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MALIGNANT SPHENO-OCCIPITAL CHORDOMA.

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I.—INTRODUCTION.

CHORDOMA, a tumour arising from vestigial remains of the primitive notochord and undergoing similar evolutionary changes, is one of the rarer and less well recognized varieties of neoplasm. A sufficient number of cases, however, are now on record to show that it is a definite entity, having a distinctive histological structure, and, in many cases at least, fairly characteristic naked-eye appearances. The literature of the subject, already fairly considerable, has recently been reviewed by one of us (Stewart,²³ 1922), and it will suffice to say here that of the twenty-six cases there referred to, in fifteen the tumour was situated in close relation to the sphenio-occipital synchondrosis, and in nine it originated in the sacro-coccygeal region. Of the remaining two, in one the tumour was in the superior occipital region, in the other there were several tumours, situated in the jaws. Since the publication of this paper, several other sacro-coccygeal cases and one sphenio-occipital case (Lemke,¹⁹ 1922) have been put on record, and it remains true to say that chordoma arises almost solely in relation to the extremities of the primitive notochord, and that in rather more than half the cases the tumour springs from the clivus blumenbachii.

Sphenio-occipital chordoma is, therefore, a rare disease, and the case now reported is, so far as we can ascertain, only the seventeenth on record. It is also the first to be published in the British Isles. Quite possibly, of course, cases of chordoma of the clivus have occurred

in which the true nature of the tumour has not been recognized, and a pituitary origin cited, since clinically the symptoms most easily fall into line with those caused by the pressure of a pituitary growth. It may be stated, however, that a search among a large series of cases of pituitary tumour published by Cushing and others has revealed only a single case in any way suggesting a chordoma in pituitary disguise (Cushing,⁷ case 17).

A short abstract of the present case has already been published (Stewart and Burrow,²⁴ 1923). We now propose to describe it in detail and to compare it, both clinically and pathologically, with previously reported cases.

II.—CLINICAL RECORD.

The patient was an ex-soldier, thirty years old, and of good physique, who was invalided from the Service on account of gas poisoning by phosgene, after serving for three years in France. He first came under our observation on November 30, 1921, when he was confined to bed in hospital, the symptoms on admission being cough, breathlessness, a sense of oppression in the chest, more or less constant headache, blindness in the left eye, loss of power in the legs, and unsteadiness when attempting to stand upright.

Personal and Family History.—He had no relatives living except a sister, who was married and in good health. The parents died of chest trouble, but the details were unknown. He was unmarried, denied lues, and had never ailed in any way since the infectious illnesses of childhood.

History of Present Illness.—The patient was quite clear that his health was good up to the time when he was gassed by phosgene while on active service in France in the winter of 1917. He admitted that he had had headaches for several months before this, but these he attributed to war conditions at the front. After the gassing he made a slow recovery in hospital. When he had been out of bed a few weeks and was going about again, he noticed that his head was continually aching, though not in a severe or paroxysmal manner. The headache he described as being throbbing in nature, worse on exertion, or when he stooped down. The breathing never entirely recovered from the time of the gassing; he wheezed, and was short of breath. Occasionally there was vomiting, but this was not a prominent symptom, and was not mentioned by him until he was asked the leading question. Early in 1920 he noticed that the vision of the left eye was much impaired; he discovered it by accident one day when he had closed the right eye and found that he could then see very little with the left eye alone. From that date the left eye gradually became blind, and vision failed totally in this eye during the spring of 1921. The sight of the right eye had failed somewhat, but he was still able to read large print when examined by us. From the spring of 1920 he became unsteady on his legs and found it a great effort to walk far, as they were awkward and weak. This loss of power gradually became more pronounced, so that his walks were shorter and shorter, and in the summer of 1921 he gave up walking altogether. In the early months of

that year he had noticed that the movements of his right hand were becoming impaired. There had been some difficulty for several months before this in handling small objects with the fingers, but from the spring of 1921 the weakness of the hand became steadily more pronounced, and by late in the summer his left hand also was quite noticeably affected. He had to take to bed in the autumn, a few weeks before he came under our observation, owing to unsteadiness in his balance, and increasing weakness of the legs. He was examined by one of the writers (J. le F. B.) on November 30, 1921.

Condition on Examination.—The man was propped up in bed breathing in a slow, laboured fashion very like the type of respiration seen in the later stages of diabetes immediately preceding the onset of coma. He presented definite cyanosis of the lips, ears, etc., and spoke in short, badly articulated sentences, pausing to breathe between them. There was a little audible wheezing, but this was not marked, and it was apparent that the dyspnoea was not due to obstruction of the respiratory passages. The legs lay extended on the bed as in flaccid paraplegia, but some motor responses were obtained when he was asked to lift first one and then the other from the bed. The arms differed from each other in posture. The right arm was adducted with the elbow extended, the forearm pronated, the wrist and fingers slightly flexed. There was œdema of the right hand and forearm. The left arm was carried more naturally, with the elbow semi-flexed and the hand resting on the chest when not in action. The intrinsic muscles of both hands, especially the right, showed some wasting, evident in spite of the œdema, but not more than could be accounted for by disuse. The head was held slightly retracted, and any active or passive movement caused pain. The most defective movement was flexion of the neck, but there was no tenderness on percussion over the cervical vertebræ. The speech was slurring and indistinct, though he was perfectly conscious and did not repeat syllables; the condition was evidently one of dysarthria. Memory and attention were excellent, and there had never been any spasms or convulsions.

Cranial Nerves.—I. The sense of smell was impaired in the left nostril, but intact in the right.

II. Sight was completely lost in the left eye; he could not even distinguish light from darkness. The fundus showed optic atrophy without any evidence of past choked disc. The visual acuity of the right eye was reduced; large print only could be made out. Rough testing of the visual fields showed a reduction on the temporal side as compared with the examiner's normal field. The fundus showed similar changes to those in the left eye, but to a much less degree.

III., IV., and VI. The pupil on the left side was dilated and immobile. There was quite definite paresis of all these nerves on the left side. The right pupil reacted sluggishly to direct light and also slowly to convergence. There was slight weakness of the right third nerve and probably of the fourth as well.

V. Sensibility on the face and in the mouth was unimpaired. There had been no facial neuralgia. The left corneal reflex was sluggish, the right normal. The muscles of mastication were all working so far as could be made out.

VII. The face lacked expression, but there was no paresis of the muscles or difference in the range of movement on the two sides. Taste was normal.

VIII., IX., X., XI., XII. No definite involvement of any of these nerves was made out, although during the last few days of life speech was very defective, and the patient had difficulty in swallowing solids. It was difficult to test the sterno-mastoids and trapezii owing to the pain caused by movements of the neck. The tongue was steady, but he could not protrude it to the full extent. The larynx was not examined.

Upper Limbs.—The right arm could not be lifted above the head, abduction from the side was badly performed, and flexion of the elbow was defective even when the weight of the limb was counteracted. The finger movements were badly performed, especially those dependent upon the action of the intrinsic muscles of the hand. There was no complete paralysis of any muscle or group of muscles. The biceps, triceps, supinator and wrist jerks were obtained on both sides, a little more easily on the right than on the left. On tapping the extensor tendons a slight finger flexion response was present on both sides. The left hand and arm could be moved fairly well, but there was some weakness of the proximal muscles.

The abdominal and epigastric reflexes were abolished.

Lower Limbs.—The legs lay extended on the bed with the feet in a position of mild "drop-foot." There was no complete loss of power in any muscle, but motor power seemed depressed without any segmental selection. The right leg was certainly weaker than the left.

The knee jerks were both normally present, the right a little more lively than the left. The ankle jerks were both easily obtained, and again the right was more lively than the left. There was no clonus. The plantar reflexes were extensor in type, giving a well-marked Babinski's sign on both sides. Gordon's and Oppenheim's signs were also positive.

The Organic Reflexes.—His swallowing difficulty towards the end of life has been already noted. Rectal control was present, but there was urinary incontinence.

The Cerebrospinal Fluid.—The pressure was slightly increased, but the fluid was perfectly clear and colourless. There was no increase in globulin, sugar was present, lymphocytes were present in normal numbers. The Wassermann reaction and Lange's gold sol test were both negative.

Diagnosis.—The provisional diagnosis made before death was tumour in the pituitary fossa with backward pressure on the pons, and forward growth involving the optic tract.

Progress.—The patient gradually became worse. The left hand lost power comparatively rapidly, the respirations became more shallow, and he died while one of the writers was at his bedside on the morning of December 5, 1921. The immediate cause of death was respiratory failure. The pulse continued to beat slowly and deliberately for nearly two minutes after the last respiration had ceased.

The Post-mortem Examination was made next morning, but apart from the tumour at the base of the skull and the notable pressure effects on the

FIG. 1.—Malignant sphenoidal chordoma. Base of skull, showing tumour springing from the region of the dorsum sellæ and pituitary fossa. The stretched and flattened optic nerves and chiasma are seen in front.

FIG. 2.—Malignant sphenoidal chordoma. Inferior aspect of brain, showing the deep depression caused by the tumour, and the stretching, flattening and distortion of the pons, crura cerebri, optic tracts and chiasma which resulted.

brain and nerves, nothing of note was found. In particular, the respiratory tract appeared to be healthy.

III.—DESCRIPTION OF TUMOUR AND BASE OF SKULL.

The central area of the base of the skull was occupied by an irregularly nodulated, ovoid tumour about the size of a hen's egg, or slightly less (*Fig. 1*). Its long axis, measuring 6.5 cm., lay transversely, while its antero-posterior diameter was 5.5 cm., and it projected upwards about 3.5 cm. from the base of the skull. Its anterior margin overhung the orbital plates and was practically in line with the most anterior part of the greater wings of the sphenoid. Posteriorly it overlapped a line joining the internal auditory meatuses, while the lateral margins of the tumour were almost in line, antero-posteriorly, with the same apertures. The tumour was irregularly bossed on the surface, and, while its intracranial part appeared completely clothed with dura, this membrane was so much thinned over the bosses that the greyish, semi-translucent, jelly-like tumour tissue showed through. On the other hand, there was no evidence that the dura mater had been penetrated at any point, and the pia mater and brain did not appear to be invaded, nor were they adherent to the surface of the growth. Here and there a number of yellowish brown areas were seen, the result of degenerative changes and old hæmorrhages within the growth. The anterior part of the tumour contained a large, dark purplish area, the result of recent hæmorrhagic extravasation.

Although it could not be definitely distinguished by the naked eye, the pituitary gland was situated on the antero-superior aspect of the tumour, just behind the optic chiasma, which could be seen in front. The tumour had evidently lifted the hypophysis completely out of its bed, causing it to become greatly flattened and stretched in the process. On its inferior aspect the tumour had extensively infiltrated and destroyed the central portion of the base of the skull, notably the basisphenoid and ethmoids, the sphenoidal sinus being filled with growth. It did not appear to have invaded the nose or pharynx.

IV.—DESCRIPTION OF BRAIN.

There was an extraordinary degree of distortion and displacement of the central portion of the base of the brain, including the pons and crura cerebri, the optic chiasma and floor of the third ventricle generally (*Fig. 2*). All these structures were stretched out over the tumour at the base of the skull and elongated, flattened, and grossly distorted in consequence. At first sight there appeared to be a large cavity at the base of the brain, deepest in front, in the region of the interpeduncular space, and shallower behind, in relation to the pons and medulla. The optic chiasma was flattened out to about a millimetre in thickness. The cerebral peduncles were elongated antero-posteriorly, as were all the structures in the interpeduncular space. The pons especially was flattened, stretched and distorted, more particularly on the left side. The medulla was hardly, if at all, involved. With the exception of the optic nerves and tracts, which showed severe pressure effects, it was very

difficult to determine to what extent the first six cranial nerves were implicated. The remaining cranial nerves did not appear to be involved.

V.—HISTOLOGY.

Numerous blocks taken from different portions of the growth showed the same type of structure throughout. The tumour was alveolar, being broken up into masses of various sizes by narrow strands of dense fibrous tissue.

FIG. 3.—Microphotograph showing chordoma cells with extreme vacuolation of cytoplasm: typical 'physaliphorous' cells. ($\times 200$.)

These carried the blood vessels, the alveolar masses of tumour tissue being devoid of both stroma and vessels. Everywhere mucoid degeneration was in progress, and the cells varied in appearance according to the stage which the mucoid change had reached. (1) In the younger, more cellular part, where mucoid change was least marked, the cells were spheroidal, ovoid or polygonal, and in loose contact with one another. They varied considerably in size, but none of them were very small. Nearly all showed some degree of cytoplasmic vacuolation, owing to the presence of droplets of mucin, and as this increased in amount the cell increased in size, until it assumed more or less the appearance of the "physaliphorous" cell of Virchow (*Figs. 3 and 4*). The nuclei of

the younger cells were large, vesicular, and rich in chromatin, but as the intracellular mucin increased in amount the nuclei became smaller both relatively and absolutely. A few giant, hyperchromatic nuclei were seen, suggesting anaplasia and malignancy, while occasional mitotic figures also occurred. No nuclear vacuolation was present, such as has been found in other cases of chordoma. (2) The next stage in the evolution of the cells was that the mucin droplets were discharged, either flowing together forming homogeneous

FIG. 4.—Another portion of the growth, showing both cytoplasmic vacuolation and the gaps formed by accumulation of intercellular mucin.

masses of varying size throughout the growth (*Fig. 4*), or simply forming a vacuolated or actually fibrillated groundwork, breaking up the tumour tissue into little groups of cells. The latter, having discharged their contents, then shrank, becoming stellate or even spindle-shaped, but more often remaining irregularly rounded or polygonal. Each consisted of a nucleus still of considerable size surrounded by a scanty layer of eosinophilic cytoplasm. The centre of some of the larger tumour nodules was completely occupied by a homogeneous or granular mucinous mass containing few or no cells.

By the use of polychrome methylene blue, thionine blue and similar stains, it was found that both the homogeneous masses and the intracellular

droplets gave the staining reaction of mucin. The blue cytoplasmic granules, so striking a feature of the more embryonic cells in Stewart's case of sacrococcygeal chordoma, were here very inconspicuous, probably because there were very few young cells present. Most of the cells showed at least a considerable degree of mucoid degeneration.

There were both old and recent hæmorrhages into the tumour at various points, the former being indicated by extensive deposits of hæmosiderin in the stroma.

VI.—RÉSUMÉ OF LITERATURE.

1. The first published case of chordoma of the clivus giving rise to clinical symptoms was that of Klebs¹⁶ (1864). The patient, a man in middle life, died following a series of tetanic convulsions.

2. Klebs¹⁷ (1889) also published the second case, where death was due to pressure on the medulla.

3. In the female mental patient, aged fifty, recorded by Grahl¹³ (1903), the history extended over three years before death, and there was paralysis of the third, fourth, and seventh cranial nerves, dysarthria and dysphagia, with death from paralysis of the medullary centres.

4. Seiffer's²² (1905) patient was a woman, aged thirty-three. The duration of the illness was four years, and the symptoms were those of intracranial pressure, headache, vomiting, and vertigo, followed by left hemiparesis and death from pressure on the medulla.

5. The case of Fischer and Steiner¹¹ (1907) was that of a schoolboy, aged sixteen and a half years, who complained of pain on moving his neck. This had existed for six months, and had been getting worse. The left arm and left leg were weak, and sensation was defective. There was a left claw hand. There was ankle clonus on the left side, with exaggerated tendon reflexes. The provisional diagnosis was tuberculosis of the spine, with pressure on the cord. Later there developed weakness of the right arm and leg also. The left eye was deviated to the left and the pupil fixed, but the face was unaffected. There was double optic neuritis. Dysphagia was present but no vomiting, while the breathing was deep and laboured. The patient died suddenly, calling out, "I am dying."

6. In the case of Linck²⁰ (1909), that of a middle-aged man, there was a swelling the size of a pigeon's egg in the pharynx, associated with right middle ear disease, for which an operation was performed. A month later a second operation was carried out, and slimy material, which proved to be chordoma tissue, obtained. The neurological findings were a diminished sense of smell, total paralysis of the left sixth nerve, diminution of the left corneal reflex, paresis of the left facial nerve of lower neurone type, left recurrent laryngeal palsy, weakness of the left trapezius and atrophic paralysis of the left half of the tongue. The remaining cranial and spinal nerves were intact.

7. The case of Frenkel and Bassal¹² (1910), which is very fully reported, was that of a farmer, aged thirty-nine, who had had symptoms for one year, viz., headache of frontal type followed by vomiting, vertigo, diplopia, and left ptosis. The external muscles of the right eye were normal, but reflexes to light and accommodation were lost. The visual acuity was $1/4$. Œdema was limited to the papilla. The left eye was blind, the fundus showing more œdema than on the right side, but no atrophy. The left second, third, fourth, and fifth nerves were paralysed. There was a lower neurone paralysis of the right seventh nerve. There was no motor or sensory loss in the trunk or limbs. Knee jerks were slightly increased. The cerebrospinal fluid was under slightly increased pressure, but was otherwise normal. The right eye gradually became involved in the paralysis. Death was preceded by coma and Cheyne-Stokes respiration. Post-mortem, the tumour measured 6.5 by 5 by 3 cm., and extended from the optic foramina to the foramen magnum.

8. Jelliffe and Larkin¹⁵ (1912) reported the case of a woman, aged thirty-six, whose symptoms extended over eight months before death. There was left hemiplegia, paralysis of the second, third, fourth, sixth, and seventh nerves, and paresis of the eighth and ninth on the same side. Epistaxis occurred from an extension of the tumour into the ethmoids.

9. Eitel⁹ (1911) recorded the case of a man, aged forty-four, who for one and a half years before death had had symptoms of brain tumour compressing the pons.

10. Wegelin²⁵ (1911) published the case of a woman, aged twenty-five, who died with signs of pressure on the pons and medulla.

11. Hässner¹⁴ (1912) noted the symptoms of dizziness, diplopia, severe headache and optic neuritis in a man aged thirty-two, who died after four years, and in whom the tumour was verified post-mortem.

12. Kotzareff¹⁸ (1918) recorded a fatal case in a man aged fifty-one. The symptoms—headache, pain and spasms in the hands and arms, and optic neuritis—had existed for nine months.

13. Daland⁸ (1919) reviewed the literature and reported the case of a woman, aged thirty, who had had symptoms for three years. There was hoarseness, with headache and swelling of the right side of the neck. There was old choked disc in the right eye, the vision of which was normal. There was a bulging into the right auditory canal. The right side of the tongue was distinctly anæsthetic. There was right recurrent laryngeal palsy, and loss of power in the right trapezius and sternomastoid. The right side of the tongue was atrophied. The tumour in the neck was curetted, and its connection with the base of the skull established. Recurrence took place in spite of X-ray therapy. The patient was alive at the time the paper was published.

14. Fabricius-Möller¹⁰ (1919) reported the case of a boy, aged sixteen, who had had a pharyngeal tumour for seven years. Removal was

followed by recurrence in a few months, but a second operation was not performed until four and a half years after the first.

15. Argaud⁵ (1918-19) reported the case of a man aged thirty, who was admitted to hospital with all the signs of a ponto-cerebellar angle tumour. At operation a tumour the size of an almond was found on the middle of the clivus, encroaching a little on the right side.

16. Lemke¹⁹ (1922) reported the case of a woman, aged forty-five, of whom there was no clinical record. Inquiry after death showed that twelve years before there had been ptosis and right facial palsy, and ten years before, squint and diminution of vision. The latter symptoms had been much worse for the last six months before death. During this time there was also left-sided paresis, dysphagia, and polydipsia. A malignant chordoma of the clivus was found post-mortem. Both the brain and the pituitary were infiltrated by the growth.

VII.—CLINICAL COMMENTARY.

The comparatively long history of about two years' symptoms, or even a little longer than this, is a feature of these cases. In sacro-coccygeal chordoma the average duration of the ailment has been much longer, viz., nine years, because the anatomical relations of the latter site are more favourable to the continued life of the patient. The symptoms of our patient, and in other recorded cases, have been, in general, those of a slowly growing tumour at the base of the skull. Headache, giddiness and eye symptoms have been the earliest manifestations, followed later by paralysis of various cranial nerves. When the pressure extends to the pons and medulla, there are added to the above-mentioned symptoms hemiparesis, or even paresis of all four limbs, and respiratory or other bulbar complications ending in death.

Diagnosis.—The slow history, with symptoms and signs of a tumour about the pituitary fossa without marked signs of pituitary derangement, should lead the neurologist to recall the possibility of chordoma of the clivus. A good X-ray film taken with the aid of a Potter-Bucky diaphragm, or similar apparatus for minimizing the secondary radiations from the tube, may show evidence of bone absorption, or the outline of the tumour, though apart from the microscope the exact pathology must remain obscure. In a few cases it will be possible to make a histological diagnosis by curetting, or puncturing, local extensions of the tumour at the base of the skull (cf. Daland's case).

VIII.—PATHOLOGICAL COMMENTARY.

The case here described illustrates very well the salient pathological features of chordoma, a lowly malignant tumour of slow growth, locally

invasive and destructive, and only rarely giving rise to metastases. The tumour tissue is intensely gelatinous or mucoid, and is prone to focal hæmorrhage and necrosis. The histological appearances are equally characteristic. The tumour is composed of large solid alveolar masses of cells, very many of which show cytoplasmic vacuolation, with, here and there, large extracellular collections of mucinous material, formed by the fusion of extruded droplets. The whole mass often presents a syncytial aspect, with complete loss of outline of the individual cells.

The histology and histogenesis of chordoma have been investigated with great thoroughness by Alezais and Peyron and their co-workers in France, and their results are embodied in an admirable series of papers extending over the last nine years (Alezais and Peyron ¹ (1914), ² (1914), ³ (1920), ⁴ (1922), and Berard, Dunet and Peyron, ⁶ (1920)). In their latest paper, based on the study of four personal and five other published cases, Alezais and Peyron ⁴ emphasize the varied yet highly characteristic histological picture which this tumour may present. (1) The commonest and fundamental type is the vacuolar, which is well exemplified by the present case. This special vacuolation, intra- as well as inter-cellular, is associated with the presence of an amorphous or granular substance which, from its reactions, would appear to occupy a position intermediate between mucin and collagen. Alezais and Peyron further suggest that certain histological aspects of this material favour the hypothesis that it may become directly transformed into collagen. All the other histological dispositions are rare, but any of them may exist alongside the one already mentioned. They include (2) regular cavities lined by prismatic or cubical epithelium, the homologue of the primitive notochordal canal; (3) solid columns of epithelial cells, which may or may not be vacuolated; (4) a sarcoma-like formation of fusiform or polymorphous cells, with a sarcoma-like relation to the fundamental intercellular substance; and (5) a gliomatous type of structure, due to the development of very fine neuroglia-like fibrillæ between the cells of the syncytium. Alezais and Peyron believe that these different appearances correspond to the classical stages of evolution of the primitive notochord: first a hollow epithelial tube, then a solid cord of undifferentiated epithelial cells, and, finally, the vacuolation and fibrillation which indicate its adaptation to a supporting rôle.

The fact that no instance of a chordoma has yet been described as occurring along the course of the dorsolumbar spine has been taken to indicate that these tumours do not arise from the nucleus pulposus of the intervertebral discs themselves. Rather it is suggested that they arise from those notochordal vestiges which were long ago shown by Müller ²¹ (1858) to occur in relation to the speno-occipital synchondrosis, and which Peyron (unpublished observation) has lately demonstrated to be

of frequent occurrence in the last coccygeal vertebra of the early human foetus.

In its anatomical characters and topographical relationships the case here reported is almost a replica of Frenkel and Bassal's, except for the absence of extension to the nasal cavities. There was no post-mortem evidence that metastasis had occurred, and this is in keeping with most of the published cases, both speno-occipital and sacrococcygeal. The encapsulation of the tumour on its intracranial aspects, and the absence of infiltration of the brain and soft membranes are in accord with the relatively low malignancy of the growth.

The relation between the frankly neoplastic chordoma and the little jelly-like nodules occasionally met with on the clivus is discussed in the following communication, "Eccordosis Physaliphora Spheno-occipitalis."

IX.—SUMMARY.

The case is recorded of a man, aged thirty years, suffering over a period of three years from the symptoms of headache, vomiting, unsteadiness of gait, failing vision, and weakness of the limbs, especially the right arm. Examination revealed optic atrophy in the left eye, early atrophy in the right eye, paresis of the third, fourth and sixth cranial nerves on the left side, rigidity of the neck, moderate increase in the tendon jerks, and double extensor plantar responses. Death ensued from respiratory failure. A large tumour springing from the clivus blumenbachii, compressing the optic tracts, crura cerebri, pons, etc., was found post-mortem. Histologically the tumour had the characters of a chordoma of low malignancy.

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