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## THE PATHOLOGY OF HERPES ZOSTER AND ITS BEARING ON SENSORY LOCALISATION.

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INTRODUCTION.

It would be useless to attempt a review of all the literature that has grown up around the subject of "Herpes Zoster," for from 1895 to the present time alone over seventy papers have been written on this subject, very few

of which have any bearing on the matter of the present communication.

Moreover, our work deals with herpes zoster from two aspects. Firstly, we have determined the pathological lesion which underlies this disease, and, secondly, we have attempted thereby to determine the cutaneous distribution of certain fibres that enter each posterior root ganglion. We shall, therefore, only allude to such communications as throw light on the pathological lesions in herpes zoster, or on the distribution of the fibres which enter the posterior root ganglia.

It was not until the appearance of von Bärensprung's classical paper (23) in 1861 that herpes zoster was stated to be definitely of nervous origin; and when von Bärensprung crowned his long series of admirably reported observations by a *post-mortem* examination (1), its association with a lesion of the posterior root ganglion was universally accepted. But as his conclusions in their passage from book to book have undergone modification, and as the position of the question he set himself to answer has been widened by our increased knowledge of the structure of the nervous system, it will be well to consider this first successful *post-mortem* examination more carefully. Moreover, we must remember that although von Bärensprung rightly placed the position of the lesion in the posterior root ganglion, he thought this structure stood in no connection with the fibres of the posterior root or peripheral nerve, but had special nerve-fibres of its own.

The eruption seems to have occupied the area we have called dorsal 7; for it ran in the form of a girdle over 2 inches in breadth between the 6th and the 9th ribs, passing the middle line behind for one or two lines at the level of the 5th to the 8th spines, to end beneath the xyphoid process. Death followed from tuberculosis forty days after the first appearance of the eruption.

The spinal cord and both anterior and posterior roots were stated to have been normal; but "Nachdem die Inter-vertebralkanäle geöffnet und die Intercostalnerven vom 5ten bis zum 9ten freigelegt waren fiel sogleich eine grössere Dicke und vermehrte Röthung des 6ten, 7ten und 8ten am

meisten aber des 7ten auf, die von einer Anschwellung des mit erweiterten stark geschlängelten Gefässen durchzogenen Neurilems vorzugsweise abzuhängen schien. Der Durchmesser des 7ten Nerve übertraf fast um die Hälfte den des 5ten und des 9ten Intercostalnerven . . . . Den 6ten und 8ten Nerv zeigten die nämliche Röthung und Anschwellung aber etwas weniger stark und auf eine kürzere Erstreckung als den des 7ten." He then states that he found the remains of extravasated blood in the ganglion, without mentioning to which of the three ganglia he alludes.

This case seems to have borne a close resemblance to No. 2 and No. 4 of our series, in both of which cases the swelling of the affected ganglion and nerve was obvious to the naked eye. Thus by little more than a naked-eye examination von Bärensprung was enabled to prove that the ganglion was affected in herpes zoster.

The next report of a *post-mortem* examination was made by Charcot and Cotard in 1865 (4). A woman suffering from cancer of the breast developed zoster over what appears to have been the 3rd and 4th cervical areas. At the autopsy secondary growths were found to have invaded many of the vertebræ, especially in the cervical region. The 4th cervical vertebra was found to be profoundly affected. The only change found in the nervous system consisted in an active injection of the capillaries of the ganglia and nerves, a "véritable neuritis" without concomitant alteration of the ganglion cells or nerve-tubes.

This case is so poorly reported that even from the point of view of a naked-eye examination it is valueless, either to elucidate the pathology or localisation of the lesion of herpes zoster. It would seem to have closely resembled case 14 of our series, where examination, even by the simple methods of that day, would have revealed marked changes in the affected ganglion.

The next case was reported by Weidner in 1870 (18). In a paper on three cases of zoster he reported two autopsies with negative results. This is not surprising, since in his first case, although the eruption lay over what we have called cervical 4, he only examined the cord ganglia and

nerves between cervical 7 and dorsal 2; and in his second case the patient died five years after the eruption.

In the same year E. Wagner (17) reported the result of an autopsy on a tuberculous patient who had developed an attack of zoster over the 9th and 10th ribs seven days before death. The six lower dorsal and the 1st and 2nd lumbar vertebræ were laid bare by tubercular caries, and the dura mater was lined with a thick layer of cheesy pus. Only the ganglia were examined microscopically, and the 9th, 10th, and 11th dorsal were said to have been affected. But it is obvious that an incomplete examination of so complicated a case could add little to the knowledge of either pathology or localisation.

In 1871, Oscar Wyss (19) reported a case of zoster of the whole first division of the trigeminal nerve, where death occurred seven days after the appearance of the eruption. The ophthalmic vein was thrombosed and the eye-muscles contained small abscesses, and the connective tissue of the eyeball was infiltrated with pus. From the point where the first or ophthalmic division leaves the Gasserian ganglion to enter the eyeball it was surrounded by extravasated blood. The second and third divisions were unaffected; but attached to the inner side of the Gasserian ganglion lay a red mass 1 cm. broad, apparently consisting of extravasated blood. Microscopically, there was an extravasation of blood into the inner aspect of the ganglion and into the first division of the trigeminal nerve. There is also said to have been "purulent inflammation" of the ganglion, pushing the ganglion cells apart.

In 1875, Sattler (16) also reported a case of herpes ophthalmicus, extremely well worked out according to the methods then known. A man of 85 was poisoned by carbonic oxide gas. Four days later neuralgia came on over the right half of the forehead, and in a few days the forehead, the side of the nose, and the eyelids, became covered with an eruption of herpes zoster. Death occurred fourteen days afterwards. The Gasserian ganglion was found to be infiltrated with small round cells, and there was marked destruction of the ganglion cells. The ophthalmic division

of the nerve was degenerated. The other two divisions were normal.

By this time it had come to be recognised that the ganglion was affected in cases of zoster, and in 1876 Kaposi (10) reported a case in which he arrived at a very odd result. A man of 54 died seven days after the appearance of an eruption that had the following distribution: "Auf der allgemeinen Decke des Unterleibes rechts über den Darmbeinkamm und mit diesem parallel laufend eine kontinuierliche Folge von Herpes-gruppen welche etwa  $1\frac{1}{2}$  bis etwa 1 Zoll vor und über der Symphyse sich erstrecken." The area affected seems to have corresponded with our dorsal 11. But he only examined the ganglia of dorsal 12 and lumbar 1 to 5, and states that hæmorrhages were present in the periganglionic fat of dorsal 12, lumbar 1, 2 and 3, and that the protoplasm of lumbar 2, the most affected ganglion, was pale and retracted. In the light of our present knowledge it is impossible that these changes could have been associated directly with the eruption over the area he describes.

In his text-book Kaposi again alludes to this case, and states that he also examined a case of herpes frontalis and found hæmorrhage and destruction in the Gasserian ganglion. We have not, however, been able to find any further account of this second case, and the first case, though frequently quoted, is valueless as a contribution to the pathology of herpes zoster.

In 1879, Chaudelux (3) reported the case of a woman who died of phthisis many months after an attack of zoster. He says the remains of the eruption lay over the 2nd and 3rd intercostal spaces on the left side, but gives no further details of its distribution. The 2nd and 3rd dorsal ganglia of the left side are said to have been double the normal size, and certain zones in these ganglia were completely transformed, ganglion cells and nerve-tubes were destroyed, and their place taken by dense connective tissue. From the figure he gives he evidently saw the condition figured by us on plate 1, fig. 2B. The spinal cord was destroyed in extraction, and the nerves, having been hardened in alcohol, gave no positive result.

In 1881, Lesser (12) published the first two satisfactory *post-mortem* examinations of cases of zoster of the trunk, and followed up his first communication by a second in 1883 (13), in which he reported a third case. In the first of these three cases the eruption lay over the right side of the neck, bounded in front and behind by the middle line, above by the lower jaw, and below by a line passing round the shoulder roughly to join the spine of the 2nd dorsal vertebra behind, with the third costal cartilage in front. This lower border dipped in front to occupy the extreme upper part of the anterior surface of the right arm. Death occurred twenty-six days after the eruption first appeared. The 4th cervical ganglion of the right side contained a focus visible to the naked eye, and situated on that side of the ganglion opposed to the anterior root. Microscopically, this focus consisted of a mass of cells surrounding what appeared to be the remains of a hæmorrhage. The remaining ganglia, the posterior roots, the nerves, and the spinal cord were stated to be normal; but at that date no method existed by which the acute degenerative changes that probably existed could have been demonstrated.

In Lesser's second case the eruption appears to have occupied the area that we should call dorsal 8, and death took place about nine days after its first appearance. To the naked eye the 8th dorsal ganglion was very red, but not swollen. On microscopical examination this reddened area was seen to consist of a hæmorrhage containing broken-down ganglion cells, and surrounded by a mass of inflammatory tissue. The case seems closely to have resembled Nos. 2, 4, and 5 of our series. Lesser thought that there was a similar though less pronounced change in the 9th dorsal ganglion, but he carefully states that there was no hæmorrhage or breaking-down of nerve elements, and our experience leads us to suspect that he was misled by the hyperæmia not infrequently present in normal ganglia; for he was evidently unwilling to believe that one ganglion could supply the whole of the area occupied by the eruption. The other ganglia, peripheral nerves, and spinal cord showed no change. Admirable figures accompany this paper, which is the first serious con-

tribution to the pathology and localisation of zoster of the trunk.

Lesser's third case (13) died three weeks after an eruption that lay over the mamma and occupied the area we have called dorsal 5. On microscopical examination the 5th dorsal ganglion was found to be markedly altered. The nervous elements of the upper half of the ganglion were replaced by connective tissue, and the sheath of the ganglion over this area was thickened. The peripheral nerve of this ganglion also showed changes, for the normal fibres were in places widely separated by fields of granular tissue. He states that the 4th ganglion also was altered, but that the 4th nerve was normal. As, however, he gives no figures in this paper, it is difficult to gather the extent of these changes, and he admits that the 4th ganglion was not so carefully examined as the 5th.

In 1883, Pitres and Vaillard (15) reported the *post-mortem* on a curious case. After mentioning a number of cases in which they had examined the nerves in the neighbourhood of bed-sores, they mention a case in which there were scars of zoster in the 6th intercostal space on the right side, and an eruption that they thought was zoster in the 11th intercostal space of the same side. On microscopical examination they state that in the 6th dorsal ganglion nerve-fibres were destroyed but the cells were perfect, that there was parenchymatous degeneration and some sclerosis of the 6th dorsal peripheral nerve and degeneration of the posterior roots of the 6th dorsal. They also state that the 11th dorsal peripheral nerve was degenerated and sclerosed, but that the ganglion and roots were normal. The cord was everywhere normal. In the light of subsequent experience it would seem that the scars in the 6th intercostal space were probably due to an old zoster, but that the eruption in the 11th space cannot be classed under the heading of true zoster. However, the case is so poorly reported that it can add but little to our knowledge.

In 1884, Curschmann and Eisenlohr (5) published two cases in which an eruption of zoster was followed by the development of small nodular swellings on the peripheral



nerves. In the first case several of these swellings were removed by operation. Microscopically they were found to consist of healthy nerve-fibres surrounded by small hæmorrhages, exudation of inflammatory cells and engorged capillaries, in fact, a condition of "perineuritis acuta nodosa." This case died a year and nine months afterwards, and they found no change in nerves, ganglia, or cervical cord.

They also report a third case in which zoster appeared two days before death over the 11th rib and last intercostal space. On *post-mortem* examination the back muscles on the same side as the eruption were found to be infiltrated with blood, and through this infiltration passed the branches of the 10th and 11th dorsal nerves. The nerve-fibres in these branches were, however, unaltered, and the 10th, 11th and 12th dorsal ganglia and the dorsal and lumbar cord were normal. But it is not improbable that these observers, like Pitres and Vaillard, were misled by their idea that zoster was due to changes in the peripheral nerves. Thus the fact that the anterior divisions of the 10th and 11th dorsal nerves passed through the broken-down muscles, caused them to imagine that these nerves must have been the seat of the lesion in spite of the fact that their peripheral branches do not supply the area over which the eruption lay (*vide* our plate 17). Probably the seat of the lesion in this case was the 9th dorsal ganglion, which they neglected to examine.

In 1884, Dubler (7) published the results of an examination of two cases. Of these we will consider the second and more straightforward case first. The distribution of the eruption, which occurred 103 days before death, was as follows:—"Rechts über den unteren Rippen und über der unteren Bauchgegend eine von oben hinten nach vorn unten verlaufende 5 cm. breite gürtelförmige Hautpartie . . . . Diese Hautveränderung beginnt hinten an der Wirbelsäule, reicht vorn bis zur Mittellinie wo sie 4 Querfinger oberhalb der Symphyse endet. Seitlich bleibt sie 3 Querfinger von der Spina Anterior Superior entfernt."

Microscopically the spinal cord was normal. The 9th dorsal ganglion showed interstitial changes, degeneration of nerve-bundles and small pin-point hæmorrhages and dots.

The 8th and 10th dorsal ganglia were normal. The 9th intercostal nerve and 9th dorsal roots were degenerated, and there was a small amount of degeneration in the 10th intercostal nerve.

Dubler's first case is less clear owing to the fact that the patient had tubercular necrosis of several ribs. The eruption seems to have occupied the area we have called the 8th dorsal, and the patient died 144 days after its first appearance. On the 7th, 8th and 9th ribs were caseous masses, due to necrosis of the bone. The 6th, 7th, 8th and 9th intercostal nerves passed through these swellings. A few nerve-fibres were degenerated in the anterior division of the 7th intercostal nerve; there was marked degeneration in the posterior and anterior primary divisions of the 8th intercostal nerve, and slighter degeneration in the anterior division of the 9th intercostal. Ganglia, cord and posterior roots were said to be normal at the level of the 6th, 7th, 8th and 9th dorsal.

In 1887, Leudet (14) published a somewhat superficial paper in which he mentions a case of herpes frontalis where he found an old inflammatory process in the frontal nerve, and a degenerative condition of the Gasserian ganglion.

Thus up till the time we began to investigate the pathology of herpes zoster there had been two well reported autopsies on cases of zoster ophthalmicus [Sattler (16), Wyss (19)], and five satisfactory reports on zoster of the trunk [Lesser, three excellent cases (12 and 13), Chandelux, one fairly reported case (3), Dubler, one excellently reported case (7)].

To these we now add twenty-one cases at all stages after the eruption.

#### PART I.—THE PATHOLOGY OF ZOSTER.

##### *Chapter 1.—Changes in the ganglion of the Posterior Root.*

If the patient has died with the eruption still out upon his skin the affected ganglion will be found to be in a condition of profound inflammation. The interstitial tissue will be crowded with small round cells which stain deeply with