HEME BODIES (ROSENTHAL FIBRES) ASSOCIATED WITH CAVITIES IN PONS AND CEREBELLUM AND ACOUSTIC NEURINOMA: WITH A REPORT OF TWO CASES *

By

AMOUR F. LIBER, NEW YORK

INTRODUCTION

FROM the time of their discovery in 1898¹ up to 1936, Rosenthal fibres have been reported in only five certain cases.^{1 2 3 4 5} They are elongated, microscopic bodies, found near syringomyelic cavities. They stain deeply with iron and chrome hæmatoxylin lakes. In all cases they have occurred in connexion with syringomyelia or syringobulbia and intramedullary tumour of the spinal cord or medulla. They are always very abundant. The nature of these structures has remained obscure. In a previous paper the author⁶ reported a typical case of Rosenthal fibres with syringomyelia, syringobulbia and an intramedullary ependymoma. This was the sixth case that could be found in the available literature. It was shown that Rosenthal fibres had most of the optic, tinctorial and histochemical characteristics of hæmoglobin and were consequently made up of a substance closely akin to, if not identical with it—that is, a heme substance. The name ‘heme bodies’ was therefore suggested in place of Rosenthal fibres.

Considering the large number of reports published about syringomyelia, heme bodies would seem to be exceedingly rare. Yet, in the article referred to above, the author expressed some doubts as to their actual rarity. If they were present in small numbers, the observer whose attention was not specially drawn to them could easily pass them by. Their staining affinities are wide, so that they might be confused with other objects which stain in the same way. This has happened in one known case, where structures first described as fragments of myelin by Leupold⁷ were later shown to be Rosenthal fibres by Kirch.⁴

Since the first case of heme bodies observed in this laboratory, they have been sought systematically in all sections of nervous tissue examined. This is not difficult to do as heme bodies, when once seen, are very easy to see and identify. They have so far been observed in three new cases. One was the

* From the Pathologic Laboratory of City Hospital, Welfare Island, New York, N.Y.

object of a report by Liber and Lisa.⁸ It concerned heme bodies associated with syringomyelia, but without a tumour.

PERSONAL CASES

The two cases presented here are of interest not only because they are the eighth and ninth cases of heme bodies reported in the available literature, but also because they demonstrate for the first time the coexistence of these structures with a tumour whose origin and situation are entirely outside of the neuraxis, namely, a neurinoma. Furthermore, the heme bodies were found in the pons and cerebellum, while in all previous cases they had only been observed in the spinal cord or medulla.

Case 1.—City Hospital autopsy no. 4545. A white male, age 53, was admitted to the hospital on June 3, 1935, in a semistuporous condition, and soon sank into a coma. Sixteen hours after admission, he regained consciousness sufficiently to ingest food, whereupon he vomited and died suddenly. The fragmentary history that could be obtained revealed a fall on the head three years earlier, followed by headache, vomiting, vertigo, weakness, blurred vision. Two months before admission, a 'brain operation' was performed, following which symptoms were stated to have grown worse.

Autopsy, done four hours after death, revealed a structure which microscopically resembled a food particle in a bronchiole of the lower lobe of the right lung. In the left lower lobe were acute alveolitis and fresh hæmorrhage. The thoracoabdominal viscera were otherwise free from gross pathology. The head showed a scar of right temporal craniotomy with a decompression. In the right cerebellopontine angle was a mass 5 cm. long and 4 cm. transversely (fig. 1). The ventral surface adhered to the basilar dura and was torn in removal. This exposed an irregular mass of clotted blood. Elsewhere, the mass was covered by a firm, whitish grey wall, 1 to 3 mm. thick. Section of the formalin-fixed brain showed that the mass lay athwart the initial portion of the great horizontal fissure of the cerebellum, over the anterior extremity of the anterior semilunar lobe, part of the biventral lobe and a small, lateral part of the flocculus. A solid pedicle connected the tumour to the upper part of the lateral aspect of the pons, which was depressed by the sharply demarcated medial end of the pedicle. The facial and acoustic nerves could not be identified on the right side, while the trigeminus, abducens, glossopharyngeus and vagus were found and were not involved in the mass. The superior cerebellar artery coursed over the dorsal surface of the tumour; short pontine twigs from the basilar artery crossed the ventral surface, and the anterior inferior cerebellar passed through a deep, narrow niche situated between the caudal aspect of the mass and the flocculus laterally, the medulla and the lower pons medially. The cephalic portion of the fourth ventricle was narrowed to an oblique slit and pushed to the left. Permission to examine the spinal cord could not be obtained.

Specimens were taken for microscopic study after seven months' fixation

in formalin. Sections were stained with H and E, Mallory's phosphotungstic hæmatoxylin, van Gieson's picrofuchsin and Loyez' iron hæmatoxylin lake

FIG. 1.—Case 1. In the right pontocerebellar angle is a large, hæmorrhagic mass encapsulated by tumour tissue. In the most cephalic section, two tiny cavities can be made out dorsal to the fourth ventricle.

for myelin. The tumour was shown to be a peripheral neurinoma, with large areas greatly altered by necrosis and hæmorrhage, the largest of which constituted the huge central mass of relatively fresh blood. There was a bundle of obliquely cut, large and medium sized, medullated fibres in contact

x 2

with the ventral aspect of the tumour, which seemed continuous with the nerve-sheath in one region. It could not be determined whether this represented the site of origin of the tumour or a secondary fusion. The nerve-bundle, far too small to constitute an entire nerve, could not be identified. Laterally, the tumour was covered with pia. Medially, it depressed the pons and cerebellum, but was everywhere sharply demarcated from the nervous tissue.

Near the tumour, the nerve-tissue was very œdematous. Neuronal elements were degenerated. There was some perivascular round-cell infiltration. Many bloodvessels had thickened walls and there was considerable

FIG. 2.—Case 1. Low-power view of part of a retroventricular cavity. The ventricular ependyma is above. In the right lower corner of the field is a heme body. Iron hæmatoxylin. $\times 100$.

vascular neoformation. Throughout the pons there was diffuse œdema of the glial mesh and dilatation of perivascular sheaths.

Dorsal to the fourth ventricle, in the upper pons, were four transversely elongated, narrow cavities. Two, one larger and one smaller, were on each side of the midline. The larger cavities were about 2 mm. $\times \frac{1}{2}$ – $\frac{1}{4}$ mm. The smaller were about $200 \times 100\mu$. The larger cavities, readily visible with the naked eye, could be followed in successive gross sections and were seen to extend longitudinally about 1 cm. Microscopically, all these cavities contained small bloodvessels cut at different incidences. Some of these vessels were very thin-walled and seemed to be venules. Others were relatively thick-walled and seemed to be arterioles. Outside of the vessels, the cavities were optically empty. The cavities were lined in places by a single row of flattened cells connected by a thin strand of substance staining like collagen with picrofuchsin and phosphotungstic hæmatoxylin. Outside of this lining was a slight condensation of the subependymal glia reticulum. The glial

nuclei were moderately proliferated and mostly of the small oval type. In some places the glial fibres were arranged radially about the cavity. Between the cavities and the fourth ventricle were small groups of cells of ependymal type.

In the glial tissue at a little distance from one of the cavities were rare, tapering, beaded, refringent bodies, staining a deep brownish-black with iron

FIG. 3.—Case 1. High-power view of the heme body seen in fig. 2. Note the characteristic tapering, beaded shape. Iron hæmatoxylin. $\times 430$.

hæmatoxylin (fig. 2). These structures had all the characteristics of typical *heme bodies* (fig. 3). Their range of staining with iron hæmatoxylin was the same as that of red blood cells in neighbouring vessels.

Case 2.—City Hospital autopsy no. 4013. The patient was a coloured female, age 23. The essential clinical features were headaches, tinnitus, loss of visual and auditory acuity, vertigo and weakness of both lower extremities, all of which had appeared three years before admission, and increased gradually. On admission, August 19, 1932, examination showed multiple cutaneous neurofibromata, bilateral papilloedema with secondary atrophy, horizontal nystagmus, absence of right corneal reflex, absence of provoked vestibular response. Spinal fluid was under pressure of 350 mm. of water. Colloidal gold was 5555543200. The Wassermann reaction was 4 plus in blood and spinal fluid. During the two months' stay at City Hospital, headache increased, blood-pressure and pulse-rate were very labile and the patient died in cardiovascular collapse.

Autopsy, done 9 hours and 45 minutes after death, revealed hydro-nephrosis of the right kidney and slight atheroma of the aortic arch. The remaining viscera were free from gross lesions. The brain showed evidence of considerable pressure, with sulci narrowed and gyri flattened. The entire ventricular system was dilated. In the right pontocerebellar angle was an irregular, moderately firm, greyish yellow mass, about $2 \times 1 \times 1$ cm., connected to the pons by a stalk which proved to be the acoustic nerve. The ventral surface of the cerebellum and the right lateral surface of the pons

and the medulla were strongly depressed and pushed toward the left, but not invaded by the tumour. The caudal portion of the fourth ventricle was deviated toward the left and strongly compressed. The cerebellar process of the ventricle was very distended and pushed far forward, so that on a section of the upper pons it appeared as a separate cavity beside the narrow cephalic portion of the fourth ventricle.

In the ventral portion of the right cerebellar hemisphere, just above the depression caused by the tumour, was a cavity $1 \times 1 \times \frac{1}{2}$ cm., filled with whitish homogeneous, translucent, semisolid material, which tended to

FIG. 4.—Case 2. A portion of a coronal section through the cerebellum and pons. The tumour has been reflected ventralward, showing the depression it produced. In the cerebellar white matter is a cavity containing whitish, gelatinous substance.

separate from the surrounding tissues (fig. 4). The cavity was everywhere surrounded by the cerebellar white matter and did not communicate with the ventricle or with the subarachnoid space. Ventrally the cavity came to within 3 mm. of the cortex. There was a narrow, firm, white layer about the cavity.

Small, fairly firm nodules were found on the left acoustic nerve, in the right semilunar ganglion and on several of the roots of the cauda equina. Microscopically these nodules, as well as a biopsy specimen of a subcutaneous nodule and the tumour of the right acoustic nerve, all proved to be typical neurinomas, with whorled and palisaded fusiform cells and a collagenous ground substance.

Except for the cauda equina and conus medullaris, the spinal cord could not be obtained.

The cerebellar cavity was studied after the specimen had remained in formalin for three years and eight months. The preservation was excellent. A portion of the cavity with the surrounding tissues was imbedded in paraffin and the sections stained with H and E, iron and chrome hæmatoxylin lakes and Mallory's phosphotungstic hæmatoxylin.

Microscopic examination showed that about the cavity was a layer of rather loose, radially arranged, long glia fibres with small, elongated glia nuclei (fig. 5). The central gelatinous substance was homogeneous and stained strongly with eosin and with hæmatoxylin after iron or chrome

FIG. 5.—Case 2. A portion of the cavity seen in fig. 4. The lumen, containing gelatinous matter, is on the right. The lining of the cavity is made up of loose, radially arranged glia. Alum hæmatoxylin and eosin. $\times 100$.

mordanting. It did not give the fibrin stain with phosphotungstic hæmatoxylin, but stained a dirty yellowish-grey or green.

In the radiate glial layer about the cavity were fairly numerous, rather small *heme bodies*, from 5×2 to about $12 \times 3\mu$. They presented the refringence peculiar to these bodies and stained deeply with iron and chrome hæmatoxylin lakes, and always within the same range of colour tone as the red blood cells in the neighbouring blood vessels.

The staining reactions of the central gelatinous substance of the cavity suggested that it too might contain some free hæmoglobin-like matter, possibly derived from laked blood. However, it was certain that the cavity did not represent a blood-vessel lumen or a perivascular space, for it was everywhere lined by glia.

In this case and in the preceding one, elective microchemical staining for heme pigments, by the Brown peroxide-acid ferrocyanide method or the Lepehne benzidine method, was inapplicable because of the prolonged

formalin fixation. The heme bodies were well stained by the Miller technique for hæmoglobin, but, on this material, the method proved relatively inelective.*

COMMENT

The cases here reported are, as far as can be ascertained, the first in which heme bodies coexisted with a tumour situated and originating entirely outside the neuraxis. In one case, that of Tannenberg³, the principal tumour, an intramedullary capillary hæmangioma, was associated with several meningeal hæmangiomas which were very small and apparently caused no serious compression. In the case of Kirch⁴ the tumour was mostly extramedullary and pushed the spinal cord to one side, but it was a glioma and arose from within the cord.

In the case of Liber and Lisa⁵, heme bodies were associated with syringomyelia, but without any tumour, either intra- or extramedullary. There was an extensive plastic panmeningitis, causing subarachnoid block and marked compression of the cord.

The findings in the case of Liber and Lisa and in the two cases reported here lend more weight to the suggestion of the author that heme bodies are probably not so rare as would appear from previous reports. Furthermore, while it is evident that intramedullary tumour, as such, is not an essential concomitant of heme bodies, *compression* and *cavitation* of some sort have always been present. The cavities in Case 1 (*supra*) are probably derived from dilated perivascular spaces and as such are not strictly comparable to syringomyelia. The mechanism of backing up of cerebrospinal fluid, suggested by Cushing⁹, would seem particularly applicable in this case.

The cerebellar cavity in Case 2, with its surrounding layer of gliotic tissue, would undoubtedly have been termed syringomyelia had it occurred in the spinal cord. Its origin is as obscure as that of syringomyelia itself, though the coexistence of the tumour suggests that compression may somehow have been at work, particularly as the cavity occurred at a place where the pressure must have been most intense. A second alternative is that the cavity may be a congenital anomaly whose germinal determination is the same as that of the neurofibromatosis. Although there was serological evidence of syphilis, there was neither gross nor histological evidence to confirm or explain the positive serology. The interpretation of this finding must then remain doubtful. Even though syphilis may have been present it is questionable whether it had any bearing on the pathogenesis of the cavitation.

In both cases the heme bodies showed their characteristic topography with relation to the cavity. They were situated in the glial tissue, mostly at a little distance from the lumen of the cavity, rarely in the innermost glial layer.

* For a discussion of the methods for histochemical demonstration of heme substances, see the author's previous article.⁶

In conclusion, it would seem that heme bodies are less rare than was at first supposed. They occur in glial tissue as a result of the interplay of some peculiar nexus of factors. Among the latter, those which seem essential are compression from any cause, perhaps accompanied by interference with drainage of tissue fluids, and some special factor or factors leading to cavitation. So far, heme bodies have only been observed in the spinal cord, medulla, pons and cerebellum. The latter two situations were observed for the first time in the cases reported here.

My thanks are due to Dr. James R. Lisa for his generous advice and helpful criticism and for permission to use his autopsy protocols; to Dr. Jacob Levine for the biopsy report in Case 2; to Dr. William Steinach and Dr. L. Vosburgh Lyons for the clinical material.

SUMMARY

1. Two cases of heme bodies (Rosenthal fibres) about cavities in the central nervous system, accompanying acoustic neurinomas, are reported.

2. In one case the cavities, located in the upper pons, probably represented dilated perivascular spaces. In the second case the cavity was in the cerebellum and was lined by a gliotic layer.

3. These cases are respectively the eighth and ninth of heme bodies reported in the available literature.

4. The presence of heme bodies outside the spinal cord or medulla is reported for the first time.

5. Heme bodies are less rare than was at first believed.

6. The three essential concomitants of heme bodies seem to be cavitation, compression, regardless of its cause, and the presence of glial tissue.

BIBLIOGRAPHY

¹ ROSENTHAL, W., 'Über eine eigenthümliche, mit Syringomyelie complicierte Geschwulst des Rückenmarks,' *Beitr. z. path. Anat. allg. Pathol.*, 1898, **23**, 110.

² BIELSCHOWSKY, M., and UNGER, E., 'Syringomyelie mit Teratom und extramedullärer Blastombildung,' *Jour. f. Psychol. u. Neurol.*, 1920, **25**, 173.

³ TANNENBERG, J., 'Über die Pathogenese der Syringomyelie, zugleich ein Beitrag zum Vorkommen von Capillarhämangiom im Rückenmark,' *Zeits. f. d. g. Neurol. u. Psychiat.*, 1924, **92**, 119.

⁴ KIRCH, E., 'Über die pathogenetischen Beziehungen zwischen Rückenmarksgeschwülsten und Syringomyelie,' *Zeits. f. d. g. Neurol. u. Psychiat.*, 1928, **117**, 231.

⁵ MACKAY, R. P., and FAVILL, J., 'Syringomyelia and intramedullary tumour of the spinal cord,' *Arch. Neurol. and Psychiat.*, 1935, **33**, 1255.

⁶ LIBER, A. F., 'Nature of the Rosenthal fibres in cases of syringomyelia with intramedullary tumour,' *Arch. of Pathol.*, 1936, **21**, 863; *Jour. Nerv. Ment. Dis.*, 1937, **85**, 286.

⁷ LEUPOLD, E., 'Ein Beitrag zur Kenntnis der Syringomyelie,' *Beitr. z. path. Anat. allg. Pathol.*, 1919, **65**, 370.

⁸ LIBER, A. F., and LISA, J. R., 'Rosenthal fibres in non-neoplastic syringomyelia: Considerations on the pathogenesis of syringomyelia.' Presented at the Section of Neurology and Psychiatry of the N.Y. Academy of Medicine, Dec. 1936. To appear in *Jour. Nerv. Ment. Dis.*

⁹ Personal Communication by Dr. Louise Eisenhardt.