Miliary Aneurysms

Miliary Aneurysms, in Relation to Cerebral Haemorrhage.

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Sir William Gull (1859) was the first to demonstrate the rupture of a miliary aneurysm as the origin and source of a cerebral haemorrhage. Previously Cruveilhier (1851) had seen "aneurysmes sous l'aspect d'ampoules" in a case of similar nature, and others had noted the occurrence of dilatations of the cerebral vessels in various diseases of the brain, such as haemorrhage, softening—both natural and experimental—and in cerebro-spinal meningitis.

Charcot and Bouchard (1868) published a paper based on the examination of 77 cases of cerebral haemorrhage. In every one of these they found ruptured miliary aneurysms in the lacerated brain substance forming the walls of the haemorrhagic area, and they concluded that the formation of these aneurysms is an essential preliminary to the occurrence of the haemorrhage. According to these authors miliary aneurysms are small rounded or spindle-shaped swellings of a diameter varying from 0.2 to 1 mm., occurring on vessels of about 0.25 mm. diameter, the numbers in individual cases varying from two to hundreds; they are found especially on the branches of the lenticulo-striate artery—Charcot's "artery of cerebral haemorrhage"—but are also seen in the vessels of the pia mater over the convexity, in the cortex, pons, cerebellum, centrum ovale, middle cerebellar peduncle, crus cerebri, and medulla. As Mott points out, this order pretty closely coincides with the order of frequency of the seat of haemorrhage.

Charcot and Bouchard believed that the aneurysms develop as a result of a primary sclerosing peri-arteritis, with secondary changes in the media; that atheroma of the larger arteries may co-exist, but that this has no direct causal connection either with the aneurysms or with the haemorrhage, though arteries stiffened by atheroma may transmit the shock of the heart-beat to vessels less able to bear it, and moreover already weakened by peri-arteritis.

A group of investigators, amongst whom Zenker was prominent, believed that the primary change is of the nature of an endarteritis; another, including Eichler, regarded it as a combined lesion, peri- and endo-arteritis. Others blame primary changes in the media,
which may be of the nature of granular or fatty degeneration, or of colloid, hyaline, or amyloid transformation, or calcification, or simple atrophy.

Of the more recent writers, Mott supports Gowers' opinion that the important factor is the loss of contractile and elastic elements, with resulting fibrous overgrowth in the intima and adventitia, but states that the vessels often show indubitable evidence of peri-arteritis, as described by Charcot. Miliary aneurysms "are formed if the muscular and elastic coats are degenerated; the wall of the vessel yields to the pressure of blood; an immature fusiform or sacculated aneurysm develops and is liable to rupture at any time. Probably the reason that these aneurysms are formed especially in the brain is that the walls of the cerebral vessels are relatively thin, and there are but few muscle fibres and vasomotor nerves."

Ford Robertson found miliary aneurysms in large numbers in the thickened pia mater in three cases of senile insanity, and maintains that they can never be pronounced absent by naked-eye examination alone. He believes that the primary change in the vessel is a hyaline degeneration of the intima, this interfering with the passage to the media of nutritive material from the circulating blood, so that, being weakened, the coats of the vessel yield before the blood-pressure. When fully developed the walls of the miliary aneurysm are composed of fibrous tissue only, the muscular and elastic tissue having disappeared. They rarely rupture in the soft membranes, but may readily do so within the brain on account of their lack of support.

Kaufmann describes miliary aneurysms not only on the cerebral vessels, but also on those of the intestine, lungs, and kidneys.

Beattie and Dickson, following the teaching of Greenfield, describe miliary aneurysms as generally resulting from degenerative changes in the walls of arteries, associated with increased blood-pressure; they are of the saccular variety, and are found specially in the brain and retina. They are usually multiple, and occur on arteries which show sclerotic changes, or are minute bulgings of the middle and inner coats, or of the inner coat alone, through degenerated outer coats.

In Pembrey and Ritchie's *Text-Book of General Pathology*, miliary aneurysms are described as round or spindle-shaped, and caused by degenerative changes in the intima, associated with atrophy and sclerosis of the media.
Orth describes aneurysmal dilatations of the smallest cerebral arteries, and even of capillaries; but he also indicates that cerebral haemorrhage can occur without recognisable pathological changes in the vessels.

Charlewood Turner was the first—as far back as 1882—to cast doubt upon the importance of miliary aneurysms as immediate factors in the causation of cerebral haemorrhage. He thus long anticipated Eppinger, to whom Pick gives credit for initiating scepticism as to the truth of the hitherto accepted pathology of cerebral haemorrhage. Turner confirms the statements of Charcot and Bouchard as to the presence of peri-arteritis and its probable importance in relation to the dilatation of the vessel, but he adds, "it seems doubtful whether the extravasation of blood occurred from the rupture of one or more miliary aneurysms resulting from that arterial lesion, or more directly from rupture of vessels weakened by inflammatory softening of their walls. In one case of haemorrhage no miliary aneurysms were found. In other cases in which they were found all those examined microscopically had thickened walls in which mingling of fibres and spindle-shaped nuclei with the leucocytes gave evidence of a lesion of earlier date and of a less active stage."

Within recent years German investigators have again questioned the truth of the accepted nature of miliary aneurysms.

Eppinger went so far as to maintain that miliary aneurysms as such do not exist, but are either "so-called" dissecting aneurysms, with accumulation of blood between media and adventitia (appearances also described incompletely by Turner), or are solid swellings in the adventitia, due to collections of cells or degenerated material, blood, fat, or pigment, in the adventitial lymphatic. These may initiate chronic peri-arteritis, with resulting solid swellings of the vessel, the lumen of which may become obliterated. These formations are termed "pseudo-aneurysms" by Kromayer and Ford Robertson, as distinct from "false aneurysms" as generally understood.

In Aschoff's Text-Book of Pathology, Ernst states categorically (p. 341) that for fatal haemorrhage only larger super-miliary aneurysms come into consideration—partly spurious, partly dissecting aneurysms, or rather intra-mural haematomata. The latter are collections of blood, either within the adventitial lymphatic, which he refers to as Virchow-Robin's space, or within the space produced artificially by the penetration of the blood between the mesodermal connective tissue, accompanying the vessel, and the
surrounding glial tissue, the so-called His' epi-cerebral or peri-vascular space. At page 58 of the same volume Benda states that, exceptionally, true saccular or dissecting aneurysms are found.

These statements in Aschoff's text-book are based on the results of the careful investigations of Pick and Ellis, which were carried out during 1909-10. Pick introduced a new method of isolating the diseased vessels, viz. by shaking up the disorganised brain substance in saline solution, slowly, for 8 to 10 hours. These authors found that all the aneurysms discovered in their cases (in all 41) were either false aneurysms or dissecting aneurysms. Primary atrophy of the media, or colloid, hyaline, or amyloid degeneration of that coat, or primary changes in the adventitia, were never found; but they found constantly atheromatous changes in the intima, with secondary changes in the media. The fatal haemorrhage originated either by rupture of atheromatous vessels or of super-miliary false aneurysms. As regards miliary aneurysms, whose character could be distinguished only by the microscope, they were either various formations simulating aneurysms, or dissecting aneurysms, or spurious aneurysms, i.e. encapsulated haematomata.

From time to time, as opportunity offered, I have been examining the vessels from cases of cerebral haemorrhage, but this has been done with greater interest since Pick's paper appeared. I demonstrated some of my results before the Edinburgh Pathological Club in 1912, and at the International Medical Congress in 1913. The results obtained so far correspond very closely with those of Pick and Ellis, and may be now described, the preparations employed for the purpose being selected from five of the cases examined.

Case I.—Male, æt. 55, died April 1908. Probable syphilitic history. Right-sided subdural haemorrhage; pontine haemorrhage, chiefly on right side, with numerous shot-like firmer masses of clot apparently older than the surrounding haemorrhage. Nodular atheroma of all visible branches of cerebral arteries. Marked hypertrophy of left ventricle. Aorta atheromatous. Most of the medium-sized and smaller arteries of the body atheromatous. Terminal arterioles in the organs, for the most part, showed marked hyaline degeneration of the intima. Arterial sclerosis in kidneys, with secondary atrophic changes in these organs, and mixed chronic nephritis.

The pons was examined by means of large paraffin sections. Microscopic examination showed numerous haemorrhages in the
Fig. 1.—Small Aneurysmal (Miliary) Dilatation of a Minute Artery. Case II.

It possesses some of the characters of a true miliary aneurysm. See text. (X 105.)

Fig. 2.—Arteriole showing Complete Rupture, and Occluded by Blood-Platelet Thrombus and Fibrin.
f, fold in section. (X 75.) See Fig. 3.

Fig. 3.—High Power View of Termination of Ruptured Vessel shown in Fig. 2. Elastic Tissue Stain.

The elastic lamina, e, is split up into layers, and fractured. b, blood-platelet thrombus; f, fibrin; x, fold in section. (X 400.)
Fig. 4.—Capillary Dilated and with Ruptures in Wall.
Perivascular space contains blood. (x 135.)

Fig. 5.—Branches of Lenticulo-Striate Artery from Hemisphere in which no Haemorrhage had Occurred. Case V. (natural size).

Fig. 6.—Vessels from Similar Situation in Hemisphere in which Haemorrhage had Occurred. Case V. (natural size).
Fig. 7.—Small Haematomata in Adventitial Spaces. Larger One simulated a Miliary Aneurysm to Naked Eye.

The ruptured vessel is seen in the lower left-hand quadrant of the figure. c, elstica, ruptured; c, occluding thrombus; b, blood which has escaped from the distended adventitial space. ($\times$ 32.)

Fig. 8.—Arteriole showing Dissection of Coats by Haemorrhage.

e, elastic lamina, split into layers; m, media; a, adventitia (letter "a" is placed in adventitial space); x, point of rupture through wall of adventitial space, found in a section further along the series. ($\times$ 138.)
Fig. 9.—Larger Artery showing Intima and Elastica Dissected up at "r."

b, blood between elastica and media; a, adventitia; m, media.

(x 77.)

Fig. 10.—Small Arteriole showing Dissection of Intima and Elastica from Deeper Coats, and Displacement in Direction of the Blood-Flow, at (1). At (2) Rupture of Intima, Elastica, and Media, with Hemorrhage.

e, elastica. (x 62.)

Fig. 11.—Artery showing Rupture in Angle Between it and a Branch.

r, rupture; e, elastica split up into layers.

(x 135.)
Fig. 12.—Small Arteriole showing Rupture of Media and Intima, with Formation of Small Aneurysmal Bulging, a, in which a few Leucocytes have Collected. (x 135.)

Fig. 13.—Arteriole showing Nodular Atheroma. m, media; e, elastica; i, thickened intima (letter "i" is placed in lumen of vessel). (x 75.)

Fig. 14.—Arteriole showing almost Complete Obliteration of Lumen as a Result of Obliterative Endarteritis. Collection of "foam-cells," c, just internal to elastic lamina, which is stretched. A similar condition extends into a small branch. (x 74.)
substance, many limited by the outer wall of the adventitial space. These corresponded to the shot-like masses observed at the post-mortem examination. In the midst of these collections the sections of the arteries were seen, some moderately dilated, others ruptured from over-distens on. Others, and these numerous, were blocked by proliferative endarteritis, or by endarteritis accompanied by thrombosis. Peri-arteritis was commonly seen, and to greatest advantage in vessels a short distance from the hæmorrhages. In some of these arterioles the adventitial space was filled up with vascular connective tissue, apparently of new formation, the smaller vessels often showing hyaline transformation. Frequently also fibrin was seen filling the adventitial space. Hyaline degeneration of intima and of adventitia was seen in many arterioles. No amyloid reaction was detected in any of these vessels.

In this case the hæmorrhage had originated by rupture of diseased vessels, these sometimes undergoing rapid preliminary dilatation. In a few instances the blood had dissected its way between elastica and media (cf. Fig. 8). The varying character of the changes in the coats of different arteries was remarkable.

CASE II.—Male, æt. 52, died January 1909. Alcoholism, three months. Chronic Bright's disease, two years. Hemiplegia, three days. Left-sided cerebral hæmorrhage in common situation. Myocardium, diffuse fatty degeneration. Hæmorrhages under endocardium. Chronic mixed nephritis.

Microscopic examination of vessels washed out of wall of hæmorrhagic area, and of serial sections of the wall, showed the following appearances:—

In parts at a little distance from the hæmorrhage the adventitial spaces of the arteries were dilated from oedema. Most of the arterioles showed a moderate degree of endo- and peri-arteritis. Some showed slight increase of connective tissue in the middle coat, with hyaline degeneration. Most of the minute terminal arterioles were approximately healthy, but some showed distinct peri-arteritis. In the hæmorrhagic areas rounded and oval collections of blood (haematomata) surrounding the arterioles were found, as in Case I., the blood coming from ruptures in the vessels. These ruptures were usually closed by thrombosis. Fibrin was seen in some of the adventitial spaces. In a few instances the elastica was split up into layers and separated from the media by effused blood.

On one very minute arteriole a rounded aneurysmal dilatation was found, 0.2 mm. in diameter, this being about three times the diameter of the vessel. The distended coats of the vessel were
Theodore Shennan

followed over more than half the circumference of the dilated part, but in the remainder the wall appeared to be formed of thinned adventitia alone. This structure was the only one seen in any of the cases which approximated at all closely in its appearance to the classic description of miliary aneurysms (Fig. 1).

In this case the haemorrhage had taken place as a result of rupture of diseased vessels, sometimes with a preliminary dissection through their coats.

**Case III.**—Male, æt. 57, died February 1913. Alcoholic; very adipose. Left-sided haemorrhage into basal ganglia. Moderate hypertrophy of left ventricle, with chronic fibroid changes in the myocardium. Kidneys, old infarcts; only moderate amount of chronic interstitial change. Bladder, numerous coalescing hemmorhages over fundus.

The lacerated brain substance was shaken up in saline solution, according to Pick’s method, and the isolated arteries cut serially in paraffin. Appearances similar to those described in the other cases were found. An arteriole with a knob-like termination was examined specially, as its appearance corresponded to that of a miliary aneurysm. The knob proved to be a dome-like thrombus occluding the ruptured vessel. At first sight the vessel appeared to be healthy, but on appropriate staining the elastica was found to be split up into layers, and was fractured in the neighbourhood of the rupture (Figs. 2 and 3). Further, the intima showed slight patchy thickening, and the inner layers of the adventitia throughout were hyaline.

**Case IV.** had a history, and showed naked-eye appearances similar to those described in the last case. In addition to the microscopical appearances described in connection with that case, I found great dilatation of the capillary blood-vessels, with small ruptures in their walls (Fig. 4).

**Case V.**—An old formalin-preserved brain, with haemorrhage into the basal ganglia. No history or post-mortem record available. This brain gave the best results of any I examined, and most of the illustrations are from preparations made from it. The vessels were pulled out of the lacerated tissue surrounding the haemorrhage, or were carefully dissected out.

The branches of the lenticulo-striate artery on the side without haemorrhage (Fig. 5) showed no aneurysms, or swellings simulating aneurysms, but some of the arterioles were slightly thickened; whereas those from the side on which haemorrhage occurred showed marked alterations (Fig. 6), the smaller vessels displaying rounded, spindle-shaped, or irregular purplish swellings. The separate lizard-shaped vessel, to the left of Fig. 6, shows in its lower part its approximately
normal size, and, above, the great enlargement due to dissection of the blood along the adventitial space. The vessel at the top left-hand corner of the figure, in addition to atheromatous thickening, had a rounded berry-like swelling upon it, about 2 mm. in diameter. This, unfortunately, gave way while it was being photographed. When examined under the microscope the smaller swellings proved in most cases to be hæmatomata, and, with care, the site of the rupture of the vessel connected with the hæmorrhage could be demonstrated (Fig. 7). Other vessels showed the characters of dissecting aneurysms, as illustrated in Fig. 8. The elastic lamina is seen to be split up into several layers, and to have given way at the bottom of the figure. It is separated from the media by extravasated blood, and the media also has given way near the point of rupture of the elastic layer. The inner layers of the adventitia remain attached to the media, and they are not thickened to any extent. Blood has also escaped into the adventitial space, and from this has penetrated to the brain substance. The intima of this vessel in other sections showed slight patchy thickening. Fig. 10 shows dissection of blood through the coats of a smaller vessel, and Fig. 11 shows rupture of a vessel in the angle between its branches. In addition, local ruptures of intima and media were found, leading to the formation of minute aneurysmal bulgings at one side of the vessel (Fig. 12). In the case of some arterioles localised yellowish swellings were due either to nodular atheroma, as shown in Fig. 13, or to a form of proliferative endarteritis, with a collection of "foam-cells" next to the elastic lamina (Fig. 14).

Conclusions.—Cerebral hæmorrhage results from

1. Rupture of diseased arterioles, which may undergo a preliminary local dilatation. This dilatation probably in most cases immediately precedes the rupture, and is not pre-existent in the form of an aneurysm. These local dilatations vary greatly in shape and size, but are usually of larger size than is associated with the term "miliary." The importance of the last point seems to be over-emphasised by German writers. Or—

2. It may follow the formation of a dissecting aneurysm, which develops in a manner similar to that of dissecting aneurysms occurring on the large arterial trunks.

True miliary aneurysms are not at all common, if, indeed, they exist at all, at the sites of cerebral hæmorrhage.

Miliary aneurysms may be simulated by small collections of blood or fibrin, or of cells in the adventitial space; by localised solid swellings of the coats of the vessel—nodular atheroma, endarteritis, or a combination of endarteritis and peri-arteritis— or by small occluding thrombi.
The statement of Charcot and Bouchard that peri-arteritis is commonly present is correct.

Seeing that in these cases arterioles elsewhere in the body are also diseased, it may be presumed that the reason why they have an especial tendency to rupture in the brain substance is that their walls are thinner, or at least more friable, and that they are less perfectly supported by resistant connective tissues than elsewhere in the body, and, moreover, are surrounded by a large adventitial lymphatic.

Further investigation is required before we can finally accept the statement that miliary aneurysms have no connection at all with cerebral haemorrhage.

But it appears to be necessary to prove, by employment of modern methods, whether miliary aneurysms actually exist. In the foregoing cases I found only one structure at all corresponding to the description of them. Such investigations should include not only the arteries at the site of the haemorrhage, but also, at least, those in the opposite hemisphere and those in the pia arachnoid.

The statement that miliary aneurysms are present in most cases of co-existent chronic heart and kidney disease (Rose Bradford and others) also requires further investigation and proof.

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