RARER MANIFESTATIONS OF HERPES ZOSTER

A REPORT ON THREE CASES

BY

THOMAS PARKINSON, M.D., M.R.C.P.

Medical Tutor, St. Bartholomew's Hospital

Herpes zoster usually presents as a mild illness with a characteristic rash accompanied by local pain and preceded by a varying degree of constitutional disturbance. Post-herpetic neuralgia is a common sequel, but complications are rare. Of the complications which have been recorded a concomitant varicelliform eruption is perhaps the most common. The rarer, and more serious, complications include lesions of the motor neurones, myelitis and meningitis, encephalitis, and osteoarthritis (Wilson, 1940). It is the occurrence of such complications that at once dispels the concept of zoster as a uniformly benign infection confined to the sensory neurones. Moreover, these complications open controversial aspects on the aetiology and pathology of the disease and upon the difficult problem of the relationship between zoster and varicella. The following three cases are placed on record as exemplifying certain of these rare complications. All three patients showed evidence of affection of motor neurones, and two of them exhibited a generalized eruption during the course of the disease.

Case 1

Zoster, accompanied by paralysis, in the distribution of the fifth cervical segment.

A solicitor's clerk aged 60 was admitted to hospital on July 4, 1947. He gave a history of chicken-pox in childhood. In 1918 he had sustained a shrapnel wound of the right elbow, which had left him with a complete ulnar lesion on that side and much limitation of movement of the elbow-joint.

Six weeks before his admission he had suffered from acute pain in the right shoulder. Three days later a rash appeared in the antecubital fossa and rapidly spread up the outer side of the arm as far as the right shoulder. Three days after the appearance of the rash he noticed, quite suddenly, that his right arm was weak and that he could raise the arm from the side only with difficulty. The weakness increased over the next few days until the right arm was quite useless. Since that time the rash had cleared up, but the weakness had not improved at all. After the disappearance of the rash he had felt tingling and numbness in the area of skin previously affected.

Examination showed a healthy well-built man. There was a pigmented scarring over the site of the recent rash, distributed on the outer side of the upper arm from the shoulder to the elbow—i.e., in the cutaneous distribution of the fifth cervical dermatome. There was some hypo-aesthesia to pin-prick and cotton-wool sensation in the same area. There was considerable wasting of the right deltoid, supraspinatus, and infraspinatus muscles. No abduction of the shoulder was possible, although a flicker of muscular contraction was palpable over the deltoid muscle when abduction was attempted. Slight contraction of the supraspinatus and infraspinatus was likewise palpable over the muscle bellies. The biceps and brachioradialis muscles on the right side were weaker than those on the left. Under the nomenclature suggested by the Medical Research Council (1942) the muscular contractions at this time were: deltoid 1, supraspinatus 1, infraspinatus 1, biceps 4, brachioradialis 4. There was a deep scar of the old wound on the inner side of the right elbow, and below the elbow there was a complete ulnar-nerve palsy. The biceps and supinator reflexes on the right side were impaired; the triceps-jerk was normal. The remainder of the physical examination revealed nothing abnormal. Lumbar puncture on July 6 showed a clear fluid under normal pressure. The cerebrospinal fluid contained 5 cells per c.mm. The protein was 0.055% with a slight increase

of globulin, and the chlorides 0.75%. The Wassermann reaction and Lange curve were negative.

The patient was treated by resting the arm in an abduction splint and by faradic stimulation of the muscles affected. He was discharged from hospital on July 30 to continue treatment as an out-patient, and at this time there was pronounced objective improvement. He was last seen on Aug. 16, when recovery was almost complete.

Case 2

Ophthalmic zoster with generalized eruption, followed by weakness of the levator palpebrae.

A housewife aged 48 was admitted to hospital on July 9, 1946. There was no history of previous illness, and she denied having had chicken-pox. She complained of an irritation on the left side of the forehead for the previous week, and on July 6 she had first had severe neuralgic pains over the left eyebrow. On the day before admission the left eye became swollen and painful, and a rash was noticed on the forehead. On admission the patient looked ill and had a fever of 101.8° F. (38.8° C.). There were a moderate number of vesicles on erythematous bases in the distribution of the ophthalmic division of the trigeminal nerve on the left side. The left eye showed conjunctival injection, with some photophobia and extreme tenderness to pressure. There were no other abnormal signs, and the rest of the skin was clear. During the next three days (July 10 to 12) the number of vesicles increased, the erythema spread, and the upper and lower lids became grossly oedematous. The appearance was now quite typical of a severe herpes zoster.

On July 13 the patient complained of irritation of the skin. Examination then showed that she had a generalized eruption on the trunk and proximal parts of the limbs, with a single lesion on the face. The eruption was quite typical of that seen in varicella, and the subsequent course of pustule formation and healing followed as customary in that disease. It was noted, however, that after the first 24 hours no fresh crops of vesicles arose. Whether or not the previous lesions had occurred in crops is not known, as no examination of the skin had been carried out between the initial examination and the complaint of irritation. As the herpes recovered it was evident that there was considerable weakness of the levator palpebrae muscle on the left, giving rise to obvious ptosis. The scabs from the varicelliform rash separated on Aug. 1, 14 days after their occurrence, and the patient was allowed to leave hospital. The ptosis was still present on discharge and persisted for many weeks. The patient was last seen in December, 1946, when the ptosis had completely recovered. At no time was there any oculomotor paralysis or abnormality in the pupil response.

Case 3

Zoster of trigeminal and cervical distribution accompanied by generalized eruption and followed by facial palsy.

An engineer aged 43 was admitted to hospital on July 13, 1947. In his youth he had suffered from scarlet fever, diphtheria, and chicken-pox. In February, 1945, he developed shingles over the lower half of the left side of the face, the upper part of the neck, and behind the left ear. He stated that, in spite of careful search no lesions were found in the ear or inside the mouth. Four days after the appearance of the zoster, he developed "an attack of chicken-pox," and because of this he was transferred to an isolation hospital. Within a day or two he suddenly developed a complete left facial palsy, which persisted until his discharge from hospital some five weeks later. Since that time there had been some improvement in the weakness of the face, but he had always been greatly troubled by difficulty in eating, numbness of the face, and severe neuralgia. His present admission followed a cerebral vascular accident which had occurred twelve weeks previously and which had caused aphasia and weakness of the right arm and face. The disability arising from this cerebral lesion had almost disappeared on admission.

Examination showed a pronounced left lower neurone facial weakness, together with diminished sensations over the lower

part of the face and on the inside of the left cheek. The tongue was protruded centrally. Although the patient complained of lack of appreciation of taste on the left side of the tongue, the presence of hemiageusia was not confirmed by crude tests. In addition to these signs there was an increase in the tendon reflexes and a diminution of the abdominal reflexes on the right, representing the residuum of the recent cerebral thrombosis. His blood pressure was 210/120. No other abnormal findings were present. Lumbar puncture showed a clear fluid under normal pressure. The cerebrospinal fluid contained 3 cells per c.mm.; the protein was 0.04%; and the Wassermann reaction and Lange curve were negative.

Discussion

Zoster Generalisatus and its Relation to Varicella

The occurrence of a varicelliform rash in the course of herpes zoster is a well-recognized entity. It is variously referred to as zoster generalisatus, zoster universalis, and varicelliform zoster. The condition was probably first described by Tenneson in 1893, and many examples have been recorded since. Minet and Leclercq (1911) collected 25 cases, and Parkes Weber (1913, 1916a, 1916b) described several cases and quoted 20 references. Most reports stress its occurrence in elderly patients. The extent of the eruption varies from the presence of a few aberrant vesicles to a diffuse eruption indistinguishable from the exanthem of varicella. The rash in Case 2, described above, was typical of varicella. Case 3 was not seen in the acute phase of the disease, but the eruption was evidently so like that of varicella that the patient was transferred to an isolation hospital.

The condition is of particular interest in that it provides a no-man's-land in the perennial battle between the monists and the dualists over the relationship between zoster and varicella. It has been assumed by some writers that the eruption constitutes a true attack of chicken-pox (Allen, 1944; Manning, 1944; Sharpe, 1946; and others), or that the concurrence of the two conditions is proof that zoster and varicella are but phases of one and the same disease (Le Feuvre, 1917). But, as Parkes Weber (1916a) has pointed out, this conclusion is hardly justified, as some of the cases show only a few aberrant vesicles, and evidence of an increase in cases of zoster during epidemics of varicella is lacking.

The experimental work of Kundratitz (1925) and Bruusgaard (1932) has an important bearing on this issue. These writers showed that the inoculation of children with vesicle fluid from cases of zoster produced a quasi-varicella rash and that contacts with these children also developed an eruption indistinguishable from varicella. Bruusgaard draws no definite conclusions from this work, but points out that the findings are compatible with the postulate of Haslund (1900) that the difference in the manifestations of infection with the zoster virus might well depend on the portal of entry. Haslund suggested that in zoster the virus gains access to the body via the nasopharynx and spreads to the nervous system, and that the generalized eruption is due to haematogenous dissemination to the skin.

The problem of the relationship between the two diseases is clearly not proved (cp. Wilson, 1940) and will remain so until further facts accumulate. Such data will become available only as the result of systematic investigations, and two lines of approach seem possible. The first is an extension of the work of Aitken and Brain (1933) on the complement-fixation test for the zoster virus, which they found to be positive in all of nine cases of zoster. Application of this test to cases of varicella does not seem to have been undertaken. The second line of approach, suggested by Le Feuvre (1917) and Taylor (1945), is the compulsory notification of herpes zoster, so that its

epidemiology might be compared with that of varicella. From observations made in a relatively isolated community Pickles (1939) showed that the epidemic peaks of the two diseases roughly correspond.

Motor Symptoms in Zoster

Of considerable interest and importance are the rare cases of zoster in the course of which the motor nervous system is affected. Involvement of the upper motor neurones has been described (Parkes Weber, 1915), and references to this condition are given by Carter and Dunlop (1941). The majority of recorded cases, however, refer to lesions of the lower motor neurones. These lower motor neurone pareses may be conveniently divided into three clinical types: facial palsy, oculomotor paresis, and segmental spinal-cord paralysis. The three cases described above provide one example of each of these types. As will be seen in the discussion that follows, the mechanism of the production of the motor symptoms is probably different in the three types. In facial palsy the motor fibres are incidentally involved in their transit through the geniculate ganglion, oculomotor lesions arise from peripheral spread of the infection, and spinal paralyses are probably due to actual involvement of the spinal cord by the zoster virus.

Facial palsy is by far the commonest of the motor lesions (Hunt, 1909). It was first clearly described by Ramsay Hunt (1907), and the syndrome often goes by his name. The primary lesion is in the geniculate ganglion, and the herpetic eruption occurs in the cone-shaped area of the cutaneous distribution of the facial nerve, which includes the posterior portion of the tympanic membrane and the external canal, the concha, the antitragus, and the anti-helix. In addition to this classical syndrome, facial palsy occurs as a complication of trigeminal herpes (Wilson, 1940; Spillane, 1941). In such cases presumably the Gasserian and geniculate ganglia are affected simultaneously.

An important group of cases is that in which trigeminal herpes occurs with facial palsy but without herpetic eruption in the seventh-nerve distribution. In these cases, of which Case 3 is an example, it has been suggested that the inflammation of the geniculate ganglion is extensive enough to produce paresis, but not to produce herpes (Sharpe, 1915). The significance of these cases is that they provide examples of "zoster sine herpete" of the geniculate ganglion, with abundant evidence of zoster of the neighbouring ganglia. It is but a short step to the assumption that certain cases of "idiopathic" Bell's palsy might be formes frustes of zoster. Ample substantiation of this supposition is to be found in the work of Aitken and Brain (1933), who demonstrated a positive complement-fixation reaction for zoster in four out of 22 cases of facial palsy in which there was no rash. Spillane (1941) brought other evidence to bear in support of this concept when he described a small epidemic of zoster in the course of which a single case of Bell's palsy was seen.

When oculomotor palsy occurs in the course of zoster it does so invariably as a complication of zoster ophthalmicus. The condition was probably first described by Vernon in 1868, and cases were later reported by Hall (1903), Mules (1903), and Parkes Weber (1916a, 1916b). The paresis may be slight, as in Case 2, in which ptosis was the sole manifestation, or more severe, producing complete paresis of the muscles supplied by the third, fourth, or sixth nerves (Hunt, 1909; Carmody, 1937). The clinical aspect is fully reviewed by Edgerton (1942). According to Kinnier Wilson (1940) the probable mechanism of its production is that spread takes place via the small communicating fibres between the first division of the

trigeminal nerve and the oculomotor nerves in the wall of the cavernous sinus. From analogy with geniculate zoster it is tempting to assume that certain of the oculomotor paralyses, especially when associated with ophthalmic neuralgia, might be due to "zoster sine herpette." No work seems to have been done on the complement-fixation test in such cases. It is of interest to note that this possibility was suggested by Mules (1903) some years before the classical work on geniculate zoster by Ramsay Hunt (1907).

Segmental paralysis of spinal-root distribution is rare in the course of zoster, but the complication was clearly described by Sir William Broadbent (1866), who reported a case in which paralysis of the arm followed herpes of the arm and neck. Joffroy (1882) described two cases—one affecting the deltoid and the other the small muscles of the hand. Most of the reports of cases describe cervical segment paralysis (Buzzard, 1902; Wilson, 1940), but involvement of the abdominal muscles (Taylor, 1895) and of the leg muscles (Carter and Dunlop, 1941) has been recorded. In Case 1, reported above, the cutaneous rash and the paralysis were in the distribution of the fifth cervical segment. Recovery was practically complete in three months from the onset. That the prognosis is not always so good is indicated by Carter and Dunlop (1941), in neither of whose cases had complete recovery taken place in nine months to one year.

These cases of segmental motor paralysis throw further light on the pathology of herpes zoster. The primary lesion in zoster is usually to be found in the posterior root ganglion. Head and Campbell (1900), in a study of the post-mortem changes, demonstrated that these ganglia showed round-cell infiltration, haemorrhage, and cell necrosis. They concluded that the changes in the posterior roots and horns and in the peripheral nerves were secondary and degenerative. This is undoubtedly the common state of affairs, but it fails to explain the rare cases in which there is definite clinical evidence of motor-root lesions. Further light is thrown on this problem by the work of Lhermitte and Nicolas (1924). These authors examined the spinal cord of a patient who died of an incidental disease seven weeks after an acute attack of zoster. In this case there was, in addition to the perivascular infiltration and demyelination in the posterior horns, marked evidence of inflammatory changes in the anterior horns. In spite of this there had been no clinical mention of a motor lesion. This finding confirms affection of the anterior and posterior horns of the spinal cord, and the presence of cord inflammation is borne out by the lymphocytosis and the increase in the protein content of the cerebrospinal fluid which commonly occurs (Wilson, 1940; Carter and Dunlop, 1941). The pleocytosis of the cerebrospinal fluid, the clinical manifestations of motor segmental paralyses, and the anterior horn changes in these cases bear a striking resemblance to those found in poliomyelitis. Parkes Weber (1916a) has taken this analogy even further by suggesting that the two diseases may in fact be caused by the same virus. As evidence he quoted the occasional appearance of the diffuse herpes in certain cases of poliomyelitis and the concurrence of epidemics of the two diseases. Further, he suggested that certain cases of painful muscle paresis of obscure aetiology might be regarded as cases of "zoster sine herpette."

Conclusions

In causing infection of the human body the herpes zoster virus shows a predilection for nervous tissue and the skin. In the classical form the brunt of the infection is borne by the sensory ganglia, the resulting symptoms being pain

and a cutaneous eruption in the peripheral distribution of the fibres proceeding from the affected ganglia. Study of the rarer manifestations of the disease shows that the infection often spreads beyond these confines. In some cases in which motor symptoms occur there is clinical and pathological evidence that the anterior horn cells of the spinal cord are affected in a manner similar to that in poliomyelitis. In others the infection produces an exanthem clinically identical with that of varicella.

From the available evidence it seems no more reasonable to deduce that varicella and zoster are caused by the same virus than it would be to make a similar deduction regarding zoster and poliomyelitis. It seems much more probable that the virus is capable of producing a range of clinical manifestations varying from simple motor lesions on the one hand to generalized skin lesions on the other, and that the classical form of the disease lies midway between these extremes. This clinical range might be represented as follows: poliomyelitis-like illness—zoster sine herpette—herpes zoster with paralysis—classical herpes zoster—herpes zoster with generalized eruption—varicelliform zoster (sine herpette). This suggestion is of course speculative, and it takes no account of the encephalitic symptoms which are said to occur. Nevertheless, clinically proved examples of each group are to be found in the literature, with the exception of the hypothetical poliomyelitis-like illness, and it is unlikely that evidence of this will be found in the absence of specific complement-fixation tests on such cases.

Summary

Three cases of herpes zoster showing unusual motor and cutaneous manifestations are described. It is suggested that the zoster virus produces a pleomorphic group of diseases with varying degrees of cutaneous and nervous symptoms. Further evidence on certain aspects of the disease could be obtained by immunological and epidemiological investigations.

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