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PROGRESSIVE VAGUS-GLOSSOPHARYNGEAL PARALYSIS WITH PTOSIS. A CONTRIBU- TION TO THE GROUP OF FAMILY DISEASES¹

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With the increase of our knowledge of the so-called family diseases of the nervous system, it has become increasingly evident, whatever ultimate classification may be adopted, that these diseases may roughly be divided into two groups: First, those which, although distinctly hereditary in character, are too varied in symptomatology to permit of classification as disease entities; and secondly, those which are absolutely sharply defined in their manifestations. In the first group, may in general be included the various forms of atrophy and dystrophy of hereditary type, which run into each other in such a way as to preclude the possibility of distinct individuality. On the other hand there are certain conditions which on account of their constant manifestation may properly be regarded as entities, whatever their broader relation to the hereditary group in general may eventually be shown to be. In this group, amaurotic family idiocy, family periodic paralysis,

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Thomsen's disease, are somewhat typical examples. The condition about to be described may properly be classed with this latter group because of the absolute definiteness of the signs and symptoms which so far as ascertainable have occurred in identical form in all the cases which have been observed. So far as I am aware, this type consisting in paralysis of the vagus-glossopharyngeal group as concerned in the act of swallowing, together with ocular ptosis, has not hitherto been described. The history of the case which has come under observation is as follows:

V. P., Figs 5 and 6, a French Canadian by birth, 59 years old, married, presented herself on November 11, 1913, at the Laryngological Department of the Massachusetts General Hospital, with the complaint that she was unable to swallow so well as formerly, that she was growing worse, and that she thought her "throat passage" was becoming smaller. She had noticed the difficulty over a period of two years. Examination in that department

FIG. 1. From this chart it appears that the parents of the generation to which the patient belongs had seventeen children, of whom eight died under the age of ten, seven lived to adult life, two males dying of the disease at the ages of sixty-seven and sixty-eight, respectively, a third male dying at forty-five of some other affection. Of the four females one has died of the disease at the age of sixty-eight, the patient under observation has the disease and is now fifty-nine years old. Another female died at the age of forty-seven of some other disease, leaving but one living at the age of fifty-seven who, so far as ascertained, has not been affected by the family disorder. It will be seen, therefore, that with but one exception, all the members of this family who have attained the age of fifty or more years have died of the disease. The matters of special interest are the undoubted similarity of the affection in all of the cases and the fact that although definitely hereditary in character, the disease has not been known to begin before the fiftieth year. The next generation numbers thirty-six, the oldest being forty-two. The disease has not appeared so far as known in any member of this generation. The next or fourth generation already numbers many children without record of the appearance of the family affection. An intensive study of this family for the next fifty to one hundred years is clearly a matter of much interest and importance.

showed that both the pharynx and the larynx were normal and that a bougie could be passed into the stomach without resistance. An X-ray threw no light on the matter, and a provisional diagnosis of cardiospasm was made. The patient was referred to the Neurological Department with a request for an explanation of the cause of the difficulty in swallowing.

Examination at this time and on many subsequent occasions gave the following facts: She first noticed a tendency to drooping of the eyelids about four years ago. Following this at an interval of about a year, she began to have difficulty in swallowing. Both of these conditions had grown gradually worse, so that at the present time (summer of 1914) she swallows with very considerable difficulty and is only able to take solid food by combining it with a large amount of water or tea. Otherwise, as she expressed it, "the food seemed to clog up in the passage." Beyond a tend-

FIG. 2. Mother. Died of the disease. Age 77. Ptosis. Paralysis of deglutition.

ency to constipation, she had no further complaints. Her bodily functions were normal and, except for the difficulty mentioned, she regarded herself as well.

She was the mother of ten children, and had had no difficulty at their birth. She had had no miscarriages, and had always led a life of activity and hard work.

Examination in detail was as follows: Cranial nerves: The first nerve showed no abnormality; the second, no impairment of vision; the fundus normal; the discs somewhat indistinct in outline, with marked physiological cupping and no swelling; the vessels of normal appearance. Third nerve, equal ptosis of both eyes, partially covering the pupils (see Fig 6). The eyes could be closed with sufficient muscular strength; the ocular movements were normal in all directions. There was possibly a slight nystagmus on the right when looking inward; the fields were normal. Pupils were moderately dilated and reacted promptly to light and

on accommodation, as well as consensually. Fourth nerve, normal. Fifth nerve, no disturbance either in the sensory or motor branches. Sixth and seventh nerves, normal. Eighth nerve, watch-tick heard at about four inches on each side; air conduction better than bone conduction. Ninth and tenth nerves, palatal reflexes well preserved; no disturbance in breathing, in phonation, or in other functions subserved by this group of nerves, excepting a pronounced difficulty in swallowing, particularly solid food. It was possible to take soft food and liquids, although on

FIG. 3. Son. Died of the disease. Age 67.

testing, the difficulty was apparent. Within the last few weeks, difficulty in swallowing had markedly increased. The eleventh nerve showed no defect. Twelfth nerve, tongue rather slender, protruded in the median line without tremor and with absolutely no evidence of atrophy. It was freely movable, and there was no speech defect whatever.

The arms showed no abnormality either in strength, sensation, coördination, or reflexes. The legs were normal in strength and without evidence of ataxia or other disturbance. Knee-jerks were normal. There was no Babinski response, no clonus, normal but slight Achilles; no objective or subjective disorder of sensation in the legs; no Romberg sign. There was no evidence of disorder of the internal organs with the exception of the circulatory apparatus and the kidneys. The heart was negative except for an accentuated second aortic sound. The pulse was 84 and full; the blood pressure on one occasion, 200 systolic; on another, 230 systolic, 115 diastolic.

Examination of the urine on April 25 was as follows: Pale; sp. gr. 1002; reaction slightly acid; albumin, slightest possible trace; no sugar. Sediment: small amount containing several epithelial cells, typical bladder and vaginal, and a few large round

FIG. 4. Son. Died of the disease. Age 68.

cells from the pelvis of the kidney or neck of the bladder. Several leukocytes; a few mucin shreds, a few uric acid crystals, and a small amount of amorphous urates.

On one occasion, the amount passed in twenty-four hours was estimated as three pints, which presumably was an error in observation. (It has not been possible to keep the patient under close hospital observation.)

Examination of the blood showed hemoglobin 95 per cent.; Reds: normal size and shape, no poikilocytes, micro- or macrocytes; no blasts; no organisms; no acromia; no stippling; no increase of platelets; no excess of fibrin. Whites: differential counts of 318 cells; polymorphonuclears (neutrophils, 72.9 per cent.; eosinophils, 1 per cent.); basophils (large mononuclears, 4.4 per cent.; small mononuclears, 19.7 per cent.); transitional forms, 2 per cent. Wassermann reaction in the blood negative.

Family History.—The patient's mother died at the age of 77, and for many years preceding her death, suffered from an increasing difficulty in swallowing together with a definite ocular ptosis. Death ultimately resulted from starvation (Fig. 2). Her father was normal so far as known. There were fifteen children of this marriage, of whom eight died under the age of ten. Of those living to adult life, there were four females and three males. Of these, two males and one female have died at the ages of 67, 68 (Figs. 3 and 4) and 68 respectively, with precisely the same

FIG. 5 Daughter. Before onset of the disease (patient under observation).

symptoms as those of the mother, and of the patient whose history is detailed above: namely, paralysis of deglutition with ptosis. One male of this generation died at the age of 45 of another affection; another female at 47, also of some other disease; leaving only a single female living excepting the patient. This woman is now 57 years old, and so far as ascertained is unaffected by the disease. It is a tradition in the family, which has been amply borne out by the facts so far observed, that the

disease never begins before the fiftieth year, a fact certainly of extreme interest, to which allusion will later be made. With one exception, all the members of this generation have been married and have had large families, for the sake of clearness omitted from the accompanying chart. Inasmuch as none of these have

FIG. 6. Same as FIG. 5. Definite signs of the disease. Age 59. Ptosis and progressive paralysis of deglutition (patient under observation).

reached the age of fifty years, according to the family tradition, the disease has not yet appeared.

From the foregoing family history, it appears that with one exception every member of the generation to which our patient belongs who has reached the age of fifty years has died of the disease. Although detailed information regarding those who have died is lacking, it has become definitely established in the family that starvation with drooping of the eyelids occurred in each case, with striking similarity. The definite character of the disturbance with its inevitable fatal outcome renders this testimony trustworthy. An unmarried sister of the patient died at the age of

68 in an institution under the charge of a Catholic sisterhood. The sister superior has kindly written me the following statement regarding this patient. She says in her letter, "This person (A. B., a sister of my patient) came to our institution some years ago, not because she was at the time very ill but rather because she was aged and wished to finish her days in our home. She suffered from paralysis of deglutition which resulted in starvation. She had a very peculiar affliction of the eyes also which I have never seen before. She died here about five years ago; our house physician attended her. He relieved her somewhat, but could not cure her." There can be no doubt that these symptoms were identical with those from which my patient is now suffering. No definite information is obtainable of the mother's illness or of the two brothers who have died, beyond the essential fact that they all starved to death and had a peculiar drooping of the lids.

I am unable to find any reference in the literature of the family hereditary affections to this disturbance. It is unique in the fact of the cleancut character of the symptoms and signs which have appeared in all the persons affected in the same form, namely: ptosis and paralysis of deglutition without other evidence of disorder of the nervous system. The fact that it never has occurred before the fiftieth year is likewise of peculiar interest. In the recently published "Handbook of Neurology" edited by Lewandowsky, Jendrassik writes an exhaustive article on the hereditary diseases, followed by a bibliography of nearly five hundred references, without allusion to the symptom-complex under discussion. Under the heading, "Hereditary ptosis and the hereditary ocular muscle paralyses," cases are mentioned in which ocular paralyses often associated with facial paralysis occur both as congenital affections and also developing in later life. Jendrassik himself has observed in two sisters at the thirtieth year a gradually developing ptosis followed by complete external ophthalmoplegia, paresis of the facial nerve, and loss of the patella reflexes. In these cases there is also a certain disorder of speech. It is hardly necessary to state that such cases bear only the most distant relation to those under consideration, owing to the widespread character of the paralysis and a coincident involvement of the spinal cord. Bernhardt,¹ in a paper entitled "*Beitrag zur Lehre von der familiären Erkrankungen des Nervensystems,*" in

¹ Bernhardt, Virchow's Arch., 1891, CXXVI, 59.

1891, described certain cases, all occurring after thirty, in which there were marked bulbar symptoms associated with speech defect and spasticity of the extremities. Beyond the fact of a bulbar involvement, these cases likewise evidently bear no intimate relation to the affection under discussion. Oppenheim, in his discussion of progressive bulbar paralysis, alludes also to an apparently hereditary type occurring in children as described by Fazio, Charcot, Londe, and Brissaud-Marie, evidently a family character, in which also certain stigmata of degeneration occurred. This condition is, however, so far removed from our cases that they require no further description, if for no other reason than that it appeared in childhood.

Classification.—It is difficult to classify these cases in any recognized group. The various myopathies, ably discussed with regard to their interrelation by Oppenheim and Spiller at the last international congress of medicine in London, cannot be considered to include this type. There is, in the first place, no evidence that the disease is to be regarded as a primary muscular affection; the pathology is rather to be sought in a curiously selective process of degeneration occurring in a limited number of cells of the vagus-glossopharyngeal group, and a single cell-group of the oculomotor nucleus. It should, in this connection, be borne in mind that the eyelids contain smooth muscle fibers innervated by the sympathetic, the function of which is to widen the lid opening. The paralysis of these fibers may produce a narrowing of the space between the lids, giving rise to an incomplete ptosis. When, however, a ptosis is due to this cause, there is commonly a reduction in size of the pupils, which did not occur in this case; nor was there other evidence of sympathetic involvement. It is fair, therefore, to presume that the ptosis is not due to this unusual cause, particularly in view of the associated difficulty in swallowing.

The peculiarity of the affection lies in the fact that although very chronic in course, extending over a long period of years in each instance, no other nerves are involved, thus differentiating it sharply from an ordinary type of bulbar or pseudo-bulbar paralysis. There is no record that the hypoglossal nerve is ever affected. It certainly shows no sign whatever of degeneration in the case which I have had the opportunity to observe.

A more important consideration is the possibility that the

affection might be considered a form of myasthenia gravis. The photographs of the various persons affected lend a certain weight to this idea, inasmuch as the ptosis alone is visible, which constitutes a conspicuous characteristic of the myasthenic face. It is, however, exceedingly unusual that the weakness in myasthenia gravis is limited consistently to single muscles, as is clearly the case in the affection under consideration; nor is there any evidence to show that in myasthenia gravis the disease occurs in precisely the same form on an hereditary basis. Furthermore, myasthenia gravis usually manifests itself before the fiftieth year. It is not possible to demonstrate the myasthenic reaction, or the fatigability of the muscles beyond what one would expect in any case of muscular weakness, such as our patient presents. Furthermore, the tendency to remissions, as frequently observed in myasthenia, is wholly lacking in this case. One is, therefore, justified in excluding the symptom-complex from the ordinary myasthenia gravis; and even if further investigation should prove that it might be classified in this category of disturbances, the fact of its peculiar localization and constant appearance in hereditary form, only occurring after the fiftieth year, would still render the affection unique.

Etiology.—In the present state of our knowledge, any attempt to discover an adequate cause for the appearance of such a disorder in many members of a single family must prove futile. No doubt it may properly be considered one of the abiotrophies as described by Gowers; but this manifestly does not serve as an explanation. That there is a defective vitality may readily be assumed, but why such a defect should occur with uniformity in just these nerves remains wholly obscure. It is furthermore an added mystery that such a defect should never manifest itself until well past middle life, and in otherwise perfectly healthy persons without apparent hereditary defects or other nervous disability. The theory of over-use as propounded by Edinger likewise does not offer even a workable hypothesis. Sclerotic changes in the blood vessels occur to one as a possible explanation but although such changes may well underlie the condition, the fact of chief importance is naturally not touched, namely: that just these nerves are affected by such a process and no others. It is clearly necessary to go behind any such superficial explanation if we are to arrive at a reasonable etiology, and this is at present

impossible. In our case there is strong probability of a coincident renal affection of a degenerative sort, as shown by the urinary examination; but this fact in no way helps towards a solution of the main question.

Prognosis and Course.—My patient noticed her first symptoms about four years ago. She now has a considerable degree of ptosis, as shown in Fig. 5, but is still able to swallow, although with much difficulty, and shows no signs of emaciation from lack of nourishment. It is probable that she will live several years, so that in her case the course of the disease may be approximately estimated at seven or eight years. Beyond the fact that the other members of the family dying of the disease are known to have been ill for a long period, no definite data are at hand. In this respect the degeneration does not differ from others involving cranial nerves important to life.

Summary and Conclusions.—A clearly defined disease or symptom-complex exists not hitherto described, consisting of ocular ptosis and paralysis of deglutition coming on after the fiftieth year, and leading to death without further involvement of the nervous system.

The affection is certainly to be classed among the family hereditary diseases, as shown by the fact that it has occurred in two generations, in the second affecting all but one of those who reached the age of fifty years.

The disorder is peculiarly remarkable in that although hereditary in type, it has not been known to occur in early life, and must therefore be regarded as superinduced in predisposed persons by conditions arising in the degenerative period of life.

The justification for regarding the affection as a distinct entity lies in the facts that so far as ascertainable it occurs in precisely the same form in all persons affected and also invariably in the declining years of life.