies have reported that over 10% of patients with blepharospasm and other forms of craniocervical dystonia have at least one first- or second-degree relative with dystonia.

Blepharospasm and segmental craniocervical dystonia are significantly more common in women with a male:female ratio of roughly 1:2. The average age of onset for blepharospasm is around 55 years whereas the average age of onset for jaw dystonia is only a couple of years earlier. In comparison, cervical and focal hand/arm dystonia begin approximately one and two decades earlier, respectively. Of note, these are only averages and, occasionally, patients may have disease onset in their twenties or seventies.

Treatment: Segmental craniocervical dystonia is commonly treated with injections of botulinum toxins. Successful treatment of dystonia with injection of botulinum toxins is both art and science and not all artists and scientists are created equal. Results depend on accurate targeting of affected muscles with an appropriate amount of toxin. Electromyographic guidance is normally used when injecting jaw, laryngeal, and neck muscles.

A long list of oral medications has been used to treat segmental craniocervical dystonia. Unfortunately, the magnitude of improvement typically obtained with commonly used drugs such as the anticholinergics (e.g., trihexyphenidyl and benztropine), benzodiazepines (e.g., clonazepam, lorazepam), baclofen, and tetrabenazine is often modest at best.

In recent years, deep brain stimulation (DBS) has garnered increasing attention as a therapeutic option in patients with intractable dystonia. DBS has been associated with dramatic benefit in patients with DYT1 generalized dystonia. Currently available data suggests that DBS is also an effective treatment for many, but not all patients with segmental craniocervical dystonia. DBS is associated with a small risk of stroke, infection, and the development of new neurological signs and symptoms. DBS should be seriously considered only if other treatment options, administered by skilled and experienced neurologists, are ineffective.

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