DEVIC'S DISEASE

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British and American journals describe a surprising number of cases of neuromyelitis optica, and though it has been argued that the disease is merely a form of disseminated sclerosis, most authors describe a picture so uniform that it must be recognized as a specific entity. Clifford Albutt, in Leeds in 1870, was the first person to describe the association of spinal-cord and optic-nerve disease, and was followed in 1880 by mention of another case by Erb. In 1894 a Frenchman, F. Gault, surveyed 17 cases and inspired by Devic wrote a thesis on the subject, on Devic's advice calling the condition *neuromyelite optique*. From then on there are sporadic reports of cases, Goulden in 1914 mentioning 51, Bell in 1927 70, and in 1949 Stansbury found reports of 200 cases in the literature. Scott in 1952 described 10 cases occurring in Edinburgh during the 14 years 1938-52, and in 1954 Markham and Otenasek found 10 cases in the files of the Johns Hopkins Hospital between 1925 and 1952.

Two cases have been seen recently in the Johannesburg General Hospital and are thought worth reporting. In addition an analysis will be given of 50 cases fully described in the literature.

CASE 1

Mr. D., a 21-year-old European, was admitted to a medical ward on 18 August 1955 because of weakness and generalized body-aches for 2 weeks, pain behind the eyes and headache for 48 hours, and poor vision and difficulty in micturition for 24 hours.

History. The illness had begun 2 weeks previously with influenza-like symptoms, which were treated by his doctor with Terramycin. Two days before admission he felt ill again, this time complaining of headache, vomiting and pain behind the eyes on moving them. There was a transitory incident 7 days before admission of weakness in the right arm. For 1 day vision had been poor in the right eye and he had found it hard to pass urine.

He had previously been quite well and worked as a machine operator for a tobacco company. There was no contributory family history.

Examination

He was a well-nourished adult man. Temperature 99·6°F, pulse rate 66 per minute and blood pressure 150/90 mm. Hg. Cardiovascular and respiratory systems and the abdomen revealed no abnormality.

The central nervous system showed the following:

The level of consciousness was quite normal and speech was normal.

Cranial Nerves. There was early papilloedema on the right side but the left disc was normal. Scotomata (central) were found on both sides, more marked on the right. The right pupil was large and reacted very sluggishly to light, and the left pupil was normal. The remaining cranial nerves were intact.

Motor. The motor system in the upper limbs was intact but the lower limbs showed weakness of both legs, with increased tone and bilateral ankle-clonus.

Sensory. The sensory system showed evidence of mild glove and stocking anaesthesia just above the elbows and knees, involving touch, pain, vibration and position senses. The abdominal reflexes were absent, all tendon reflexes (especially the knee and ankle) were much increased, and there were bilateral extensor plantar responses.

Investigations. The blood count was normal (haemoglobin 17·6 g.%, white cells 7,000 per c. mm. with 84% neutrophils). Cerebrospinal fluid: pressure 126 mm. of water; clear fluid and a negative Queckenstedt test; 50 cells per c. mm. (2 polymorphs and 48 lymphocytes), and sugar, chlorides, Lange curve and Wassermann reaction normal. The blood Wassermann was negative. Virus studies on stool and blood were negative. The electro-encephalogram showed a focus of irregular slow activity in the inferior surface of the mid- to posterior temporal areas. X-rays of chest, skull and sinuses were normal.

Course and Outcome

He was put on Meticorten, 60 mg. daily, and Vitamin B12, 1,000 micrograms daily.

On 22 *August* both discs showed papilloedema and on both sides the pupils reacted to light very sluggishly.

On 28 *August* there was marked improvement. Papilloedema had almost disappeared on both sides, reflexes were much less brisk, and the plantar responses were flexor. The dosage of cortisone was decreased.

By 5 *September* almost all signs had subsided, and vision was reasonably good. The cortisone was stopped.

On 9 *September* there appeared to be a relapse of the optic neuritis without further signs of myelitis. Both pupils were widely dilated and the discs were paler than normal. Meticorten was started again at the original dosage. From this time on recovery was very slow and for 3 weeks vision in both eyes was less than 6/60.

On 30 *September* the pupils were less dilated and reacted reasonably well. Vision in the right eye was 6/60 and in the left 6/36.

Both discs were paler than normal. He was discharged but advised to continue Meticorten, the dosage being reduced to 30 mg. daily.

Subsequently he has been seen several times as an out-patient and by mid-October was well enough to return to his original work. In November when last seen both discs were pale, but vision good enough for him to remain at work. On one occasion when he had been without cortisone for 4 days he complained of pain on moving the eyes. Physical signs were unchanged.

CASE 2

A European child aged 8 years was admitted to the Transvaal Memorial Hospital for Children on 13 April 1950.

History. His illness began 3 weeks before admission, when he became feverish, had a severe headache, and vomited. On about the 7th day of the illness he became drowsy and complained of pain in the muscles of the back and in the hamstrings. Convulsions had occurred at the age of 18 months and again when 4 years old, but otherwise he had always been well. Family history was non-contributory.

Examination

He was a well-nourished child with temperature 99°F, pulse rate 80 per minute, and blood pressure 120/70 mm. Hg. The cardiovascular and respiratory systems and the abdomen showed no abnormality.

The central nervous system showed the following features:

There was no neck stiffness but Kernig's sign was positive. The fundi showed early papilloedema on both sides. The gait was slightly unsteady.

Cranial Nerves. Both pupils reacted poorly to light and vision was extremely poor. An actual field-defect could not be made out.

Sensory. Sensation showed no gross abnormality but coordination was weak in the lower limbs.

Motor. The reflexes were exaggerated in the upper and lower limbs, abdominal reflexes were absent, and both plantar responses were extensor.

Investigations. The blood count was normal (haemoglobin 15·1 g. %, white cells 9,000 per c.mm., of which 75% were polymorphs). Cerebrospinal fluid: pressure 200 mm. of water; fluid clear and Queckenstedt test negative; 26 lymphocytes per c.mm.; total protein more than 100 mg.%, and chlorides and sugar normal.

X-ray of the skull was normal. The Wassermann blood-reaction was negative, as were virus studies on stools, blood and cerebrospinal fluid.

Course and Outcome

He was given Aureomycin and vitamin tablets. For about 3 weeks his condition deteriorated and though he was not co-operative enough for proper tests his vision was noted to be very poor. By 20 April he could not see a bright light and he was incontinent of urine and faeces. On 25 April the only change noted was that both discs were more blurred.

On 25 May all signs of spinal-cord involvement had subsided. Vision was reasonably good but both discs paler than normal; swelling had subsided.

On 17 June 1950 he was discharged, and apart from pale discs appeared to have recovered completely. At this time, testing showed bilateral very dense central scotomata, and vision in both eyes was 3/60.

In June 1951 he was well except for pale discs. Vision in the right eye was 6/60 and in the left 6/36.

In November 1955 he was seen again; apart from his eyes he is a normal schoolboy. Both optic discs are slightly white in colour. The peripheral fields are almost normal and full, but the central fields when tested with a 20/2,000 red object still revealed marked loss. Visual acuity is 6/24 on both sides.

CASES FROM THE LITERATURE

The following is a statistical summary of 50 cases of Devic's disease from the literature:

Ages	*Male*	*Female*	*Total*
1–10	2 (4%)	6 (12%)	8 (16%)
10–20	1 (2%)	11 (22%)	12 (24%)
20–30	1 (2%)	6 (12%)	7 (14%)
30–40	5 (10%)	4 (8%)	9 (18%)
40–50	3 (6%)	5 (10%)	8 (16%)
50 and over ..	2 (4%)	4 (8%)	6 (12%)
	14 (28%)	36 (72%)	50 (100%)

Preceding Infections

Upper respiratory tract	17	
Following prostatic abscess	1	
Following axillary abscess	1	
–	19	(38%)

Outcome

Complete recovery	11	(22%)
Survival but poor outlook	11	(22%)
Result unknown	1	
Death from myelitis	27	(54%)

Onset			*Differences between onset of optic neuritis and of myelitis*	
Optic neuritis	19	(38%)	Up to 10 days	8 (16%)
Myelitis	23	(46%)	Up to 1 month	6 (12%)
± Simultaneous	8	(16%)	Up to 1 year	7 (14%)
			Up to 2 years	2 (4%)
			± Simultaneous (remainder)	

Cerebrospinal Fluid (examined in 45 cases)

Cells (majority lymphocytes except 5 where polymorphs pre-dominated):

0–5 per c.mm.	23
5–20 per c.mm.	7
20–50 per c.mm.	6
50–100 per c.mm.	3
Over 100 per c.mm.	6 (in one 375 and in one 1,300 —remainder under 200)

Protein

Under 50 mg.%	26
50–100 mg.%	14
Over 100 mg.%	5

Lange Curve. Abnormal in 14 but no consistent pattern
Pressure. Normal except in 2 with spinal blocks
Wassermann. Consistently negative.

DISCUSSION

In the diagnosis of these cases, and in previous publications, several difficulties are encountered. From autopsies done on many cases presenting typical features of neuromyelitis optica there is no doubt that it is a demyelinating disease, but whether a specific entity should be made of it or whether it should remain just one of the group has been disputed. The diseases of the group are: (1) Disseminated sclerosis, (2) diffuse sclerosis of the Schilder type, (3) the acute dissemminated encephalomyelitides, and (4) neuromyelitis optica.

Disseminated sclerosis is rare before puberty, whereas nearly 40% of the cases of Devic's disease occur in the younger age-group; nystagmus is very rare in Devic's disease and characteristic of disseminated sclerosis; the course of Devic's is relatively uniform even if it relapses, whereas disseminated sclerosis is a long-drawn-out disease usually with long periods of complete normality; sudden binocular loss of vision is common in Devic's but very rare in disseminated sclerosis and the visual loss in Devic's is far greater.

Diffuse sclerosis has very little in common with

Devic's disease except for the demyelination. Mental deterioration is very rare in Devic's disease.

Encephalomyelitis often has some obvious cause such as an infection, and cerebral signs and symptoms are very prominent. Though papilloedema may occur, visual signs of the Devic type are very rare.

The cause of Devic's disease has not so far been determined, though various theories have been produced. The possibilities are the following: (1) Infection, (2) toxins, (3) enzymes, (4) vascular obstruction, and (5) allergies.

That infection plays a part is very likely, for many cases follow an infection of some sort. Whether this acts directly on the nervous system or is an allergic reaction it is hard to say. Though many investigators have tried, no one has yet isolated a virus in any case. Toxins or allergies may be the result of infections, drugs, poisons, etc. The enzyme theory is that an enzyme-destroying lecithin acts on the nervous system, but what enzyme and what sets it off has not been determined. Vascular obstruction is hard to believe; one cannot picture why such specific areas and no others should be picked out in every case. On the whole, an allergic response to infection seems the nearest answer to the problem.

The typical clinical features are shown by the cases. The age can be anything from 6 to 60 years, but mainly young age-groups are affected. The onset is rapid, though the disease may be preceded by an upper respiratory infection. Either the eyes or the spinal cord may be involved first—the intervening period being slight, though occasionally reaching months. There may also be a period between the involvement of the two eyes. The symptoms related to the eyes are either pain in or behind the eyes on movement from optic or retrobulbar neuritis, or rapidly developing loss of vision. The signs usually consist of slight papilloedema in the early stages, with large pupils reacting poorly or not at all to light. Associated with this is loss of vision far greater than the papilloedema would indicate, usually central, and especially colour vision being lost. The discs may return to normal but in most cases remain pale. Vision can return to normal but often remains impaired to a greater or lesser degree.

Spinal symptoms may be ushered in by pain in the back or limbs, by weakness, or by interference in sphincter control. The picture on examination may be a diffuse myelitis involving one or several segments of the cord, a complete transverse lesion at any level, the Brown-Séquard syndrome, or one or more small discreet lesions involving one or several tracts. Motor or sensory systems may be involved. Recovery may be complete or partial, or an ascending lesion may lead to bulbar paralysis and death.

The cerebrospinal fluid may be normal, but in over half of the cases described there is a rise in cells, the lymphocytes usually predominating. The protein is high in over 50% of cases. In 2 cases described in the literature there was complete spinal block—McIntyre *et al.* (1952) and Marlcham *et al.* (1954). The Lange test is often slightly abnormal but there is no specific picture. The Wassermann reaction is always negative.

The outcome varies. Many authors, particularly the earlier ones, felt death was inevitable, the cause being from bulbar paralysis, pneumonia or urinary infection. Cases recovering completely are less than 25% of those described and in many of them the discs remained pale and vision slightly impaired. In neither of our cases has visual recovery been complete and in both the eyes have pale discs.

No treatment is really effective, though in case 1 one felt that cortisone may have helped and that relapses may have been related to stopping it.

Many cases have come to autopsy and at least 30 autopsies have been described.

The lesions are seen in the spinal cord, most frequently at the dorso-lumbar level, and in the optic pathways. The optic nerves, chiasma, track, geniculate bodies and radiations to occipital lobe and calcarine cortex may be involved.

The spinal cord and optic nerves are usually swollen and softened and there may actually be constriction of the optic nerves by the unyielding dura and bony foramina.

Microscopically the lesions resemble those of a severe acute disseminated sclerosis or encephalomyelitis, but there tends to be greater involvement of grey matter than is usually seen in these conditions. The predominating pathological change is that of demyelination but nerve-cell degeneration of all degrees of severity is seen in affected grey matter. Axis cylinders are also destroyed in the softened areas and macrophage lymphocytic activity is evident. In most cases coming to autopsy the process has been too acute to allow of much astrocytic gliosis.

CONCLUSION

Neuromyelitis optica is not a rare disease, though not frequently seen in South Africa. All cases correspond to a fairly definite and typical picture of optic or retrobulbar neuritis associated with myelitis. The onset is usually rapid and the disease short-lived though relapses occur. Many patients die, though a considerable proportion recover completely. Some are left blind or crippled by the spinal deformity. Treatment has never been satisfactory though it is possible that cortisone helps.

SUMMARY

Two cases of Devic's disease have been described and the main features of 50 others given. Brief mention of the diagnosis, etiology, clinical picture, outcome, pathology and treatment has been made. One concludes that neuromyelitis optica is a specific disease distinct from the other demyelinating diseases. Its cause is unknown but is is possibly related to infection. The clinical picture is one of optic or retrobulbar neuritis with myelitis. The outlook on the whole is poor and treatment, with the possible exception of cortisone, unhelpful.

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