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Working Notes on *"An Investigation into an Unusual Disease seen in Epidemic and Sporadic Form in a General Practice in Cumberland in 1955 and subsequent years"* by A.L. Wallis; Doctoral Thesis, University of Edinburgh, 1957

Margaret Williams 1st January 2003

NB. *The doctoral thesis is 143 pages. These are not comprehensive notes; they extrapolate ONLY what is deemed of most relevance to the present study. These notes do not adhere strictly to the pagination of the thesis: sections have been amalgamated for ease of topic reference.*

SUMMARY

An infectious disease occurred in epidemic and sporadic form in a rural, single-handed general practice in Cumberland in 1955 and subsequent years.

The clinical features showed similarity to those reported from outbreaks of encephalomyelitis of unknown origin which had occurred in various parts of the world in the preceding decade.

Both sexes and all age groups were affected, and the disease affected over 200 people. The more severe attacks occurred in adults.

There were changes in the blood picture in 30% of cases.

There was objective evidence of CNS involvement in 20% of cases, with subjective neurological phenomena in > 60% of cases.

Characteristic features were the presence of muscular pain and a protracted outcome (characteristic of CBV).

INTRODUCTION

The disease was the cause of much disability and loss of working time.

It was characterised by acute myalgia; disturbance of the reticulo-endothelial system and by CNS involvement; also by psychological sequelae.

Relapses were common: those with more severe involvement of the RES and CNS had more prolonged illness with greater liability of relapses. Some patients suffered a mild illness initially, only to be followed by more severe relapse at a later stage.

Recurrence of symptoms became a well-marked feature.

The causal agent was pan-trophic, with various systems showing clinical evidence of disease.

Sequelae included debility, depression and emotional lability.

During the early stages of the epidemic, Wallis recognised that the disease was not conforming to any disease with which he was familiar.

EPIDEMIOLOGY

The disease occurred as an epidemic between January – August 1955; thereafter it was sporadic. Farmers especially presented with vertigo when haymaking.

ONSET

Onset was either abrupt or insidious, with the latter being more common in adults.

The more severe cases had an insidious onset.

Adults were more severely affected than children and adolescents.

DIAGNOSIS

Diagnosis was made on clinical grounds: in the more severe cases a definite pattern emerged. Diagnosis of this disease was made when the following features were present in the clinical picture:

1. Dizziness

2. Headache
3. Extreme lassitude
4. Drowsiness and lethargy by day and restlessness at night
5. Thickly coated tongue, dry mouth, sore throat and dry cough
6. Blurred vision with diplopia on upward and lateral gaze
7. Spontaneous severe pain in muscles of the neck, lower back and limbs
8. Muscle tenderness and some loss of muscle power
9. Parasthesiae and some degree of sensory impairment
10. Tender enlargement of lymph glands in neck, inguinal region and axillae
11. Splenic and hepatic tenderness; subcostal pain
12. Depression and emotional lability (sometimes anxiety)
13. Low grade fever or subnormal temperature
14. Tachycardia

The clinical picture varied from mild to one of considerable severity and duration.

In a minority, the onset was precipitate diarrhoea with associated nausea: in this group, upper respiratory symptomatology was minimal.

The costal margins were the site of considerable pain.

Involvement of the liver and spleen was a typical finding: both were tender to palpation; in some cases there was actual enlargement.

Morphological abnormalities were found in lymphocytes associated with an eosinophilia in 30% of cases.

SYMPTOMS

In cases of abrupt onset, signs and symptoms were:

general prostration and somnolence
severe headache
aching pains in back of neck, lower limbs, back, shoulders and upper limbs
subcostal pain
dizziness
dry, parched mouth and throat
enlarged tender lymph glands
sore eyes
blurred vision
abnormalities of taste and smell

The initial stage was followed by lethargy and weariness increasing rapidly in degree, with loss of muscular power, especially in lower limbs. Patients longed for bed, but it needed a considerable effort of will to get there: if stairs had to be climbed, the effort of doing so left them exhausted, with aching legs which felt leaden.

Patients fell into a deep sleep at first, then became restless, with vivid, disturbing dreams.

Within 48 hours, headache (usually frontal, but not infrequently temporal) was severe, as was aching pain in back of neck. Aching in back of neck was ***always*** present.

Myalgia was prominent and the affected muscles were acutely tender.
Acute myalgia commonly affected the para-spinal muscles, especially in the lumbar region and shoulder girdle.

Photophobia was present, with blepharitis in some cases. Blurred vision was present, and it required a conscious effort to bring objects into focus; it was not due to refraction errors. Sudden eye movements caused acute stabs of pain. Diplopia was present in all severe cases.

During the first week, vertigo was usually present, associated with lateral nystagmus (which was intermittent).

Hyperaesthesia was present in the skin over affected muscles.

Pins and needles commonly affected the extremities. Other abnormal skin sensations included prickling (accompanied by observable slow waves of contraction along a bunch of muscle fibres).

Attacks of sweating were normal, with drenching sweats at night: changes of night clothes were frequently needed because of frequency of drenching sweats.

<u>Physical examination of abrupt onset cases revealed:</u>

tachycardia
low grade fever
clusters of petechiae on the palate
mouth ulcers
abdominal distension
tender nodules in recti muscles
tenderness without guarding was always present on palpation at the subcostal margins and frequently over the RIF

liver and spleen were very tender in the more severe cases, being enlarged in some cases
skin was affected by rashes (both maculo-papular and urticarial)
eyes were puffy and upper lid tended to droop

The most obvious feature O/E was the degree of spontaneous muscular pain: in many cases SLR caused severe pain before the leg had been raised more than one inch and hamstrings went into spasm.

Palpation of the affected muscles frequently revealed the presence of palpable and tender nodules in muscles, with a gritty sensation to the touch.

Pain in the low back was the main myalgic manifestation, being aggravated by standing. It was sufficiently severe for patients to take to their bed and lie without moving.

Pain in the neck was severe.

Neurological examination revealed that diplopia occurred on upward and lateral gaze in a considerable number of patents: this argued the presence of some degree of muscle weakness.

Mental state examination in the early stages revealed somnolence, followed in the later stages by emotional lability.

There was an inversion of sleep rhythm, with vivid dreams being extremely common.

Progress of disease in abrupt onset.

Headache, myalgia, muscle cramps and waves of dizziness persisted, as did parasthesiae.
"Easy fatiguability was the rule".

In cases of insidious onset, signs and symptoms were:

excessive tiredness
sweating
cold hands and feet
dizziness and unsteadiness
headache
neuralgic pain (frequently referred to ear and down neck)
insomnia
cognitive problems

aching in back and legs
pins and needles in hands and feet
partial aphonia
blurred vision (this was a constant complaint)
frightened by loss of power in legs (being almost unable to bring one leg past the other)
joint pains (knee, ankle, elbow, wrist and MCP joints)
skin over fingers was cyanosed and felt cold
pain in calf muscles
myalgic pain in back, neck and shoulders
hyperaesthesia of skin (this was commonly noted)

Neurological signs and symptoms in cases of insidious onset (and in later stages of abrupt onset) were:

1. parasthesiae
2. hyperasthesiae
3. impairment of taste and smell
4. vertigo
5. blurred vision
6. loss of concentration
7. poor recent memory
8. impairment of co-ordination and unsteadiness
9. general weakness (a frequent complaint: walking, lifting and carrying were all limited)
10. inversion of sleep rhythm
11. pupils frequently sluggish in reaction to light and accommodation
12. ptosis of eyelid (not in all cases)
13. hyperacusis (commonly found)
14. nystagmus
15. neuralgic pain was commonly complained of
16. alteration in speech
17. nominal aphasia
18. ataxia
19. Romberg commonly positive
20. observable tremor
21. impaired judgment of distance
22. a variable reflex state was found during the course of the illness, being brisk in a large number of cases, with knee and ankle clonus

<u>Sensory disturbance complained of by most cases included:</u>

tingling / pins and needles
numbness / heaviness of limb

feeling of pressure on scalp as if wearing a tight skull cap
feeling of drops of water trickling on affected area
feeling of insects crawling over skin
abnormal perception of taste and smell

Objective sensory disturbances noted:

hyperaesthesiae
impairment of position sense
impairment of joint sense
impairment of vibration sense
some cases showed diminished sensation to touch and pin prick

Autonomic disturbance:

abnormal coldness in extremities
sweating / drenching nocturnal sweats
sluggish pupillary reactions

A labile emotional state and outbursts of weeping proved remarkably persistent.

Persistence in an activity was found difficult to maintain.

Complications

myocarditis (heart rate was accelerated during the illness)
dyspnoea on slightest exertion
orchitis
DVT

Treatment

No specific cure, so palliative only.

General management: bed rest was the most important factor; early mobilisation resulted in relapses. Convalescence was slow in the more severe cases.

Prognosis

Persistence of symptoms was a marked feature.

In a few cases, there was permanent neurological involvement.

It was found that an extraneous infection (eg. a common cold) caused the re-appearance of symptoms even in some cases who had been asymptomatic for months.

POST-MORTEM HISTOPATHOLOGY

There were no fatalities during the period January – August 1955, but one patient who had exhibited the illness died the following year, severe memory defect and nominal aphasia having persisted. Death was found to be due to numerous small haemorrhages in the mid-brain. Post-mortem histopathology report from this (female) case stated

> "There are in the entire diencephalon, particularly round the third ventricle, numerous small haemorrhages, which extend into the adjacent parts of the mid-brain. Similar haemorrhages can be seen in the corpora mamillare. The haemorrhages are mostly around the small vessels but some are also to be seen in the free tissue. This is a significant finding."

DISCUSSION

The main clinical features were:

Dizziness
Somnolence
Acute myalgia and muscular weakness, with loss of sustainable power in limbs
Lymph gland enlargement
Tender liver and spleen
Neurological disturbance (this was remarkable for fluctuation and for the complex nature of the involvement as shown by its effects)
Mental effects
Protracted course with relapses.

The presence of acute myalgia, muscle spasm and protracted course is characteristic of CBV.

Wallis was struck by the stoicism of those affected --- often he would find out about a relapse only when visiting another member of the family for an unrelated disorder.

Notable features were the similarity of symptoms and clinical history with other outbreaks in Akureyri, Iceland (1948); Adelaide, Australia (1949); New York State

(1950); Middlesex Hospital, London (1952); Coventry, England (1953); Durban, South Africa (1955); Royal Free Hospital, London (1955).

NB Wallis considered this was a new, unusual disease with which he was not familiar; he repeatedly sought expert advice, investigations and laboratory assistance from the highest sources available. No causative agent was isolated.

One paragraph in his thesis stands out:

> " **Consultant medical opinion rather clearly showed disinterest, an implication being that a hypothetical mountain was being erected on an imagined molehill, and that the cases could readily be explained on conventional grounds by a competent person. The psychogenic sequelae were considered to be affective disorder"**

Wallis then adds:

> **"I understand, however, since obscure illnesses have become respectable following the outbreak at the Royal Free Hospital, followed by reports and leading articles in the medical press, the consultant in question now makes such a diagnosis himself".**