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On the Etiology of Myasthenic Bulbar Palsy

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Two cases of myasthenic bulbar palsy prompt me to say something specifically about the cause of this remarkable and rare disease.

The first sufferer comes from a healthy family. It is particularly noteworthy that there is no history of neuropathological diseases in his family. Since childhood, he has suffered frequently from sore throats several times a year. In 1900 he suffered a broken nose as a result of an accident, and since that time, he has had difficulty breathing through his right nostril. Removing his pharyngeal tonsils and widening his nasal passages did not bring any improvement. In 1906, he had a mild case of diphtheria, at which time no bacilli analysis was done. Since 1912, he has suffered from alopecia. Until September 1915 he was generally fit and well, and took part in a lot of sports. Then he suddenly started experiencing double vision several times a day, particularly after intense reading, which, according to the description, could be attributed to abducens nerve palsy. After a period of rest, the double vision subsided. Healing occurred several weeks after treatment with calcium iodate and galvanic current. At the end of December 1915, he came down with influenza with a throat infection again, after which he never fully recovered. On 2nd January 1916, at the age of 20, he was conscripted. The physical exercise was very difficult for him, but he continued in the service until the end of January, when the same visual disturbances recurred, only less often, maybe 3 or 4 times a day. After an 8-day course of arsenic, these disturbances disappeared, and he went back on duty. When marching, he repeatedly became fatigued quickly and had to sit down and rest before he could continue. In the middle of March, he felt very weak and he noticed that he was unable to stretch his mouth wide, and others noticed he had a peculiar laugh too. In addition, he experienced bouts of heat and shivers, accompanied by heavy sweating. At the same time, after speaking for a long while, his speech became indistinct and he was completely unable to utter some letters, especially the letter "V." After a short period of recuperation, he was able to speak freely again for some time, until his speech eventually deteriorated and then failed him completely. A week later, he started to have difficulty swallowing, and sometimes he could get solid food down only with great effort. Liquids seeped into the nasal cavity, but that also was intermittent. On April 7th, he collapsed during exercise, and on the following day, he was so weak that he could hardly carry his weapon. For this reason he was transferred to the military hospital. The sufferer is of medium build, fairly well nourished, has a healthy-looking complexion and is continually free of fever. The heart is not enlarged, the beats are normal, the pulse is regular, pressure normal, 72 per minute. The lungs are normal, although 20 breaths are already a great strain for him. The urine is free of protein and sugar, and nothing was found at a microscopic level either.

The pharyngeal organs are somewhat hypertrophied and reddened. The uvula is displaced slightly to the right; the soft palate sags on the right. The right nasal labial fold is slightly flattened, the right corner of the mouth is somewhat deeper set, and the middle of the lower lip shows minor sagging. The mouth cannot be pulled to the right. The ability to shut both eyelids is normal. The eye movements are now free – they become weaker after prolonged movement, but don't fail significantly at this time. The pupils are equally wide and round on both sides and react promptly to light and convergence. The tendon and skin reflexes are normal, likewise there are no sensitivity dysfunctions anywhere, and the Romberg's sign is not present either. His speech, which is quite normal at first, becomes nasal and indistinct, and then some of the labial sounds cannot be pronounced at all; after a short time, whistling is not possible at all. Fatigue occurs quickly on climbing the stairs or performing arm exercises, but its intensity fluctuates.

In the right facialis area, the musculature initially reacts to the faradic current normally, but after 15 stimulations, the reaction is very weak, and after 20, hardly at all. The Wasserman blood test is negative. Nasal swabs show the presence of diphtheria bacilli, throat swabs do not. The follow-up examinations at the University clinic produced the same results over the next three months. And his condition has not changed up to now.

The other sufferer is 16 years old and is still attending secondary education. According to his information, he had influenza with a sore throat and throat coating that was not examined for bacteria. After a few days he went back to school. A week later he was suddenly unable to stand; then his left leg, followed shortly by his right leg, was paralyzed so that his toes and whole foot dropped down and could not be moved of their own volition. Then the paralysis migrated up to his arms and fingers, reached his eyes—causing double vision—and he became unable to read at a close distance and generally could not see well at all. Eventually, the entire left side of his face, the left side of his tongue and the left side of the soft palate were paralyzed. The left side of his mouth drooped, he had no sense of taste in the left half of his tongue, and liquids flowed into his nose. After six months, there was improvement. Three months after that, the paralysis recurred almost in the same sequence, but with less intensity, and lasted for only two and a half months. Then he was reasonably well, though he noticed that he sometimes suddenly felt tired while walking or running, and had to rest. Similarly, when speaking he gets stuck in the middle of a sentence and is able to continue only after a period of rest. At the beginning of May 1916, he came down with a sore throat again, shortly afterwards double vision, and in fact the left image continuously—not intermittently—deviated slightly toward the left, but at the same height. After exertion, it deviated even further to the left. However, his difficulty with swallowing now occurs infrequently, as does the penetration of liquids into the nasal cavity; and the weakness in his arms and legs appears seldomly too, but always after exertion.

The sufferer looks pale and somewhat emaciated. Lungs, heart and urine show no signs of disease. The nasal labial fold is a little flattened on the left, the left palpebral fissure is slightly wider than the right; although both eyes can be closed equally well, after many repetitions, the closure of the left eye is weaker. Similarly, wrinkling the forehead is less effective on the left. The left half of the palate droops a little but the uvula remains in the middle. Speech is nasal, and laughing produces a mask-like facial expression. His left eye is unable to follow completely toward the left periphery, but otherwise the eye movements are quite free. The pupils are round, equally wide, react normally, and show no sensory impairment. The left facialis area and the other musculature are stimulated normally by the faradic current, and there is no fatigue reaction. The nasal swabs contain diphtheria bacilli but the throat swabs do not. The two following examinations, conducted several weeks apart, have so far produced the same results. After a 6000 I.U. diphtheria serum injection, he collapsed with cardiac insufficiency and sweating, which persisted for nearly two hours. After this incident, the paralysis has not subsided and the bacilli have not disappeared yet. Even local treatment has proved ineffective so far.

In the clinical presentation, the first case shows the typical signs of myasthenic bulbar palsy with generalized myasthenia: intermittently occurring and increasing weakness when using the tongue and lip muscles; persistent weakness in the facial area around the mouth and eyes, which escalated to paralysis on exertion; initial weakness in the musculature of the extremities, which disappears again when movement is ceased; and initial persistent paresis of the eye musculature, which increased with prolonged reading. This case belongs to the types of myasthenic bulbar palsy first described by Karplus, where the first sign of paralysis of the extraocular muscles is double vision. This is the most common case according to existing studies. Later, a nasal smile (first described by Gowers) caused by zygomatic failure appeared, followed by the other symptoms—one after another.

The second case initially showed the symptom complex of Landry's paralysis, which clears up, but then briefly repeats a second time. After another remission, the symptom complex of myasthenic bulbar palsy appeared; first came the paralysis of the eye muscles again, then the bulbar symptoms, and finally sporadic weakness in the arms and legs—this time, with persistent paresis only of the eye and facial muscles, for now at least—and otherwise weakness occurring only after exertion, which can escalate to paralysis, but disappears again after rest, thus presenting the typical signs of myasthenia.

A great number of names have been given to the symptom complex of myasthenic bulbar paralysis (Oppenheim compiled 17 in his monograph). The number of causes attributed to it is equally great; however, even more authors still assert bluntly that they have found no explanation, even during autopsy. The majority who seek to explain the disease declare the causes: neuropathic diathesis (a weakness of the nervous system with a particular tendency towards diseases), over-exertion, alcoholism and above all infection or intoxication.

It is indicated that typhus, pneumonia, erysipelas, malaria, many instances of influenza, as well as angina and diphtheria preceded the infections—the last times 2-3 months previously; the other time, one and a half years before, with post-diphtheria paralysis following on immediately.

In both of these cases in the literature, no etiological connection is assumed, and the preceding diphtheria is only mentioned as a side issue. Since the inception of the myasthenic disease, diphtheria bacilli have never been detected until now. And here I come to the main point and the reason for presenting my two cases. In both sufferers, diphtheria bacilli were detected several times during the course of the disease and both are to be regarded as carriers of diphtheria bacilli.

As the literature indicates, the myasthenia appears without the body showing signs of fresh infection and in the absence of fever and the other symptoms. We are close to assuming – as Boedecker and Hoffman did - that we are not dealing with a fresh disease, but with an intoxication. In my sufferers too, the myasthenia arose after the actual diphtheria, but we must assume that the myasthenia itself is created and maintained by the toxins of the diphtheria bacilli they carry. Therefore, in the future the throat and nose must be examined in every case for diphtheria bacilli or perhaps even other infections or post-infectious intoxication.

Even in greater doses, as with the cases of post-diphtheria paralyses, the diphtheria serum has remained ineffectual. It remains to be seen whether or not recovery will occur once the sufferers are rid of the bacilli. This determines at the same time whether the persistence of the bacilli in the body is the basis of and prerequisite to this disease. Since the bacilli carriers are sometimes free of their bacilli years later, it is possible that the 7 cases of recovery published in the literature myasthenic bulbar palsy are just such cases. Let's use this perspective to test the pathological-anatomical discoveries made with myasthenic bulbar palsy and compare them with the changes established in cases of diphtheria paralysis.

The following have been described with myasthenic bulbar palsy: atrophic changes in the roots of the hypoglossal nerves and in several peripheral motor nerves, a partition at the aqueductus sylvii with duplication of the central channel; a serious etiological meaning can hardly be ascribed to the latter, and still less to the other noteworthy findings of tumors on all possible organs.

In the cases of diphtheria paralysis, findings have been: neuritic processes, also on the spinal root of the accessory nerve; myelitic foci; and in the acute and fatal cases, changes in the nerve cells of the central organs, as has already been highlighted previously, especially by Raymond (Arch. gen. de med, 1905), and before him Dejerine. Oppenheim says (in his textbook p. 696):

“After extensive research, it can hardly be doubted that the fundamental basis of diphtheria-related paralysis lies in neuritic processes. The toxin here first affects the nerves that are adjacent to the center of infection and which are directly immersed in it. However, paralysis of accommodation can occur initially after intestinal diphtheria. Signs of interstitial and parenchymal neuritis, and sometimes also bleeding, were found in the nerves. Klimoff claims to have found lesions of the cardiac ganglia. It certainly cannot be assumed that the diphtheria paralyses are based on a primary myositis even though substantial changes were found in the muscles—one time even exclusively in the muscles. The experimental research of recent times has evidenced, aside the neuritic processes, changes in the roots, the meninges and especially in the spinal cord (myelitic center). Also, research carried out according to more modern methodologies has uncovered a considerable degree of degeneration in the spinal root of the accessory nerve, and in the spinal cord itself. A few times, as in the Kotha and Hasche cases, the findings were negative. Bolton discovered changes in the nuclei of the medulla oblongata in acute diphtheria-related toxemia. Furthermore, Guillain and Laroche proved in one case, which was fatal due to the severe bulbar symptoms, that the material, which had a toxic effect in animals, was contained in the bulb.” “After all, we cannot disregard that the diphtheria toxin affects the entire nervous system—the most severe changes arise presently at this place, then soon at another place, but most often on the peripheral nerves, and in addition, it can damage certain areas toxicologically without changing them structurally. Thus, it has already clearly been stated that the diphtheria toxin in particular (and this applies also to other bacterial toxins, especially of the typhus bacilli group) can change or merely damage (which cannot be detected microscopically yet) all possible parts of almost the entire nervous system. Therefore, it no longer seems so remarkable that sometimes one symptom complex appears more often, than the other symptom complex appears, which conforms more or less to an established pattern of a localized group of nerve nuclei—or one

that even permits us to ignore the text book forms and then must be described as “mixed form”—or one that jumps between improvement and deterioration and then suddenly flares up again at any time.

Both of my sufferers show that with many diphtheria bacilli carriers, particularly strange types of paralysis develop as a result of chronic mild toxic effects. These paralyzes are noteworthy in that repeated acute attacks are interspersed with periods of improvement, so that the whole thing can be regarded as a mitigated form of an undulating career of enduring toxic paralysis.

Internal secretions and metabolic disorders have also been promoted as explanations for mysathenias: First, the combination of Basedow’s disease with myasthenia was noticed several times; then, lymphorrhoeas and other pathological/anatomical findings in the pituitary gland, the adrenal glands, and the thyroid, and noticeable deformities seemed to point even more clearly to this. Chwostek moved the seat of the disease to the parathyroid gland and assumed a hyper-secretion there. Therapeutic intervention proceeded according to these assumptions. Even when improvements are indicated after adrenalin, hypophysin and the other substances have been administered, success has nevertheless remained unreliable. In the same way, the extirpation of tumors has produced only transient improvements, not recovery. At the same time, it should be briefly mentioned that infiltrations of the lymphocytes and other changes in the musculature in all possible infectious diseases occur without functional disorders. And these changes are never found directly in the muscles belonging to our symptom complex.

Attempts have been made to illuminate the darkness of this disease by researching metabolism. A lack of glycogen in the liver, increased calcium elimination, and the signs of acid poisoning were found, meaning that it could be assumed the liver was producing auto-intoxication., and to a great extent this is primarily the result of undernourishment caused by the difficulty in swallowing associated with this disease. .

These seeming contradictions might be explained in the following fashion, i.e. that myasthenic muscular weakness, recidivistic muscular weakness and myasthenic electrical reaction can occur in all possible conditions, for example, in myopathies (O. Foerster), but also in the course of traumatic peripheral paralyzes (O. Foerster), and particularly during their restitution. Therefore, it seems that the myasthenic behavior, so to speak, represent a first step on the way to lasting paresis or paralysis, no matter what the cause, and is the expression of relatively minor damage to the motor apparatus. Such minor damage can, of course, arise from differing causes: trauma, intoxication, or insufficient hormone production, a view which O. Foerster has just presented at the International Congress in London, 1918.

The literature is presented comprehensively in Oppenheim’s monograph and in his Textbook of Nervous Diseases, 6th Ed., 1918, as well as in the cited works.