ADIE'S SYNDROME

Report of Four Cases

W. JAMES GARDNER, M.D. and F. L. SHIVELY, JR., M.D.

Adie's syndrome is characterized by two features: a tonic pupil and absent tendon reflexes. This condition has been recognized by neurologists for many years, but there has never been an adequate explanation of the etiology and pathogenesis. In 1902, Saenger[1] and Strasburger[2] simultaneously described the condition. Since this description, the syndrome has been given various names, such as the tonic pupillary reaction, pupillotonia, myotonic convergence reaction, and tonic convergence of pupils apparently inactive to light. In 1931 Adie[3] gave an adequate and concise description of the condition. From a study of twenty-two cases, he found that these cases seemed to fall into two definite groups: (1) The complete form with a typical tonic pupil and absence of tendon reflexes, and (2) the incomplete forms which he further subdivided into (a) the tonic pupil alone, (b) atypical phases of the tonic pupil alone ("iridoplegia," "internal ophthalmoplegia"), (c) atypical phases of the tonic pupil with absent reflexes, and (d) absent reflexes alone.

In Adie's syndrome the dilatation of the pupil is unilateral and it does not respond to light when the usual methods are used for eliciting the light reflex. After the patient has been placed in a darkened room for a long period of time, the pupils become equal in size. If a bright light is flashed into the affected pupil following this procedure, it responds slowly. As soon as the light is removed, the pupil returns to its original size. The most important feature of the tonic pupil is that it responds to convergence and accommodation only after prolonged effort. The pupil is never miotic and responds to mydriatics and miotics.

Because of the apparent loss of the light reflex with or without loss of the tendon reflexes, these patients are frequently thought to be suffering from syphilis of the central nervous system. Frequently, the tonic pupil has been erroneously called an "Argyll-Robertson pupil," "atypical Robertson pupil," etc. This is not good practice because (1) the pupil does not correspond to the postulates of Argyll-Robertson and (2) the use of such terms implies that the patient has syphilis. Adie has gone so far as to say, "The true Argyll-Robertson sign is an infallible sign of syphilis." The Argyll-Robertson pupil, as described by its original author, is small, usually bilateral, constant in size, and unaltered by light or darkness. It contracts promptly on convergence and dilates promptly when the effort to converge is relaxed. It dilates slowly and imperfectly to mydriatics. Thus it differs in every respect from the tonic pupil (Table 1).

TABLE 1

COMPARISON OF THE ARGYLL-ROBERTSON PUPIL AND THE TONIC PUPIL

Features	*Argyll-Robertson Pupil*	*Tonic Pupil*
Pupils		
1. Size of abnormal pupil	Small 75 per cent	Large 95 per cent
2. Abnormal pupil unilateral	5 per cent	90 per cent
3. Constant in size	Yes	No
4. Response to light	No contraction	Contraction only after prolonged stimulation
5. Response to darkness	No dilatation	Abnormal pupil may equal size of opposite pupil
6. Response on convergence	Immediate contraction	Very sluggish contraction
7. Response following convergence	Immediate dilatation	Reaction variable
8. Response of mydriatics	No dilatation	Immediate dilatation
9. Response to miotics	Slow contraction	Immediate contraction
10. Wassermann reaction	Positive	Negative

Adie, in 1932[4], published a second paper in which he reviewed forty-four reported cases, in nine of which there were absent tendon reflexes. Most of the patients had been examined by ophthalmologists, with little or no mention of the reflexes. When the reflexes were absent, they more than likely were regarded as further evidence of syphilis of the central nervous system. In Adie's own series, the tendon reflexes were absent in 68 per cent, or thirteen of nineteen cases. Loss of the Achilles reflex is the most common finding. Adie states that with both Achilles reflexes present he has never seen loss of any other jerks.

Case Reports

Case 1: A forty year old white woman came to the Clinic complaining of headache. She was very emotional and was upset easily. She complained of being chronically tired, becoming irritated very easily, and weeping upon the least provocation. Her husband was a chronic alcoholic.

Physical examination revealed the blood pressure to be 140 mm. systolic and 85 mm. diastolic. The right pupil was irregular and larger than the left. It did not react to light, but there was some reaction when it was subjected to prolonged convergence. The biceps, triceps, abdominal and patellar reflexes were diminished. The Achilles reflex was absent bilaterally. The Babinski reaction was negative. No sensory or motor changes were present.

Laboratory examination showed that the blood counts and the blood chemistry were within normal limits. Roentgenograms of the skull were normal. A spinal fluid examination exhibited normal dynamics. Wassermann and colloidal gold tests of the spinal fluid were negative and Wassermann and Kahn tests of the blood gave negative reactions. Urinalysis revealed nothing of significance.

Based upon these findings, a diagnosis of the complete form of Adie's syndrome was made.

Case 2: A sixteen year old white girl came to the Clinic with the complaint of "aching eyes" which had been present for four months. Approximately nine months prior to her admission to the Clinic she noticed that her right pupil was enlarged. She sought the advice of an ophthalmologist who refracted her eyes. The pupils were contracted for a few weeks after refraction, but the right pupil then returned to its original size. The remainder of the history was noncontributory.

Neurological examination revealed no objective evidence of an organic lesion of the central nervous system. The tendon reflexes were normal. There was no evidence of involvement of the third, fourth, or sixth cranial nerves. Ophthalmologic examination revealed the right pupil to be larger than the left and to be fixed to light. Examination of the visual fields showed a relative central field loss in the right eye which gave rise to the opinion that perhaps the patient had a retrobulbar lesion. Examination of the retina of the right eye showed a spot of old chorioretinitis just below the nerve head. Further examination revealed that the right pupil responded to the postulates set forth by Adie. With these findings, a diagnosis of the incomplete form of Adie's syndrome was made.

Case 3: A nineteen year old white girl came to the Clinic complaining of headache and blurring of vision. The headache was located just above the left eye and had been present for five months. It was continuous in nature and occasionally radiated to the parietal area. Occasional attacks of nausea and vomiting had been associated with the headache. The vomiting was described as

being projectile in character. About one month prior to admission to the Clinic, blurring of vision occurred. She also complained of photophobia. An ovarian dysfunction was present but this was not deemed pertinent to the present illness.

On physical examination the patient had a normal temperature, the pulse rate was 92 and the blood pressure 120 mm. systolic and 78 mm. diastolic. The pupils were irregular. The left pupil was dilated and did not react to light or accommodation upon the first examination. The right pupil was normal in all respects. Examination in the Department of Ophthalmology showed the left pupil to have no direct or consensual reaction to light. However, the pupil did contract after three minutes of fixed accommodation. Only a slight increase was noted in the size of the left pupil after the patient had been placed in a dark room for thirty minutes. At the end of this time, the pupils were equal in size. The left pupil reacted sluggishly to light after prolonged stimulation. Both pupils contracted promptly following the instillation of two drops of eserine.

The biceps, triceps, abdominal, patellar, and plantar reflexes on the left side were markedly diminished. The Achilles reflex on the left was absent. There were no pathological reflexes. No sensory or motor changes could be elicited.

Laboratory tests showed the blood counts and the blood chemistry to be normal. Urinalysis was negative in all respects. The Wassermann and Kahn tests of the blood gave negative reactions. Roentgenograms of the skull were reported negative for any intracranial pathology.

With these findings, a diagnosis of the complete type of Adie's syndrome was made.

Case 4: A twelve year old white girl came to the Clinic complaining of unequal pupils which had been present for a period of one year. The patient was the second child. She had been delivered without any obstetrical difficulty, and had developed normally in every respect. At the time of examination there were no complaints referable to the vision. The patient did have an occasional frontal headache but it was not believed to have any relation to the pupillary asymmetry. No nervous manifestations could be elicited. The family history was entirely negative and the remainder of the history was nonessential.

Physical examination showed a pulse rate of 78 beats per minute and a blood pressure of 100 mm. systolic and 60 mm. diastolic. The only significant findings pertained to the eyes and the tendon reflexes. The right pupil measured 6 mm. in diameter. It was round and, when stimulated by light, the direct and consensual response was absent. When the pupil was subjected to a strong light over a prolonged period of time there was only a slight contraction. The pupil responded to accommodation and convergence after prolonged effort. The left pupil measured 4 mm. in diameter and was normal in all respects. The visual fields were normal. There were no pathological changes in the fundi. The patient was then placed in the dark room for a period of thirty minutes but no change was noted in the size of the pupils. When the right pupil was stimulated by homatropine and eserine, it responded immediately. Examination of the tendon reflexes showed the biceps and patellars to be diminished. The Achilles reflexes were absent. There were no pathological reflexes and no sensory or motor changes.

The blood counts and the blood chemistry were within normal limits. Wassermann and Kahn tests of the blood gave negative reactions. The urinalysis was normal.

With these findings, a diagnosis of the complete form of Adie's syndrome was made.

Discussion

Although many theories have been advanced, the etiology and pathogenesis of Adie's syndrome still remains obscure. Many times the condition is asymptomatic. Moore[5] quotes a case of a patient who had been aware of the pupillary asymmetry for a period of forty-seven years, the condition being entirely asymptomatic. Kennedy[6] and his associates noted the frequency of emotional disturbances and vasomotor lability in their group of cases. Inman[7] also noted the relationship between emotional instability and the tonic pupil. Adie, however, stated that the nervous factor played no part in the etiology. The explanation for the loss of the tendon reflexes upon an unstable autonomic nervous system remains a problem of much conjecture.

As far as can be determined, Adie's syndrome is not congenital or hereditary. However, cases have been reported in which the patients have stated that the pupils have *always* been unequal. Adie states, "My impression is that the abnormal pupillary reaction may appear at any age." Women predominate over men. In Adie's own series (nineteen cases), women comprised 79 per cent of the cases. In his review of the literature (forty-four cases), 70 per cent of the cases were women. All four of our cases occurred in the female sex.

In a few instances, the onset appears suddenly with blurring of vision and upon examination a tonic pupil is found with or without absence of the tendon reflexes. The general health of these patients is remarkably good. In our series, we believe Case 1 has a very definite "nervous factor" which, according to Kennedy and others, accounts for the presence of the syndrome. However, in the other three cases, no factors of emotional instability were exhibited.

Adie believes that the reaction is an expression of a unique kind of perversion of pupillomotor activity. He states, "the curious manner in which stimuli are stored in excess and slowly emitted points to some change in the activity of the cells in the vegetative portion of the oculomotor nucleus. We are driven to the viscera for analogous types of innervation." He further states that the associated absence of tendon reflexes does not alter this opinion.

The treatment of Adie's syndrome, providing all other neurological diseases have been eliminated, is reassuring the patient. Particular attention should be given to patients in whom a previous diagnosis of syphilis has been made. An attempt should be made to control any emotional instability in the patient.

Conclusions

We have not attempted to explain the etiology or pathogenesis of this condition. This small group of cases recently has come to our attention and consequently has stimulated our thinking along this line.

Every possibility must be considered in an attempt to reach a diagnosis. Then, by exclusion, the patient may be placed into this category. Further study and more careful examination may reveal this syndrome to be more prevalent than it appears at present.

The actions and reactions of the tonic pupil have been discussed, particularly with reference to the Argyll-Robertson pupil with which it is so easily confused. In the table which is included, an attempt has been made to show the differences between the two totally different pupillary reactions.

The age of onset cannot be determined and the cause is unknown. There are no sequellae. The syndrome predominates in women.

Finally, we want to stress the fact that Adie's syndrome is a symptom-complex which superficially simulates tabes dorsalis, and is not due to syphilis.

References

1. Saenger, A.: Ueber myotonishe Pupillenbewegung, Neurolog. Centrabl., 21:837, 1902.
2. Strasburger, J.: Pupillentrögheit bei accommodation und convergence, Neurolog. Centrabl., 21:738, 1902.
3. Adie, W. J.: Pseudo-Argyll-Robertson pupils with absent tendon reflexes; Benign disorder simulating tabes dorsalis, Brit. M. J., 1:928-930, (May 30) 1931.
4. Adie, W. J.: Tonic pupils and absent tendon reflexes: Benign disorder sui generis; its complete and incomplete forms, Brain, 55:98-113, (March) 1932.
5. Moore, R. F.: Non-luetic Argyll-Robertson pupil, Brit. M. J., 2:843-844, (November 7) 1925.
6. Kennedy, F., Wortis, H., Reichard, J. D. and Fair, B. B.: Adie's syndrome: Report of Cases, Arch. Ophth., 19:68-80, (January) 1938.
7. Inman, W. S.: Non-luetic Argyll-Robertson pupil, Brit. M. J., 2:1179-1180, (December 19) 1925.