SARCOIDOSIS OF THE BRAIN AND SPINAL CORD

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THE dermatological lesions of sarcoidosis were first described by Boeck in 1899, and in 1905 Winkler reported the manifestations of this disease in the nervous system (cited by Salvesen), while others at about the same time described involvement of other organs by sarcoid tissue.

Among 20 cases of sarcoidosis at autopsy, Aszkanazy (1952) found three to have central nervous system lesions. However, Löfgren (personal communication with Höök) (1955) stated that he found clinical evidence of central nervous system involvement in only two of 300 cases of sarcoidosis, that is, under 1 per cent., but his cases were mostly in the primary stages of the disease. Carstensen and Norviit (1953) in 15 cases of sarcoidosis, found increased protein and a pleocytosis in the cerebrospinal fluid in six cases, although only two of these cases had signs of central nervous system involvement, indicating that it may be more common than is generally supposed, and may be easily missed if the cerebrospinal fluid is not examined.

Colover (1948) surveyed 115 cases of sarcoidosis affecting the nervous system found in the literature, adding three cases of his own. The lesions in these 118 cases were:

- (a) Cranial nerve lesions; anosmia (2); ptosis (6) and other oculomotor lesions (3); sluggish pupil responses without active iritis (3); trigeminal impairment or loss (5); facial paralysis (58, of which 22 were bilateral); nerve deafness (8) and disturbance of vestibular branch of acoustic nerve (4); dysphagia, or vocal cord paralysis (38) and twelfth nerve lesions (7).
- (b) Peripheral nerve lesions (localized) (4).
- (c) Intra-ocular lesions (33).
- (d) Pituitary and hypothalamic lesions (22).
- (e) Meningeal involvement (9).
- (f) Spinal cord and brain lesions (13).

Jefferson (1957) reviewed the literature and recorded seven cases of his own, illustrating the

diversity of presentation of neurological sarcoidosis; of his recent cases, two showed cranial nerve lesions alone, three had central lesions alone, one had both central and cranial nerve lesions, and one had a meningeal sarcoid granuloma.

Diagnosis

The diagnosis of neurological sarcoidosis is not an easy one, as the lesion may be in any part of the nervous system, resulting in many methods of presentation (Colover, 1948). Disseminated sclerosis shows similar spontaneous remissions and exacerbations, and retrobulbar neuritis is common to both diseases. In tuberculous meningitis, the presenting symptoms may be similar, accompanied by ptosis, ocular muscle palsies, facial palsy, or hemiplegia, but the cerebrospinal fluid sugar is always normal in sarcoidosis. Sarcoidosis may imitate spinal and cerebral tumours, and cases of sarcoidosis have been operated upon by neurosurgeons in mistake for a space-occupying lesion (Ross, 1955), particularly as the first sign of the disease may be an epileptiform attack, as in two cases described by Jefferson (1957).

The diagnosis may be made easier by the presence of sarcoid lesions in other parts of the body, most commonly the lungs, skin, uveal tract and parotid gland. A persistently high cerebrospinal fluid protein level is usual, often associated with a pleocytosis.

Although the Mantoux reaction is usually said to be negative, Hoyle, Dawson and Mather (1954) have shown that this is not always so. They recorded a series of 90 cases of sarcoidosis, 62 being confirmed histologically, and found that 28% were insensitive to Old Tuberculin 1 in 1,000 strength, and 44% were insensitive to 1 in 100.

Wood and Bream (1959) have recently reported the changes found on myelography in patients with sarcoidosis affecting the spinal cord.

The diagnosis of sarcoidosis can now be confirmed by means of the Kveim test. The reliability of this test was reviewed by Nelson (1949),

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who found that it was positive in 11 out of 15, i.e. 75% of patients with active sarcoid, and that it was negative in all of nine cases in which sarcoid was clinically inactive.

James and Thomson (1955) obtained positive biopsies after a Kveim test in 12 out of 16 cases of sarcoidosis, and negative biopsies in 47 controls, 28 of whom were tuberculous patients. They also recorded variations in the appearance of the Kveim site, simultaneous with clinical fluctuations on the disease, and by serial biopsies studied the histological response to different methods of treatment.

Treatment

Sarcoidosis tends to undergo spontaneous remissions, and it is therefore difficult to assess the effect of treatment; however, Siltzbach (1952) reported the effects of cortisone therapy in 13 patients with uveal tract, skin, lung or peripheral lymph node involvement with serial tissue biopsies. In all cases he found subjective and objective improvement of varying degrees, and 70% showed relapse when treatment was stopped. Mather, Dawson and Hoyle (1955) have treated 93 patients with radiographic evidence of sarcoidosis in the chest with streptomycin and cortisone, and all showed clinical and radiographic improvement; in three cases with disease of over two years' duration the epithelioid follicles seen on previous liver biopsy completely disappeared.

A less encouraging report came from Stone, Schwartz, Feltham and Lovelock (1953), who found that in the majority of seven cases treated with cortisone their clinical condition became worse, which they concluded to be due to acceleration in the development of pulmonary fibrosis.

Matthews (1959) has reported three cases of neurological sarcoidosis treated with cortisone, with partial improvement in each case, but found it difficult to assess the benefit of active therapy. A case of sarcoid encephalo-myo-meningitis, recorded by Carstensen and Norviit (1953) apparently showed a dramatic response to cortisone.

Case Reports

CASE No. 1

M.B., female, a housewife, aged 31 years when she was first admitted to the Bristol Royal Infirmary, as an emergency, on 17.4.55. For three years she had had attacks of unconsciousness followed by frontal headache every few weeks, which had recently become more frequent and much more severe. Eleven days before admission she had had a very severe attack, the headache persisting, and associated with vertigo which caused her to fall when she attempted to walk, and loss of consciousness for a few minutes.

Examination: No pyrexia. Blood pressure 110/70. No abnormal physical signs were demonstrated, although her general practitioner had found bilateral extensor plantar responses and slight incoordination

of movements on the left side of the body six days before admission.

Investigations: Hæmoglobin, 101%; W.B.C., 7,600/c.mm.; E.S.R., 26 mm./hr. (Wintrobe); Wassermann and Kahn negative. C.S.F. pressure, 145 mm. water with no spinal block; protein, 200 mg./100 ml.; W.B.C. 6/c.mm. (all mononuclears). Lange curve, 3444321100. Skull X-ray: normal. Chest X-ray: multiple small opacities in the apices of both lungs, consistent with lobular consolidation or deflation.

Progress: Following admission she continued to have headaches, associated with vomiting. A second lumbar puncture on 28.4.55 showed a pressure of 60 mm. water, protein 160 mg./100 ml., Lange 1124431100. On 2.5.55 she was transferred to the Frenchay Neurosurgical Unit where she was found to have increased tone in the lower limbs with ankle clonus, bilateral exaggerated reflexes and extensor plantars. A left carotid arteriogram showed no abnormality. On 12.5.55 an air encephalogram was attempted but there was found to be a spinal block. Following this, ventriculography showed the ventricles to be enlarged and suboccipital craniotomy was performed; adhesions were found between the arachnoid and the dura mater at the level of the foramen magnum, which were divided. After the operation she made a good recovery and her headache rapidly disappeared. The diagnosis at this time was considered to be adhesive arachnoiditis with communicating hydrocephalus. She was discharged on 28.5.55 but continued to vomit once a day after meals and her gait remained unsteady.

In September, 1955, ventriculography was repeated and showed no change from the previous picture. Ventricular C.S.F. protein, 65 mg./100 ml.; lumbar C.S.F. protein, 202 mg./100 ml. No block was demonstrated. At this time both plantar responses were still extensor but she was able to walk unsupported, though unsteadily.

When seen in the Out-patient Department on 11.10.55 slight enlargement of the thyroid was noticed and her hair was thought to be rather dry; the plasma cholesterol estimation was subsequently found to be 400 mg./100 ml. No change was found in her neurological signs.

On 31.12.55 she was readmitted to the Bristol Royal Infirmary for investigation of her myxoedema. Examination showed a slightly unsteady gait, nystagmus, an increased left knee-jerk, bilateral extensor plantar responses and diminution of touch and pain sensation below the left knee. The E.S.R. was then 39 mm./hr. Urinary 17-ketosteroid excretion was 4.6 mg. in 24 hours.

On 11.1.56, following an attempted water excretion test, she complained of severe headache and vomited once; she was pale and looked ill, but apart from a tachycardia there was no change in the physical signs. Early the next morning, however, she suddenly collapsed, becoming cyanosed with stertorous breathing, a pulse rate of 150 per minute and an unrecordable blood pressure. She died soon afterwards.

Autopsy: There was enlargement of the hilar glands and histology showed the gland structure to be replaced by epithelioid follicles. Lung sections showed similar non-caseating lesions with no acid-fast bacilli visible. The superior surface of the brain was normal, but there were arachnoid adhesions round the foramen magnum and in other areas thickening of the dura and arachnoid were seen, sections of which showed patchy lymphocytic infiltration and epithelioid follicles. Similar lesions were found scattered throughout the brain and spinal cord.

CASE NO. 2

P.R., female, was 53 years old when admitted to the Bristol Royal Infirmary on 8.8.53. In 1948 she noted a tender lump in the left axilla which apparently disappeared spontaneously. In 1952 she began to have headaches over the vertex, lasting about six hours, coming on every few weeks. Two months before admission she developed persistent pain over the right eye, accompanied by nausea, and the following day the eye was red and swollen and she was unable to see with it. She was admitted to hospital where an iridectomy was performed and the sight improved. One month later, on 1.7.53, the right eye again became painful and she was admitted to a nursing home with iritis; four days later she developed iritis in the left eye also and the vision in both eyes became misty. Two infected teeth were extracted at this time. On 12.7.53 she developed a 'pneumonitis' at the base of the left lung which subsided over the next 14 days after treatment with aureomycin and penicillin. On 21.7.53 she noticed bilateral deafness, the right worse than the left, which was considered to be due to bilateral cochlear lesions. Mentally she was at this time often very depressed and sometimes experienced the sensation that she was 'floating' and found it difficult to stand, though she never actually fell. Lumbar puncture showed an increased C.S.F. pressure with cells 250/c.mm. (mostly lymphocytes) and protein 70 mg./100 ml.

It was then considered that a space-occupying lesion was the possible cause of these signs and symptoms and she was transferred on 1.8.53 to the Frenchay Neurosurgical Unit. There she was found to have an enlarged left jugulo-omohyoid lymph gland, which was neither tender nor painful. Both eyes showed vitreous opacities and the fundi were not seen. The pupils were irregular with no reaction to light and there was a bilateral anterior and posterior uveitis; the eyes were treated with atropine and cortisone. On 3.8.53 the C.S.F. showed a cell count of 90/c.mm. (lymphocytes 96%) and protein 60 mg./100 ml. Chest X-ray normal.

On 8.8.53 she was seen by Dr. A. M. G. Campbell who diagnosed sarcoidosis and she was transferred to the Bristol Royal Infirmary.

Family history: The patient's father died of tuberculosis and his mother and two sisters also suffered from this disease.

Examination: She had a pyrexia of 101° F., and an erythematous maculo-papular rash over the face, neck, trunk and limbs, which was confirmed to be chicken-pox when other members of the ward subsequently developed it. There was a slight swelling of the right parotid gland which subsided within a few days. Marked bilateral conjunctival and corneal injection was still present with haziness of the cornea and fixed pupils. She could distinguish light from dark with both eyes and could just count fingers held up against the light. She had signs of a partial nerve deafness in both ears. The reflexes were normal except for an increased left biceps jerk; the plantars were flexor. There was diminished sensation to pinprick over the right middle and lower abdomen, over the distribution of T. 10-12. No other abnormal neurological signs were found; the chest was clinically clear.

Investigations: Haemoglobin, 90%; W.B.C., 2,800/c.mm. X-ray of the hands showed minor changes in the phalanges characteristic of sarcoidosis.

Progress: She was given subconjunctival midricaine and cortisone for several weeks with no appreciable amelioration of the irido-cyclitis and on 27.8.53 cortisone was commenced systemically. Between 13.9.53 and 23.9.53 she was given three intravenous injections of

T.A.B. vaccine with fairly good febrile responses. Following this she felt faint on several occasions and was once disorientated for about one and a half hours, apparently feeling that she could not speak or move, though there was never any medical evidence of paralysis. While in hospital she completely lost all her naturally red hair, but eventually grey hair grew in its place. On 5.10.53 the C.S.F. protein was 20 mg./100 ml., and the cell count 4/c.mm. By the time she was discharged on 15.11.53 she was almost totally blind, but all her other symptoms had subsided except for occasional pains in the top of the head.

After her discharge she gradually improved in general health, but continued to have pain in both eyes for about a year, during which time she gradually became completely blind. When I saw her in March 1960, she was managing to work for about two hours each day, but was easily exhausted. She complained of occasional aches 'in her bones' and the transitory appearance of 'lumps' in various parts of her body persisting for a few days. She also sometimes developed crops of slightly irritating raised red spots, each lasting for about a week, biopsy of which, however, showed no evidence of sarcoidosis. Her eyes were sunken and the eyeballs soft with opacity of the cornea completely obliterating the pupils. A Kveim test was negative.

CASE NO. 3

S.E., female, a laboratory technician, had been working for the previous six months with *Mycobacterium tuberculosis* cultures. She was aged 21 years in April, 1954, when she complained of smarting of the left eye for several months. In July she developed blurred vision in the same eye and examination of the fundus showed swelling of the left disc with many small haemorrhages. In August, 1954, she was admitted to the Bristol Eye Hospital. She also complained of a 'heavy feeling' in her head for about six weeks before admission.

Previous history: When aged 7 years she had whooping cough with pneumonia and the following year had some cervical glandular trouble which was treated with tablets.

Examination: Increased vascularity was observed around the left limbus and papillitis of the left disc was present with early retinal oedema on the left; the right fundus was normal. No other abnormal physical signs were found. The visual fields were normal.

Investigations: Chest X-ray showed enlarged left hilar glands, confirmed by tomography. X-rays of the hands and feet were normal. Mantoux (1 in 100) was negative. C.S.F. pressure, 105 mm. water with free rise and fall; protein, 20 mg./100 ml.; cells, 5/c.mm.; serum calcium, 9.8 mg./100 ml.; phosphate, 3.7 mg./100 ml.

Progress: She was treated with atropine and cortisone drops to both eyes and on 8.8.54 was transferred to the Bristol Royal Infirmary where it was noted that the papillitis was bilateral. On 12.8.54 systemic cortisone, P.A.S., and streptomycin were commenced.

By 18.8.54 the vision was no longer blurred though the appearance of the discs was unchanged. On 3.9.54 the visual fields were unchanged and by the time she was discharged on 18.9.54 there was only slight swelling of the left disc and none of the right. When seen in Out-patients two weeks later all signs of iritis had disappeared, though the left papillitis persisted. X-ray of the chest at this time showed an increase in the hilar glandular enlargement. By 30.11.54 the left disc was normal. Mantoux (1 in 100) was negative. In July 1955 chest X-ray was normal.

When I saw her in April 1960 she was perfectly well

with normal vision, except that she sometimes saw black spots before her eyes and found a sudden bright light painful. Her fundi were normal. A Kveim test was negative.

CASE NO. 4

M.B., female, aged 32 years, a bank clerk, whom I saw at the Bristol Royal Infirmary Out-patient Department on 21.1.60. In November 1950 (when aged 22 years) she first complained of blurring of vision and inability to see to the left. She also had some difficulty in making her speech clear and had frequent headaches and occasional attacks of tinnitus. Examination showed a left facial weakness and the tongue deviated to the right; the left pupil was larger than the right and blurring of the left optic disc was noted. A lumbar puncture showed the protein level to be 15 mg./100 ml. and the cell count 8/c.mm. The facial palsy recovered after seven weeks. When examined in February 1951 the pupils were fixed; visual field estimation showed enlarged blind spots in both eyes and the left optic disc was papilloedematous. The reflexes in the right leg were increased and the right plantar response was extensor. Chest X-ray showed glandular mediastinal swelling, but films of the hands were normal. The C.S.F. protein and cells were again normal. The following month she had severe bilateral irido-cyclitis, and when seen in July 1951 her E.S.R. was 30 mm./hr. and examination of the eyes showed vitreous opacities and deposits in the anterior chamber and on the cornea. A diagnosis of sarcoidosis was made. She went back to work in November 1951 and over the next three years only complained of occasional blurring of the vision. In September 1954 she presented with two palpable lumps in the right axilla which were not biopsied and she was successfully treated with penicillin. Her E.S.R. was then 30 mm./hr., and a chest X-ray showed small opacities in the right mid-zone consistent with sarcoidosis. In July 1956 she again had a small gland palpable in the right axilla.

When seen on 21.1.60 she was quite well except for occasional blurring of vision in the left eye when she was tired.

Examination: The pupils were unequal, the right being larger than the left, both were irregular and both reacted to accommodation, but not to light. The fundi were normal. The right biceps and right knee reflexes were increased, but both plantars were flexor. No other abnormal physical signs were demonstrated. A Kveim test was negative. Chest X-ray showed no change from the films taken four years previously with mediastinal glandular enlargement and appearances suggesting pulmonary collapse or fibrosis in the right lower zone.

CASE NO. 5

H.M., male, aged 52 years, had been a stonemason until about ten years before, seen on 30.1.60 at the Bristol Eye Hospital. Six years previously he had had 'flu' and since that time he had noticed 'pin-pricks' in both eyes when tired. Four years before admission, while at work in his office, he experienced a sudden muzziness in the head, could not think clearly and noticed blurring of vision on the right side, affecting both eyes. This state lasted for 24 hours and then passed off, but he continued to see what he described as 'geometrical patterns' on the right side of each visual field for about a month and this was then replaced by a 'black spot' situated in the same position. He attended the Eye Hospital in November 1959 complaining of blurring of vision and redness of the right

eye which was treated successfully with atropine and prednisolone drops.

Examination: No abnormal physical signs were found apart from the visual fields. These showed a dense, strictly congruous, right homonymous scotoma in each visual field, mainly in the right upper quadrant, but extending into the lower right quadrant and coming right up to the fixation point; these changes strongly suggested a lesion in the radiation or cortex on the left and were consistent with a temporal lobe lesion. In addition to these features the right visual field showed some generalized retraction of both upper quadrants with a sharp edge between the upper and lower quadrants on the left. This appearance was consistent with nerve fibre bundle lesions of the right optic nerve.

Investigations: Chest X-ray showed bilateral hilar glandular enlargement. Mantoux (1 in 1,000) positive. C.S.F. protein, 26 mg./100 ml.; cell count nil. Air encephalography showed a possible lesion at the tip of the left temporal lobe. Conjunctival biopsy showed nodules typical of sarcoidosis.

Progress: Prednisolone therapy was commenced on 5.1.60 with a dose of 15 mg. t.d.s. which was gradually reduced to 5 mg. t.d.s. The visual fields were charted on 18.2.60 but showed no change from those recorded four weeks earlier. A Kveim test performed on 30.1.60 was negative, probably because steroid therapy was commenced before the test was completed.

CASE NO. 6

H.D., male, aged 51 years, a Devonshire farmer, was admitted to the Bristol Royal Infirmary on 22.8.59. In October 1954 he collapsed while at market and complained of persistent pain in the epigastrium and left side of the chest. He was admitted to hospital and treated with penicillin. A barium meal was normal. Four weeks later he was transferred to another hospital and at this time he was confused, with slurred speech, and complained of severe intermittent headache with vertigo and a cough productive of thick sputum. He had bilateral extensor plantar responses, a positive Kernig's sign and a pyrexia of 100° F. Repeated C.S.F. examinations showed a consistently high protein level, varying from 150 to 200 mg./100 ml., the cell count being normal. X-ray changes in the lungs were interpreted as being those of miliary tuberculosis, but sputum and C.S.F. cultures for tubercle bacilli were negative. He was diagnosed as tuberculous meningitis and was treated with streptomycin, P.A.S. and I.N.H. with apparently a little improvement. At the end of this period sarcoidosis was considered as the diagnosis. While in hospital his eyes became inflamed and congested.

During the succeeding four years he continued to do some work on his farm, but complained of increasing lumbar pain and his gait became progressively more unsteady. He had three more attacks of unconsciousness which were apparently relieved by lumbar puncture. He also complained of hesitancy and frequency of micturition.

By January 1959 his backache was severe, pain radiating down both legs; he was again admitted to hospital. His legs then became very weak and he was eventually unable to stand. In August the C.S.F. protein was 2.36 g./100 ml., and a myelogram showed a partial spinal obstruction with appearances consistent with widespread adhesions. Tomography of the chest showed massive widening of the mediastinal shadow.

On 22.8.59 he was transferred to the Bristol Royal Infirmary under the care of Dr. A. M. G. Campbell. **Examination:** The fundi showed bilateral optic atrophy. The knee and ankle reflexes were absent and both

plantar responses were extensor. There was gross wasting of the thigh and calf muscles and the power in the lower limbs was very diminished and the tone increased. There was a slight left facial weakness. He had some dysarthria and dysphagia and sensation was diminished on the left side of the body. The vibration sense was diminished at both ankles. Blood pressure 185/130 mm. Hg.

Investigations: Hæmoglobin, 113%; E.S.R. (Wintrobe), 13 mm./hr.; plasma proteins, 5.9 g./100 ml.; albumin, 2.95 g./100 ml.; serum calcium, 8.5 mg./100 ml.; plasma inorganic phosphate, 2.8 mg./100 ml. X-rays of the hands showed typical changes of sarcoidosis.

Progress: On 23.8.59 prednisolone 10 mg. t.d.s. was commenced and the power in his legs improved dramatically: after a week he was walking short distances with help. C.S.F. examination on 7.9.59 showed a free rise and fall of fluid and a protein level of 630 mg./100 ml. His knee and ankle reflexes were then present and equal and the plantars both flexor. The power in his legs was good and he was walking up to 20 yards without help. His backache had subsided and he was discharged home on prednisolone 10 mg. t.d.s. on 30.9.59.

He was readmitted on 14.10.59 for assessment of his progress. In an attempt to establish a histological diagnosis a liver biopsy was performed, but although this was atraumatic six hours later he went into status epilepticus with peripheral circulatory collapse. His circulation responded to large doses of steroids, but his recovery to consciousness was very slow and he remained confused and dysarthric. The liver sections showed no evidence of sarcoidosis. He gradually improved and on 4.11.59 was transferred to a hospital nearer home. On 10.12.59 he was discharged home for Christmas, after a Kveim test had been performed, but he died a week later, following a period of unconsciousness of about 12 hours' duration, and a post-mortem examination was not obtained.

CASE No. 7

B.P., male, aged 34 years, a newsagent, was admitted to the Bristol Royal Infirmary on 14.11.59. One month previously, immediately after getting up in the morning, his vision became suddenly blurred and he became dysphasic, felt dizzy, vomited several times and felt shooting pains down both legs. He lay down and went to sleep and though his wife found him difficult to rouse he felt quite well on waking again. He had two similar attacks during the following three weeks. His wife stated that she had noticed that his attitude had altered recently towards his work, being then not as painstaking and responsible as previously. He said his fluid intake had increased over the previous few weeks.

Previous history: In 1949 he was admitted to the Infirmary with a persistent cough. Mantoux (1 in 1,000) was slightly positive and chest X-ray showed bilateral hilar gland enlargement. A diagnosis of sarcoidosis was made. The patient discharged himself.

In 1955 he was admitted to the Infirmary for investigation of a fever of sudden onset accompanied by rigors and vomiting. Chest X-ray showed no abnormality, the hilar enlargement previously noted having subsided. No cause for the pyrexia was found and he quickly recovered.

Examination: He had a left ptosis and a slight right facial weakness. The arm and leg reflexes were slightly increased on the right side of the body, but both plantar responses were flexor. No other abnormal physical signs were found.

Investigations: Fluid balance and urine examination

were normal. Blood sugar after 24 hours' starvation, 75 mg./100 ml. C.S.F. pressure, 195 mm. water; C.S.F. protein, 182 mg./100 ml.; C.S.F. cell count, 86/c.mm. (90% lymphocytes). X-ray of chest was normal.

Progress: He had no further attacks while in hospital, but was very lethargic, sleeping most of the time. He was discharged on 3.12.59 without treatment, to await the result of a Kveim test, which was subsequently found to be positive. Lumbar puncture was repeated on 16.1.60 and the C.S.F. pressure was 245 mm. water, with a sluggish rise and fall; the protein was 156 mg./100 ml., and the cell count 64/c.mm. (100% lymphocytes). Since his previous admission he had had no more attacks and had gradually become less lethargic, so that at that time he felt quite well and it was considered that treatment was not indicated.

Discussion

Seven cases of sarcoidosis affecting the central nervous system are described in this paper. Cases 1, 4 and 6 had developed generalized spinal and cerebral lesions with arachnoiditis; case 2 showed signs of generalized lesions with meningitis with permanent damage to the optic nerves. In case 3, also, both optic nerves were involved, while in case 5 only one optic nerve was damaged together with evidence of a lesion in the region of one temporal lobe. Case 7 showed signs of deposits in the region of the hypothalamus.

Three cases were proved histologically (1, 5, 7). The Kveim test was positive in only one case (7), probably because in three cases (2, 3, 4) all signs of active disease had ceased several years previously, while in one case (6) the patient died before the test was completed, and in another (5) treatment with prednisolone was commenced a week after injection of the antigen. The conjunctival biopsy in case 5 proved the diagnosis.

The onset in each case varied considerably. Case 4 presented like a case of disseminated sclerosis, though the chest x-ray suggested sarcoid. Four cases (1, 2, 5, 7) simulated intracranial space-occupying lesions, case 1 undergoing a craniotomy. Case 6 was treated for a year as a case of tuberculous meningitis, the first symptom in this case being epileptiform fits similar to two cases described by Jefferson (1957).

In all seven cases, sarcoidosis was demonstrated also in sites other than the nervous system. Case 2 illustrated the well-known uveo-parotid syndrome (Ross, 1955) and case 3 presented with iritis, while case 4 developed iritis during the course of the disease. Six cases (1, 3, 4, 5, 6, 7) at some time had demonstrable pulmonary involvement, though in case 7 this was only apparent in x-rays taken 10 years before the nervous system was involved.

Case 6 showed the typical picture of diffuse arachnoid adhesions on myelography, as described recently by Wood and Bream (1959). X-rays of

the hands showed characteristic changes in two cases (2, 6).

Study of the cerebrospinal fluid is of great value, particularly in differentiation from disseminated sclerosis, when the protein is rarely raised to such a high degree. Four cases (1, 2, 6, 7) showed an abnormally high C.S.F. protein, in case 6 this being raised to as much as 2.36 g./100 ml. Two cases (2, 7) showed an abnormally high C.S.F. white cell count, the majority being lymphocytes.

The Mantoux reaction (1 in 1,000) was only recorded in three cases (3, 5, 7), being negative in one case and positive in two.

In the cases recorded the results of treatment are obviously difficult to assess. Case 6 showed a dramatic temporary response to prednisolone while case 5 showed no change after four weeks, treatment, and cases 4 and 7 went into a spontaneous remission, although case 7 has not yet been followed up long enough to know how permanent this remission may be; case 4 lost all physical signs of nervous disease. With these cases in mind, it does seem that where arachnoid adhesions have developed, as in cases 1 and 6, the prognosis is poor, but that without this compli-

cation the disease may become quiescent for long periods and the outlook is not as pessimistic as has sometimes been stated.

The importance of the Kveim test must be stressed, both as a reliable means of diagnosis, and as a method of eliciting whether the disease is still active (Nelson, 1949; James and Thomson, 1955).

Summary

The purpose of this paper is to draw attention to sarcoidosis affecting the central nervous system with the difficulties of diagnosis and prognosis, and to emphasize that it is probably more common than is generally believed. Until cases are recognized and carefully followed up it is impossible to gain any further knowledge regarding the course and successful treatment of this disease.

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