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Dysphagia

Neurologic Causes of Dysphagia

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Abstract. Pharyngeal dysphagia may be caused by any of a wide variety of neurologic diseases, but the possibility of neurologic disease is often overlooked in the evaluation of dysphagia. This is especially unfortunate because some of the neurologic causes of dysphagia are treatable. This review organizes the neurologic causes of dysphagia into a simple framework that facilitates consideration of these diseases. Methods of evaluating neurogenic dysphagia, including history taking, physical examination, and laboratory testing, are to be considered separately in a subsequent article.

Key words: Neurologic disease – Dysphagia – Choking.

The cerebral cortex controls voluntary aspects of feeding, such as food preparation and swallow initiation. Corticobulbar tracts descend bilaterally from the cortex to the "bulb," which includes the pons and medulla. These tracts carry messages to the bilateral brainstem centers that command the muscles of swallowing. These brainstem centers include both well-recognized cranial nerve nuclei, such as the nucleus ambiguus, as well as ill-defined groups of neurons nearby that are vital for regulation of swallowing. The input from each cerebral hemisphere to the brainstem nuclei is distributed bilaterally, so that centers on both sides of the brainstem continue under cortical influence even when one cortex or its descending corticobulbar tract is impaired.

In addition to the descent of messages regarding motor function, there is ascent of sensory information from brainstem to higher centers. This sensory feedback about bolus characteristics, head position, and muscle activity is essential for normal swallowing performance.

The brainstem can initiate swallowing without cortical input, and it governs the involuntary phase of swallowing after swallow initiation. Muscles on each side of the tongue, palate, pharynx, and larynx are controlled by cranial nerves from ipsilateral brainstem motor nuclei. Cranial nerves communicate with their target muscles across neuromuscular junctions by release of the neurotransmitter acetylcholine that binds to muscle receptors. If the stimulation of muscle contraction by acetylcholine is properly orchestrated by the cortex and brainstem, then a bolus is propelled from the oral cavity through the pharynx and into the esophagus without penetration into the nasopharynx or larynx.

The esophagus has an intrinsic neural network that regulates peristalsis, although the brainstem is capable of overriding inherent esophageal motility. For example, the esophageal peristaltic wave is interrupted whenever a new pharyngeal swallow occurs.

In simple terms, swallowing has three phases: oral, pharyngeal, and esophageal. The oral (voluntary) phase is influenced by both the cortex and brainstem, the pharyngeal (involuntary) phase is controlled by the brainstem, and the esophageal phase is mediated by both the brainstem and intrinsic esophageal neurons. As a general rule, neurologic disease causes dysphagia by interfering with the oral and pharyngeal phases of swallowing, and whatever esophageal impairment occurs is less likely to be the primary source of symptoms.

Dysphagia may result from disease of the cerebral cortex and brainstem, cranial nerves, neuromuscular junction, or muscles of swallowing. Using this framework, specific neurologic diseases

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causing dysphagia are reviewed. First, the terms "bulbar palsy" and "pseudobulbar palsy" require definition. *Bulbar palsy* is a syndrome of weakness of lower brainstem-controlled muscles, including those of the face, tongue, palate, pharynx, and larynx. Its prominent symptoms are dysphagia and dysarthria. Bulbar palsy implies dysfunction of the motor unit, which is a lower motor neuron and the muscle it innervates. Diseases causing bulbar palsy may affect cranial nerve nuclei, cranial nerves, neuromuscular junctions, or muscle. The pharyngeal (involuntary) phase of swallowing is most impaired.

Pseudobulbar palsy is similar to bulbar palsy in that dysfunction of muscles results in dysphagia and dysarthria. However, the dysfunction is due to corticobulbar tract (upper motor neuron) disease, rather than motor unit disease. As long as one corticobulbar tract is functional, swallowing can proceed fairly normally, because each tract by itself supplies both sides of the brainstem with cortical input. Pseudobulbar palsy must therefore be caused by *bilateral* corticobulbar tract disease, and the oral (voluntary) phase of swallowing is most affected.

Diseases of the Brain and Brainstem

Vascular disease

Stroke is probably the most common neurologic cause of dysphagia. If only one cerebral hemisphere is affected by a stroke, then swallowing is usually preserved because the brainstem still receives input from the other hemisphere. However, there may be impairment of the oral phase of feeding, such as swallowing *apraxia*, a disorder of voluntary motor control in which the patient behaves as if he or she has forgotten how to feed. In addition, unilateral cerebral stroke may cause contralateral face and tongue weakness that results in poor bolus control within the oral cavity. If a unilateral cerebral stroke is massive or if there is coexisting disease in the other cerebral hemisphere, then more profound dysphagia may occur.

Carotid artery atherosclerosis is the most common cause of hemispheral stroke. It is best treated preventively by reduction of such risk factors as hypertension and by use of antiplatelet medication, such as aspirin in low dosage. Acute stroke management is primarily supportive, and oral feeding should be done cautiously if at all in the immediate poststroke period, at least until the patient is neurologically stable.

Lacunar strokes are tiny lesions deep in the brain caused by hypertensive small vessel occlusive disease. These lesions are often multiple and bilateral, and they tend to occur in the deep white matter from which the corticobulbar pathways descend. Bilateral lacunar strokes are therefore a cause of pseudobulbar palsy.

Brainstem stroke due to either atherosclerotic large vessel disease or hypertensive small vessel disease may result in pseudobulbar palsy, if the corticobulbar tracts are interrupted bilaterally in the upper brainstem, or bulbar palsy, if the lower brainstem nuclei themselves are damaged. The lateral medullary (Wallenberg) syndrome is a common and easily recognizable type of brainstem stroke that is usually due to unilateral vertebral artery occlusion. Along with dysphagia, these patients present with some combination of dysarthria/hoarseness, vertigo, ataxia, nausea/vomiting, hiccups, ipsilateral Horner's syndrome (ptosis and miosis), ipsilateral facial numbness, and contralateral body numbness.

Intracranial hemorrhage has many causes and takes many forms, including subdural, subarachnoid, intraparenchymal, and intraventricular bleeding. The occurrence of dysphagia in these cases, as in any type of stroke, depends on the location and extent of brain injury and the presence of secondary complications, such as local mass effect and increased intracranial pressure.

Patients with stroke and dysphagia are often excellent candidates for swallowing rehabilitation, because their usual prognosis is for at least partial spontaneous recovery. Competence of pharyngeal swallowing can be facilitated by specific exercises and modification of feeding habits and diet. Dynamic imaging of swallowing (cine- or videofluoroscopy studies) is helpful in guiding rehabilitation efforts by providing visual evidence of the effect of therapeutic maneuvers upon swallowing performance.

Multiple Sclerosis

Multifocal white matter lesions occur in multiple sclerosis (MS) as a result of immune-mediated damage to myelin, the insulating material of nerve fibers in the CNS. The course is usually relapsing and remitting, but may be steadily progressive. There is as yet no consistently effective treatment, although immunosuppression may prove to be of benefit in selected patients.

The symptoms of MS vary according to the location of disease in each case. Dysphagia may be caused either by bilateral corticobulbar tract

lesions or lower brainstem lesions. Patients with relapsing/remitting disease and dysphagia may require temporary nasogastric tube feeding and may benefit from swallowing rehabilitation as recovery begins. Chronically progressive MS patients with dysphagia are more likely to eventually require gastrostomy for feeding.

Motor Neuron Disease (MND)

Also known as *amyotrophic lateral sclerosis* (ALS), MND is a common cause of insidious dysphagia and dysarthria, especially in the elderly. The disease is idiopathic, untreatable, and progressive over its course, which typically lasts several years. Both upper and lower motor neurons in the brainstem and spinal cord may be affected, and the impact of MND is therefore widely variable, depending on the type and location of involvement.

Either bulbar palsy, pseudobulbar palsy, or a combination of the two are seen in cases of MND. The disease may be unrecognized until late in its course if the limbs are relatively spared. Gastrostomy is often necessary in order to maintain hydration and nutrition and to avoid aspiration pneumonia and asphyxia.

Movement Disorders and Neurodegenerative Diseases

Parkinson's disease is a treatable condition involving degeneration of dopamine-producing neurons in the substantia nigra. The classical syndrome includes hand tremor at rest, muscle rigidity, slowness of movement, and postural instability, but patients often either lack certain elements of the syndrome or possess additional features, such as dysphagia. Treatment with L-dopa relieves the symptoms and feeding is improved not only by reducing oral and pharyngeal impairment but also by enhancing upper extremity function.

A variety of less common, untreatable neurodegenerative diseases affecting the brainstem also may cause dysphagia: these include *spinocerebellar degeneration, olivopontocerebellar atrophy* and *progressive supranuclear palsy. Huntington's disease* is a hereditary condition dominated by dementia and involuntary movements, but dysphagia invariably develops at some point in its course. In children, a myriad of *metabolic diseases* and enzyme defiiciencies lead to progressive neurologic dysfunction, including feeding impairment.

Dementia may occompany other neurologic deficits, as in the case of Huntington's disease, or it may be the sole manifestation of a neurodegenerative illness, such as *Alzheimer's disease*. Dysphagia in Alzheimer's disease primarily results from oral (voluntary) phase impairment. Management is supportive, although there is hope that replacement of the deficient neurotransmitter, acetylcholine, may someday be possible, analogous to the correction of dopamine deficiency in Parkinson's disease.

Movement disorders, such as *dystonia* and *dyskinesia*, are characterized by involuntary, localized muscle contractions. These conditions may be either idiopathic or related to a definable cause, such as chronic neuroleptic medication exposure in the case of tardive dyskinesia. If the involved musculature is facial, oral, lingual, or palatopharyngeal, then difficult feeding results. Treatment with anticholinergic and other medication is often of benefit.

Infections

Poliomyelitis, a viral infection of motor neurons, is rarely seen in its acute form today, but many survivors of bulbar polio have residual dysphagia. Some of these individuals even have slowly worsening pharyngeal dysfunction due to *progressive postpolio muscle atrophy.* This condition, which typically begins several decades after the acute illness, is thought to be due to a gradual loss of motor neurons that survived the initial illness, but have undergone premature degeneration as a result of "overwork" in compensation for depletion of the total motor neuron pool. The progressive postpolio syndrome has been confused with motor neuron disease, but it is much less rapidly advancing and disabling than MND.

Neurosyphilis can involve any part of the CNS, including corticobulbar tracts and the brainstem. The initial illness may have been unrecognized or inadequately treated, so it is important to consider neurosyphilis in cases of dysphagia of uncertain cause. The disorder can be stabilized and possibly reversed with appropriate antibiotic treatment, usually penicillin.

Encephalitis and *menigitis* caused by any of a variety of bacteria or viruses may lead to dysphagia, along with other neurologic deficits. Uncommon in the United States, such *parasitic and mycobacterial infections* as toxoplasmosis and tuberculosis may impair swallowing, depending on the location of lesions. Many of these infectious diseases are responsive to antimicrobial therapy.

Structural Lesions

Intrinsic brainstem *neoplasms*, such as gliomas, and such extrinsic tumors as acoustic neuromas

may compromise brainstem swallowing centers. Some of these lesions are treatable by surgery and radiotherapy. Developmental abnormalities of posterior fossa structures, including *Arnold-Chiari malformations* and *syringobulbia*, are associated with brainstem dysfunction, and surgical decompression may be possible.

Medication Effects

Benzodiazepines and other CNS *depressant drugs* can reversibly impair swallowing performance, especially in patients with other underlying neurologic problems. A careful medication inventory is part of the basic evaluation of a dysphagic patient. *Local anesthetics* applied to the pharynx and larynx for endoscopic procedures may temporarily reduce the sensory input from these sites that is essential for safe management of oropharyngeal secretions and food.

Other Disorders

Cerebral palsy is a term referring to nonprogressive brain damage acquired early in life from virtually any cause. Many pediatric patients with dysphagia fall into this category. *Head trauma* often results in brainstem contusion or hemorrhage that impairs swallowing. Any disease process that affects bilateral corticobulbar pathways or lower brainstem nuclei can cause dysphagia.

Diseases of Cranial Nerves

The motor signals generated by cerebral and brainstem swallowing centers are carried to the muscles of mastication and swallowing by paired cranial nerves: V (jaw), VII (face), IX/X (palate, pharynx, and larynx) and XII (tongue). These nerves may be interrupted anywhere along their course from the brainstem and subarachnoid space through exit formamina in the skull base to the neuromuscular junctions at the target muscle.

Neoplasms

Neoplastic meningitis is diffuse spread of tumor in the subarachnoid space where cranial nerves may be infiltrated and damaged.

This condition commonly occurs in leukemia and lymphoma, but may also develop with such metastatic solid tumors as lung and breast carcinoma. *Base of skull tumors*, such as meningioma and chordoma, and such retropharyngeal tumors as nasopharyngeal carcinoma can compress cranial nerves as they pass through the skull on their way to muscle. Some of these neoplasms are responsive to surgery, radiotherapy, and/or chemotherapy.

Infections

Chronic meningitis due to such organisms as tuberculosis and fungi is typically most intense in the basilar meninges where cranial nerves traverse the subarachnoid space.

Bacterial processes, such as diptheria, and such viral infections as reactivated herpes zoster (Ramsay Hunt syndrome) are uncommon causes of dysphagia due to cranial neuropathies.

Inflammatory and Immune-Mediated Disorders

Sarcoidosis is an idiopathic, multisystem granulomatous disorder that may infiltrate cranial nerves as part of sarcoid meningitis. Corticosteroids are usually effective in treating sarcoidosis. The *Guillain-Barré syndrome* is an immune-mediated demyelinating disease of peripheral nerves, often including lower cranial nerves. Impairment of nerve function may be so severe as to necessitate mechanical ventilation, but the large majority of patients recover well within weeks to months. Plasmapheresis early in the disease course hastens or improves recovery.

Diseases of the Neuromuscular Junction

Normally, acetylcholine is released from cranial nerve terminals, and this neurotransmitter then diffuses across neuromuscular junctions, where it binds to receptors on muscle endplates and stimulates muscle contraction. Diminished release or inadequate binding of acetylcholine leads to muscle weakness.

Myasthenia gravis is an autoimmune disorder in which abnormal antibodies directed against acetylcholine receptors interfere with receptor binding of the neurotransmitter. Weakness is often fluctuating and tends to occur in muscles of the eyes, pharynx, and proximal limbs. A variety of medications are effective in treating myasthenia, and some patients are virtually cured by removal of the thymus gland, which seems to be largely responsible for production of the causative antibodies.

Botulism results from a neuromuscular junction poison, botulinum toxin, which is elaborated by certain anaerobic bacteria. Most often, preformed toxin is ingested in improperly prepared food that has been contaminated by bacteria. An infantile form of the disease is due to intestinal colonization by bacteria, which then produce the toxin within the patient. The toxin impairs release of acetylcholine from nerve terminals, thereby interfering with

stimulation of muscle contraction. Both the toxin and the causative bacteria can be counteracted with medication.

The *Eaton–Lambert syndrome*, as is botulism, is characterized by impaired acetylcholine release at the neuromuscular junction. It often occurs in the setting of malignancy, such as small-cell carcinoma of the lung, and an immune-mediated process is suspected. Treatment of the underlying malignancy and modulation of the immune system can be of benefit.

Such medications as aminoglycoside antibiotics are capable of inhibiting neuromuscular junction transmission, although they rarely cause symptomatic weakness unless there is underlying neuromuscular disease.

Diseases of Muscle

Inflammatory Myopathy

Polymyositis and *dermatomysitis* are autoimmune, inflammatory muscle diseases that most often occur spontaneously, but may also be associated with underlying malignancy or collagen vascular disease, such as systemic lupus erythematosus. The muscle weakness is often insidious and diffuse, and muscles are not usually painful or tender. Recognition of this condition is important, because corticosteroids and immunosuppressants are quite effective in restoring muscle strength. *Sarcoid myopathy* is often part of systemic sarcoidosis, and it too responds to corticosteroids if the muscle has not been irreversibly damaged by long-standing disease. Inflammatory myopathy can arise from infection, such as the treatable parasitic disease *trichinosis*.

Metabolic Myopathy

Deficiencies of enzymes essential for normal muscle function can lead to either episodic or progessive muscle weakness. The term *mitochondrial myopathy* describes a group of diseases in which muscle cell energy production is impaired because of a mitochondrial enzyme defect. *Ragged red fiber disease* is synonymous with mitochondrial myopathy: its name refers to the characteristic appearance of affected muscle fibers when a muscle biopsy specimen is examined microscopically. There are CNS abnormalities associated with some forms of mitochondrial myopathy, such as the *Kearns-Sayre syndrome*, in which dysphagia can result from both pharyngeal myopathy and disordered brainstem control of swallowing. The mitochondrial myopathies are probably more common than was previously appreciated, and one variant is slowly progressive, isolated dysphagia in the elderly. Treatment in the future may be possible with replacement of the defective enzyme.

Dysthyroid myopathy, which may predominantly affect pharyngeal muscles, results from either hypo- or hyperthyroidism. Thyroid disease and myasthenia gravis often coexist, and myasthenia must be considered as a cause of pharyngeal impairment in a patient with thyroid disease.

Muscular Dystrophy

Myotonic dystrophy is the most common form of muscular dystrophy resulting in dysphagia in adults. It is an autosomal dominant disorder that causes weakness of facial, pharyngeal, and distal limb muscles, unlike most myopathies, which result in mainly proximal weakness. "Myotonic" refers to delayed relaxation of muscle following contraction so that an affected individual may have difficulty releasing his or her grip after a firm handshake. Associated nonneuromuscular features of myotonic dystrophy include frontal balding, cataracts, gonadal insufficiency, and cardiac conduction defects. The disease is idiopathic and untreatable, but swallowing problems can be managed with rehabilitation and, if necessary, tube feeding.

Other forms of muscular dystrophy, such as *Duchenne's muscular dystrophy*, are less likely than myotonic dystrophy to involve pharyngeal muscles and cause dysphagia. The signs and symptoms of *oculopharyngeal dystrophy* are ptosis, limitation of eye movements, and dysphagia, and it often occurs within families. At least some causes of oculopharyngeal dystrophy are forms of mitochondrial myopathy.

Summary

In evaluating a patient with dysphagia of unknown cause, neurologic disease must be suspected. Neurologic disease leading to dysphagia may be located anywhere from the brain to the muscles of swallowing. When neurologic disease is thought to be present, an attempt should be made to localize the disease to one of four anatomic categories: brain/brainstem, cranial nerves, neuromuscular junction, and muscle. Then, the various processes causing disease in each compartment can be considered, leading eventually to a diagnosis. A subsequent article will discuss methods of evaluation that provide the information necessary to sort out the many possibilities and arrive at the correct diagnosis of a patient with neurologic dysphagia.