Virchows Arch. path. Anat. 335, 345—335 (1962)

From the Armed Forces Institute of Pathology, Washington, D. C., U.S.A.

Hemangiomas and Related Lesions of the Adrenal Gland

By

ALFRED PLAUT

With 15 Figures in the Text

(Received August 15, 1961)

There is much difference of opinion as to what constitutes an angioma. Organs vary so much in the structure and function of their vasculature that one might expect these variations to be reflected in the structure of their blood vessel tumors. This seems to be the case with the adrenal. Textbooks and monographs deal with adrenal angioma in cursory fashion, if at all. Among the case reports I found in the literature, eight appeared acceptable (DIECKMANN; IHRINGER; LUCKSCH; MARTEN and MEYER; MENON and ANNAMALEI; MÜLLER-STÜLER (bilateral); TAVERNARI; VOLKMUTH). These tumors were found accidentally at necropsy of adults, mostly old people. The files of the Armed Forces Institute of Pathology between 1943 and 1958 list one adrenal angioma in every 10,000 autopsy protocols.

Materials and Methods

Of the 30 cases on file at the AFIP, 17 were suitable for study. The fact that all angiomas came from male patients is of no statistical importance because men predominate in our material. Since necropsies are not performed at the AFIP, no intact gross specimens were available. The lesions were studied in paraffin sections — some in single ones, others in step series and occasionally in series. Techniques used were hematoxylin-eosin, VAN GIESON's, MASSON's trichrome, WILDER's reticulum, and WEIGERT's stain for elastic tissue.

Observations and Discussion

A variety of angiomatous lesions were encountered. More than half of them were of the cavernous type (cavernoma), which does not need further description or illustration. Half of these had a diameter of 1 to 2 cm; the others measured between a few millimeters and 1 cm. One cavernoma-like lesion was diffuse and had severely compressed the surrounding adrenal tissue. There were two locally destructive capillary hemangio-endotheliomas (Figs. 10, 15) and one very small similar tumor (Fig. 9). Diffuse tumor-like phlebectasia occupied large atrophic portions of two adrenal glands (Figs. 1, 13).

No relationship with clinical data and other autopsy findings was noted. Detailed descriptions can therefore be dispensed with, and the text can be essentially restricted to description and discussion of theoretically interesting observations. In a morphologic study like this one, only the simultaneous occurrence of changes can be proved, while statements about time sequence and causal relationship remain mostly conjectural. Data appear sufficient, however, for showing that not all these benign tumors do arise "without recognizable external sufficient cause" (ALBRECHT) but are associated with previous local changes.

Fibrosis. The walls of the blood-filled spaces in cavernous angiomas generally retain the character of capillary walls, and when I found them fibrosed in many of the adrenal lesions I thought this was a secondary change. But finding a distinct fasciculata pattern of the reticulum in the solid portion of a mostly

Fig. 1

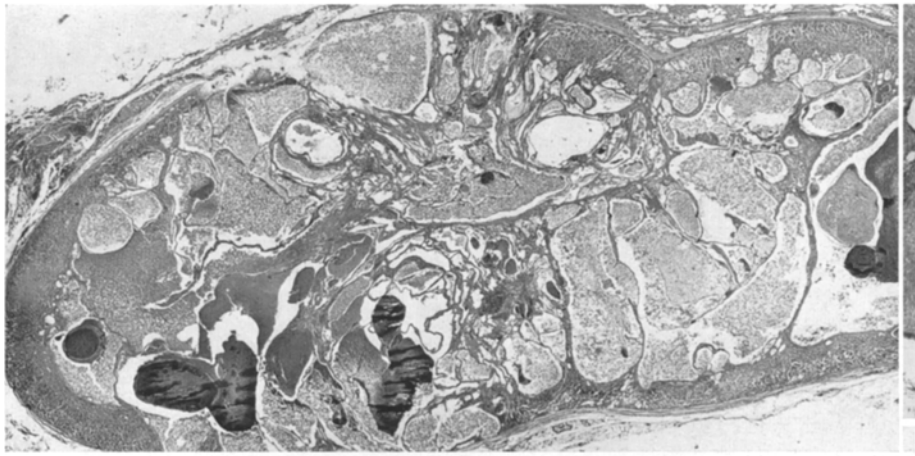
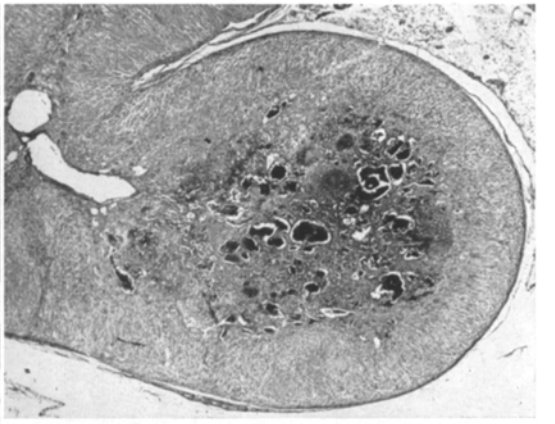


Fig. 2



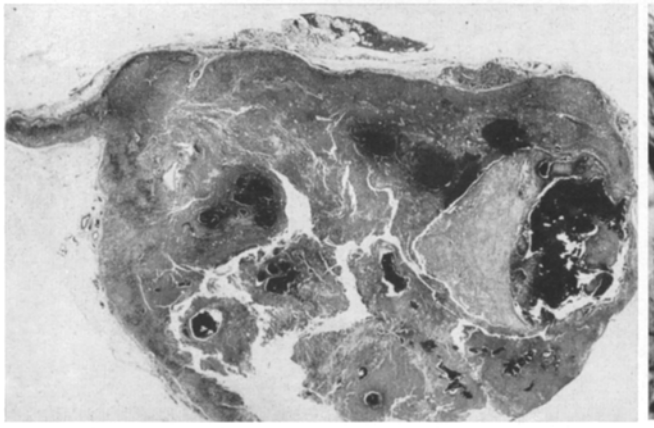


Fig. 3

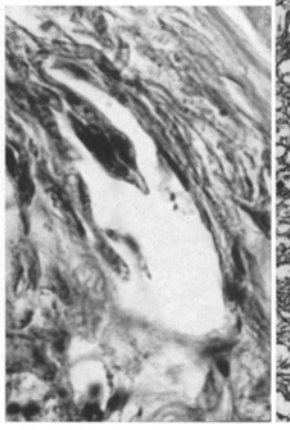


Fig. 4

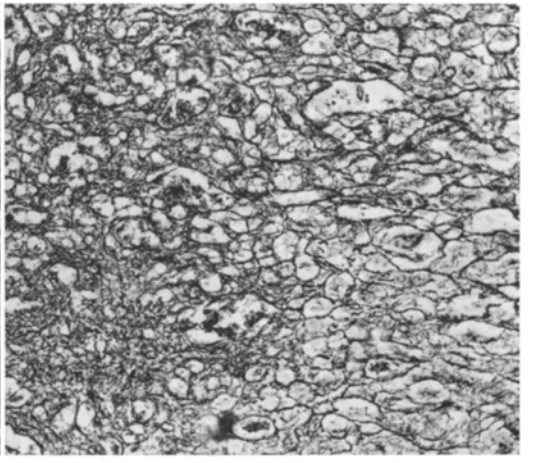


Fig. 5

Fig. 1—5. Fig. 1. AFIP Neg. No. 58—8827. Male, 19 years, shot through the neck. The adrenal tissue is displaced by irregularly shaped, mostly wide venous spaces. Most of them are filled with blood; some contain phleboliths. The periadrenal vessels are not distended. Hematoxylin-eosin stain. Mag. 8 ×. — Fig. 2. AFIP Neg. No. 58—13070. Male, 50 years, tuberculosis of lungs. Hemangioma with mediumsized and small spaces and with solid-appearing areas. Other levels show communication with the normal vein at the left edge. Van Gieson stain. Mag. $10^1/_2$ ×.— Fig. 3. AFIP Neg. No. 58—9192. Male, 61 years, rheumatic heart disease. The tongue-shaped protrusion in the left upper corner is normal adrenal. The large portion consists of about equal parts of hyperplastic cortex and of wide vessels with fibrotic walls. MASSON'S trichrome stain. Mag. 4 ×. — Fig. 4. Same case as Fig. 1. AFIP Neg. No. 58—8831. Single capillary bud with trace of lumen. Hematoxylin-eosin stain. Mag. 600 ×. — Fig. 5. Same case as Fig. 2. AFIP Neg. No. 58—13238. The pattern of the reticulum in a solid area has been transformed into a dense, irregular network. WILDER'S reticulum stain. Mag. 100 ×

cavernous angioma showed that the fibrosis had orginated in normal cortex, not in the established angioma. Furthermore, fibrous areas and layers, even circular shells, were found outside angiomas, sometimes separated from them by normal or by compressed and atrophic cortex. Areas of netlike fibrosis with varying distention of vessels in otherwise normal cortex also suggest the primary nature of the fibrosis. The walls of normal-appearing or distended large veins in the neighborhood of angiomas often were thick and fibrosed, and, as continued sectioning showed, they merged imperceptibly into cavernomatous structures.

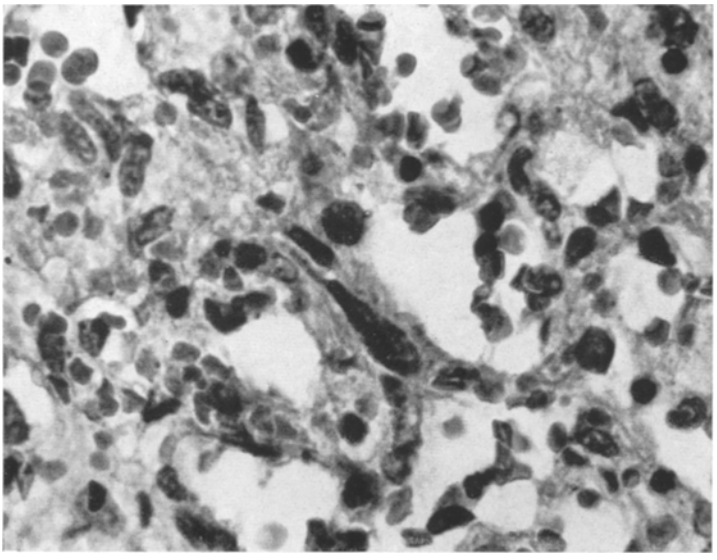


Fig. 6. Same case as Fig. 2. AFIP Neg. No. 58—13236. Under higher magnification, some areas, notably near the periphery, are occupied by small, irregularly shaped spaces, some of which contain red cells. The numerous nuclei vary greatly in size, shape, and structure. Hematoxylin-eosin stain. Mag. 700 ×

Such relationship between fibrosis and angioma was the same in truly blastomatous angio-endotheliomas as in cavernomas. Angio-endothelioma compressed and invaded areas of fibrosis as well as it did normal cortex. The way in which fibrosis and angioma are connected is unknown. It may be significant that the pattern of reticulum was much altered in a fibrotic area of a mostly cavernous angioma (Fig. 5). In order to make sure that fibrosis and angioma are linked in some way — as far as the adrenal is concerned — the routine adrenal sections of 45 men between 50 and 70 years of age were studied. In all but 2 of the 45, neither fibrosis nor distention of vessels was found. In one of the two, thin networks and arches of fibrosis caught the eye, and continued search revealed distended veins in the area. In the other one, wide veins attracted attention, and the fibrosis was found later. Changes that appear as fibrosis in the light microscope may represent different processes; the "fibrosis" that precedes an angiomatous process may be different from the one that transforms an angioma into a scar.

Other Concomitant Changes. As in the case of fibrosis, one might assume that atrophy is a secondary process when found with cavernoma-like structures. But

this mechanical explanation collapses when we find the atrophy in portions without widening of vessels as well (Figs. 13, 14), and at least some of the atrophy appears to be primary. The connection between the two processes is unknown.

In a number of cases, the thickening of the adrenal was caused largely by adenomatous cortical hyperplasia, and the angioma was situated in the hyperplastic nodule (Fig. 3). Associated fibrosis in some cases was also restricted to the area of hyperplasia. Myeloid cells in cortical capillaries of man and other mammals may likewise be restricted to the hyperplastic nodules. Hemopoiesis, which can be found in angiomas of different organs, e.g., the leptomeninx, was present in adrenal angiomas in a few cases in the areas of newly formed capillaries (Fig. 12). Finally, it is worthy of note that the myelolipoma (defined as a bonemarrow-like structure without bone in the adrenal cortex of patients without hemopoietic disorders) was found 4 times in the 30 cases of adrenal angioma; that is a thousand times more often than expected.

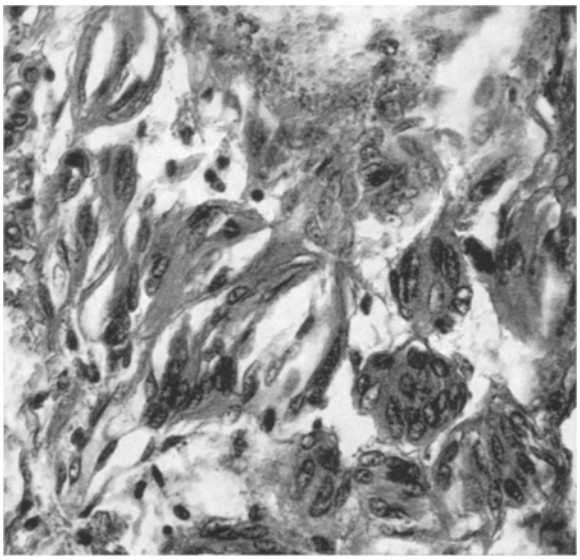


Fig. 7. Same case as Fig. 1. AFIP Neg. No. 58—1324. Solid and sprouting endothelial formations. Hematoxylin-eosin. Mag. 375 ×

The Relationship Between the Formation of Angiomas and the Dynamics of Adrenal Circulation. The question of continuity between the spaces of a cavernoma and the surrounding blood vessels has occupied many pathologists. Surgeons can answer the question for angiomas of skin, since ligation of an afferent and an efferent vessel makes the removal of a skin angioma almost bloodless (PACK and MILLER). Single sections of a cavernoma often do not show continuity with surrounding vessels, but study of many sections leaves no doubt about such continuity in adrenal angiomas. The results of injection experiments with liver cavernomas have not been uniform. Careful serial sections of liver cavernomas, however, have shown a single narrow artery which, without branching or change of caliber, went to the center of the cavernoma and there opened into one of the vascular cavities (KUSKE). In the adrenal lesions under study, continuity with adjoining capillaries was often evident, and distention of such peripheral capillaries was one of the mechanisms by which the cavernomas increased in size. Occasionally, distended capillaries connected the angioma with a large normal vein while all other capillaries in the neighborhood were narrow. This suggests a connection between the formation of the cavernoma and the blood stream in this vein. The relative frequency of angioma-like structures in arteriovenous anastomoses (lung, muscle) points to causative hemodynamic factors. The arteries within the adrenal are too small for furnishing efficient arteriovenous anastomoses,

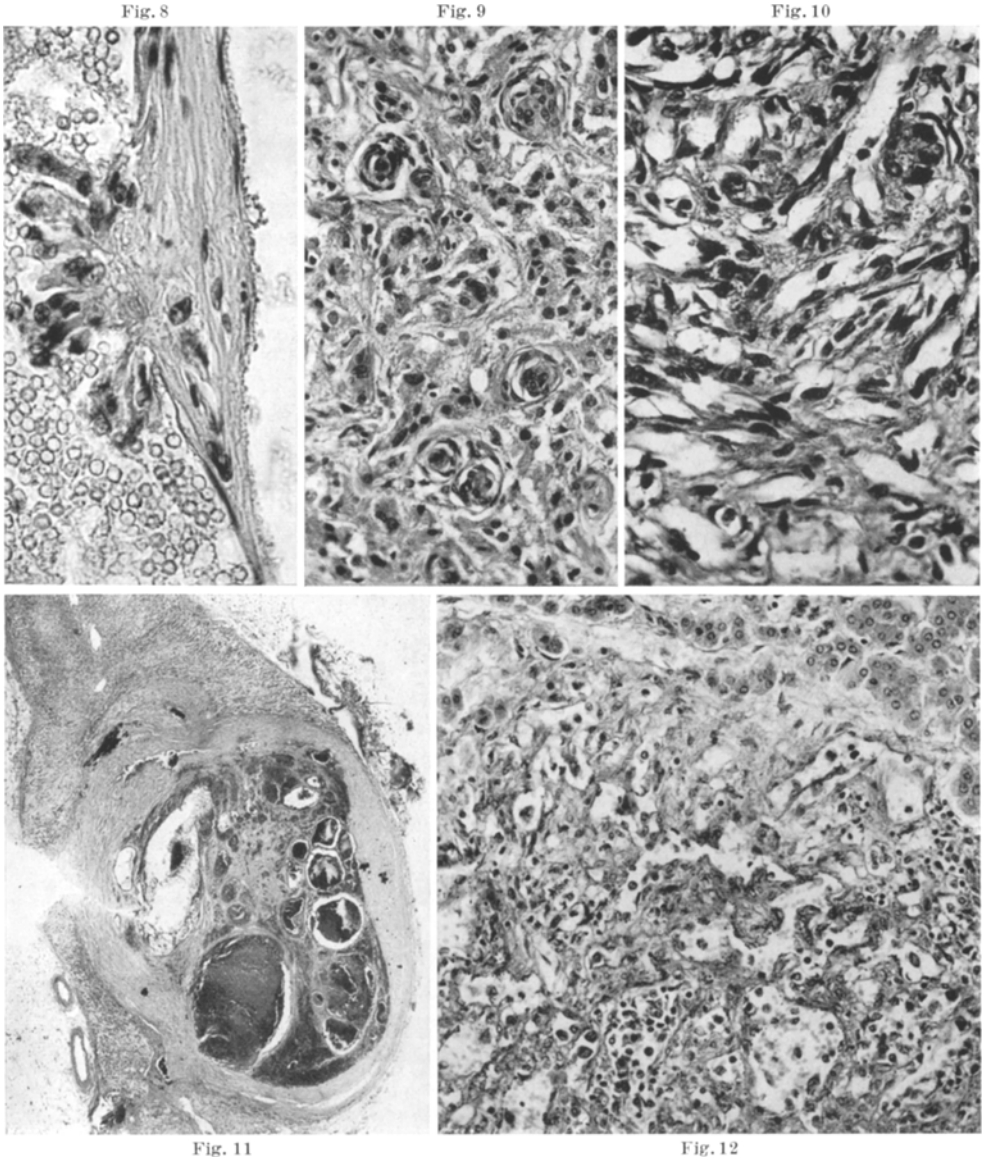


Fig. 8—12. Fig. 8. Same case as Fig. 1. AFIP Neg. No. 59—1926. Capillaries sprouting from the endothelial lining of a wide cavernous space. This takes place not only at the edge of the cavernoma but in its center also. Hematoxylin-eosin stain. Mag. 440 ×. — Fig. 9. AFIP Neg. No. 58—138073. Male, 60 years. Shock after gallbladder operation. From a light-staining area that caught the eye in a routine section of a normal-appearing adrenal. Several whorled angioendotheliomatous structures. Hematoxylin-eosin stain. Mag. 215 ×. — Fig. 10. AFIP Neg. No. 58—7462. Male, 58 years, tuberculosis of lungs. Diffuse capillary angioma with large, dark-staining nuclei. Hematoxylin-eosin stain. Mag. 350 ×. — Fig. 11. AFIP Neg. No. 58—8311. Male, 62 years, hypertensive heart disease. A partly fibrosed cavernoma is surrounded by a dense, thick shell of connective tissue. In spite of this the surrounding cortical tissue is compressed. Hematoxylin-eosin stain. Mag. 9 ×. — Fig. 12. AFIP Neg. No. 59—1933. Male, 48 years, osteomyelitis. Undifferentiated tissue with irregular vascular spaces in a partly cavernous hemangioma. Such areas were numerous. Hemopoiesis in lower portion to left of midline. Hematoxylin-eosin stain. Mag. 175 ×

but the thick, irregular musculature of adrenal veins cannot fail to create sudden and violent changes of blood pressure and blood flow. Adrenal veins in the adult

human have columns of longitudinal muscle and some oblique bundles, but no circular muscle. The divergent descriptions of the arrangement of these muscle bundles are explained by their great variation. Thick masses of muscle may protrude into the lumen. Variously extensive and variously thick musculature is found even in the wall of small veins. Thin-walled capillaries open directly into large muscular veins, perforating the thick muscular layers at different angles. It is obvious that even slight contraction of the muscle of the large vein must close such capillaries and create local stasis. Such small vessels may be found wide in their course outside the large vein while their intramural portion is narrow. The function of this elaborate muscular apparatus is unknown. Some

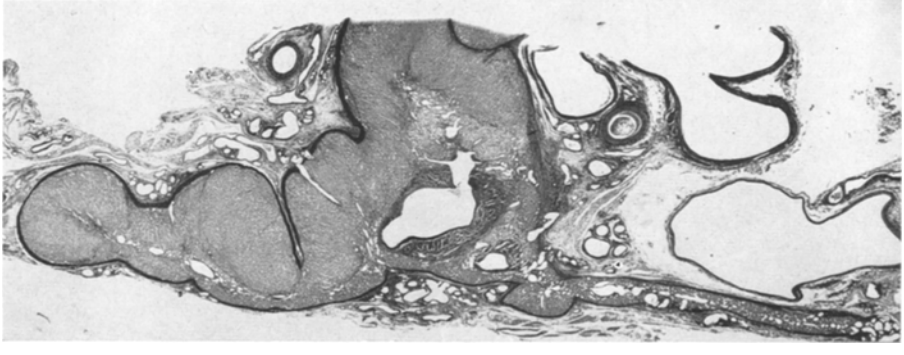


Fig. 13. AFIP Neg. No. 58—8825. Male, 49 years, tuberculosis of lungs. This adrenal gland, at autopsy, gave the impression of being "partially replaced by small cystic spaces." Distended veins are scattered through a very thin portion of this gland and also partly surround it. The veins in the remainder of the organ look normal. Van Gieson stain. Mag. 8 ×

people speak of constriction of the vein by this muscle, others of dilatation (HARTMAN and BROWNELL). The possibility that both may take place has also been voiced (VÉLICAN). The rapid rise of blood adrenalin levels in animal experiments seems to indicate a propelling mechanism of adrenal veins, but it also occurs in the cat, whose adrenal veins have very little muscle. In adult man, muscle bundles continuous with venous muscle sometimes crisscross the medulla; their contraction may squeeze the medulla like a sponge and may widen veins to whose wall they are attached. The effect of muscular contraction in the wall of a vein upon the blood flow must be different in the adrenal because the muscle often does not occupy the whole circumference and because the wall between the muscle bundles is as thin as that of a capillary. While considering the special nature of circulation in the adrenal and its possible role in the formation of blood vessel tumors, we must not forget that such tumors are rare and that probably numbers of other factors are needed before an angioma is formed. The experimental approach is not feasible because only the rhinoceros, the kangaroo, and adult apes have adrenal venous muscle comparable to that of man. Such extensive, specialized muscular structures of veins inside a secreting organ have, to my knowledge, no parallel in the mammalian body. The slow development in prepuberal life bespeaks endocrine correlations, and adrenal angiomas do not seem to occur in children.

There is another item in the complex picture of adrenal circulation which may manifest itself in the life history of tumors of the adrenal vessel. Not all venous blood is necessarily carried by the single adrenal vein. Capsular veins

were described almost a hundred years ago, but modern literature has neglected them. It is not known how much blood they carry nor where they carry it. The location and extent of their anastomoses, especially with the portal system of the liver, have not been sufficiently investigated. Experiments concerning the fate of adrenal secretions when carried to the liver have not given uniform results (MARK; EVERSOLE and GAUNT; MARDEN, HOPKINS and SCOTT). These veins are part of the picture in two cases that show atrophy of the cortex and diffuse widening of adrenal veins (Figs. 13, 14). In one of these cases the capsular

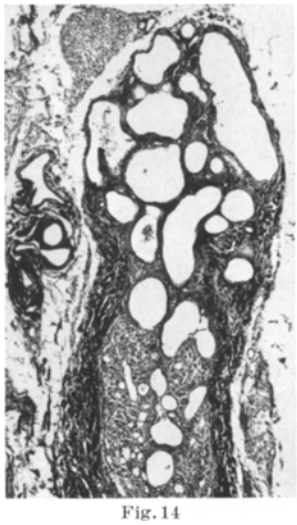


Fig. 14

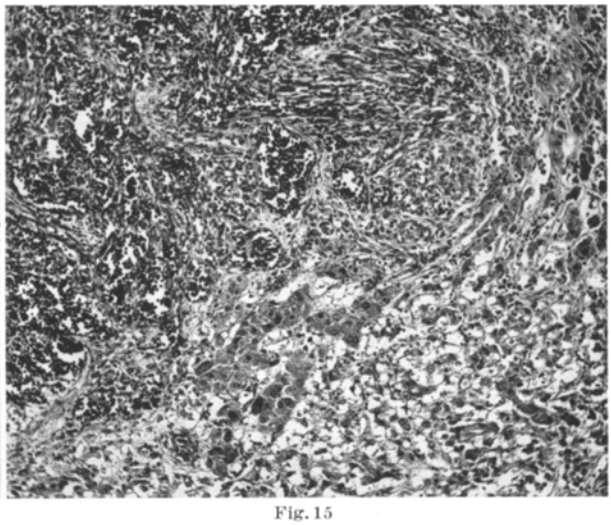


Fig. 15

Fig. 14. Same case as Fig. 13. AFIP Neg. No. 58—8830. Outer end of the atrophic portion (right lower corner of Fig. 9). Some of the septa between vessels in the snakehead-like portion contain remnants of cortex, which cannot be recognized at this magnification. This specimen shows no parallelism between the width of vascular spaces and the degree of cortical atrophy. Van Gieson stain. Mag. 40 ×

Fig. 15. AFIP Neg. No. 58—13574. Male, 33 years, lymphatic leukemia. Large portions of the adrenal are destroyed by diffuse and focal capillary angioma. Remnants of cortex are recognizable below the center and near the right margin. Hematoxylin-eosin stain. Mag. 85 ×

vessels were unusually wide and communicated with distended vessels inside the organ, while in the other, capsular veins were barely visible. Thus in the latter case all the blood contained in the distended veins must have left the organ through the central vein, while in the other patient the outflow was divided between the central vein and the many wide capsular veins. It is unknown what difference that may have made functionally. Occasionally, atypical vascular structures leave one in doubt about the direction of the blood stream: In two instances, a subcapsular area about 2 mm in the largest diameter was occupied by a labyrinth of moderately distended vessels that communicated with a large muscular vein inside the adrenal but also with wide veins that penetrated the capsule. The amount and direction of blood flow in such a structure is certainly unknown.

Postnatal Causation Versus Hamartoma. Angiomas, except for the aggressive angio-endotheliomas, are customarily classed not with "true tumors" but with tumor-like malformations, hamartomas. When this term was coined at the beginning of the century, COHNHEIM's theory that many tumors were caused by

embryologic flaws was widely accepted, and the concept of hamartoma fitted well into the general picture. Today the situation is reversed: We find more and more environmental causation of congenital malformations, and we search for external causative factors in neoplastic diseases. While previously we tried to correlate oncology with embryology, we now look for factors that start or steer embryologic processes in the manner in which carcinogens lead to the formation of tumors. Both ways of thinking do away with sharp separation of prenatal and postnatal happenings, but the emphasis has shifted. Thus the concept of hamartoma has lost much of its appeal. When we call a lesion a hamartoma we renounce efforts at finding decisive postnatal causative factors. Adrenal angiomas, to my knowledge, have not been found in children, and even the accepted prototype of vascular hamartoma, the cavernoma of the liver, is much more frequent in the old than in the young. Experienced pediatric pathologists (GRUENWALD; POTTER; STRAUSS) have seen scarcely one in thousands of autopsies, and the widely accepted belief that the liver cavernoma is congenital is difficult to explain. Pertinent statements in the literature are not substantiated by illustrations or detailed descriptions. The age distribution and the genesis of the clinically unimportant small liver cavernomas are not talked about much in textbooks of pathology, and only few deny or doubt their congenital nature (KAUFMANN; MOORE). The early appearance of skin angiomas has probably helped to put angiomas in general into the hamartoma class. But angiomas should be considered according to the organ in which they are located (VIRCHOW), and the variety of angioma-like lesions in the adrenal, considered together with the complexity of adrenal circulation, emphasizes the correctness of this century-old statement. Hamartomas are not supposed to involve a greater area than originally affected. But the adrenal cavernomas described in this paper expand not only through distention of vascular spaces but also through active growth (Fig. 7). Areas of compact vasoformative tissue, which are believed by some to be part of a malformation, appear to me as new growth. These are opposing impressions for which convincing proof is hard to adduce. But the search for postnatal causative factors gives at least more promise for future enlightenment than the malformation hypothesis does. The above-mentioned frequently found fibrosis, which obviously preceded the angioma, also speaks against the hamartomatous nature of adrenal angiomas.

Tumors and Reactive Growth. The old definition of a benign tumor as an organoid structure "without recognizable sufficient causation" (ALBRECHT) is at variance with our more dynamic attitude of searching for the conditions under which tumors are formed, be they benign or malignant. We look for conditioning factors in the surrounding tissues, and it follows automatically that angiomas will be studied in relation to the vascular system of the organ in which they are located. The division between reactive growth and tumor growth often is arbitrary, and the more we learn about causation of tumors the less appealing becomes the separation of the two types. In the case of blood vessel tumors, we may expect causative hemodynamic factors, and if we at least make progress in understanding the genesis of angiomatous structures, we need not be concerned with whether to call them "true tumors" or not.

In the embryonic development of blood vessels, chemical factors (inductors) probably are responsible for the first steps, namely, the appearing of capillary

spaces. We can assume similar conditions in the genesis of angiomas: chemical factors for the early phases like capillary budding, hemodynamic factors for the further shaping of vascular walls and spaces. The importance of hemodynamic factors in the formation of angioma-like structures in general is demonstrated by the "angiomas" in arteriovenous shunts. The beginnings of angiomatous change in the adrenal are often found in the vicinity of veins with thick musculature whose lumen may narrow or widen abruptly, and when, as I have seen repeatedly, the capillaries between the vein and the angioma are wide, while all other capillaries are narrow, the idea readily offers itself that a circulatory disturbance in this vein is somehow connected with the formation of the angioma. We have no inkling of the chemical factors underlying adrenal or other angiomas, but the production of angiomas by painting with methylcholanthrene (RIGDON, WALKER, and TEDDLIE) shows the possibility of chemical causation.

Round Structures, Expansion, Proliferation. The adrenal cavernous angiomas generally have a fairly regular spherical shape. It seems natural to explain this as even expansion of an essentially fluid body in a mechanically homogeneous medium. But the above-mentioned fact that considerable compression of cortical tissue can be observed outside a thick fibrotic shell surrounding an angioma (Fig. 11) makes one doubt the mechanical explanation. One would hardly expect the pressure of the fluid to be transmitted through a thick layer of dense connective tissue. Conversely, the lack of compression around widely distended thin-walled vascular spaces of a cavernoma appears paradoxical, but we do not know how slowly the distention took place. In one cavernoma-like tumor, the surrounding tissue was severely compressed, and this was the one with the most widespread budding (Figs. 4, 6, 7, 8). Probably this active new growth led to rapid increase in size, though we do not know to what extent rapid filling of vascular spaces may have done the same. Rings of condensed reticulum and of connective tissue within an angioma are probably indicative of multiple growth centers. New formation of blood vessels is required in order to call a lesion angioma. This is easily found in some specimens (Figs. 4, 8), but not in others. BORST assumed that the tumorous process may have come to a standstill. Zones of little-differentiated mesenchyme with small vascular spaces between cavernoma and adrenal cortex represent growth centers, and it is significant that blood formation occurs in such areas (Fig. 12). In our material, every third cavernomatous adrenal structure showed active blood vessel proliferation, and it was probably present in more of them. Both known precursors of vessels were found: small lined spaces in undifferentiated mesenchyme and endothelial budding (Figs. 4, 6, 7, 8). When such newly formed capillaries are haphazardly inserted into the circulation they may easily become distended and thus form a cavernoma. The continuity of cavernoma spaces with large muscular veins does not necessarily indicate the size of the vessels from which the cavernoma has arisen, because even the main adrenal vein has capillary-like tributaries that traverse its thick muscle coat. The variety of morphologic types of capillaries as revealed by the electron microscope (BENNETT, LUFT, and HAMPTON) may also play a role in the formation of vascular tumors. The term "capillary angioma" is often understood to mean that the component vessels are narrow, but when they become distended, as in the cavernoma, their walls may nevertheless retain the character of capillaries. In the adrenal gland there is little difference between the wall of a capillary and

that of a vein, except for the muscular portions, and histogenetically there is probably little difference between a capillary angioma and a cavernous angioma.

The differences in the occurrence of proliferative processes underline the above-mentioned thesis that angiomas must be studied with an eye to the organ in which they are located. While proliferation is frequent in the adrenal angioma, RIBBERT found none in the cavernomas of liver, and skin cavernomas are said to be without proliferative structures also (GANS and STEIGLEDER). Angiomas do not fit all customary concepts; neither does their mother tissue, the blood vessels. Other mesenchymal tumors are histioid; they consist of certain cells and their products. Angiomas, however, are organoid. This difference is little recognized, and it is the same with the "altruistic" nature of blood vessels. Blood vessels, unlike nerves, will grow profusely even into highly malignant tumors and maintain their nourishment (EWING). While the lumina in adenomatous tumors, as far as I know, do not communicate with pre-existing glandular lumina, the blood vessels of angiomas — spontaneous ones and experimentally produced ones — do communicate with pre-existing vessels, and pressure atrophy of vessel walls is hardly sufficient to explain this.

Conclusions and Summary

A variety of hemangiomas and hemangioma-like structures occur in the adult human adrenal gland. They seem to be more frequent than in other viscera, except the liver, and their variegated pictures contrast with the uniformity of liver cavernoma.

A study of 30 such cases from the files of the Armed Forces Institute of Pathology again shows the futility of attempts at sharply separating "truly neoplastic tumors" from related lesions. Structures that seemed to have the earmarks of simple angiectasia yielded, on closer examination, pictures of neoplasia. Localized or diffuse angiectasia, focal or widespread fibrosis, atrophy and nodular hyperplasia of the cortex accompanied, and probably preceded, the formation of angioma in many cases. Angioma and myelolipoma, both rare lesions, were found together far more often than coincidence can explain. Changes that took place in postnatal life appear more important in the genesis of adrenal angiomas than congenital ones.

Zusammenfassung

Verschiedene Hämangiome und hämangiomartige Gebilde kommen in der Nebenniere des erwachsenen Menschen vor. Sie scheinen häufiger zu sein als in anderen inneren Organen, mit Ausnahme der Leber; ihre Mannigfaltigkeit sticht ab von der Einförmigkeit der Leberkavernome. Dreißig solche Fälle aus dem Material des Armed Forces Institute of Pathology wurden untersucht. Dabei ergab sich wieder die Nutzlosigkeit der Versuche, „wirklich neoplastische Tumoren" scharf von verwandten Gebilden abzutrennen. In Strukturen, die zunächst ganz wie eine einfache Angiektasie aussahen, fanden sich bei genauerer Untersuchung Bilder, wie wir sie von echten Tumoren kennen. Umschriebene oder diffuse Gefäßerweiterung, herdförmige oder weitverbreitete Fibrose, Atrophie und Hyperplasie der Rinde kommen in vielen Fällen zusammen mit den Angiomen vor und gingen ihnen wahrscheinlich voraus. Angiome und Myelolipome fanden sich viel häufiger zusammen, als der Wahrscheinlichkeit nach zu erwarten wäre. Im

postnatalen Leben entstandene Veränderungen erscheinen wichtiger in der Genese von Nebennierenangiomen als angeborene.

References

ALBRECHT, E.: Die Grundprobleme der Geschwulstlehre. Frankfurt. Z. Path. **1**, 221—247, 377—425 (1907).

BENNETT, H. S., J. H. LUFT and J. C. HAMPTON: Morphological classification of vertebrate blood capillaries. Amer. J. Physiol. **196**, 381—390 (1959).

BORST, M.: Das pathologische Wachstum. In L. ASCHOFF, Pathologische Anatomie, 8. Aufl., Bd. 1, S. 641. Jena: Gustav Fischer 1936.

DIECKMANN, H.: Histologische und experimentelle Untersuchungen über extramedulläre Blutbildung. Virchows Arch. path. Anat. **239**, 451—474 (1922).

EVERSOLE, J., and R. GAUNT: Methods of administering desoxycorticosterone and the problem of its inactivation by the liver. Endocrinology **32**, 51—56 (1943).

EWING, J.: Neoplastic diseases, edit. 4, p. 249. Philadelphia: W. B. Saunders Company 1940.

GANS, O., u. G. K. STEIGLEDER: Histologie der Hautkrankheiten, 2. Aufl., Bd. 2, S. 451. Berlin-Göttingen-Heidelberg: Springer 1957.

GRUENWALD, P.: Personal communication.

HARTMAN, F. A., and K. A. BROWNELL: The adrenal gland, p. 48. Philadelphia: Lea and Febiger 1949.

IHRINGER, G.: Zur Pathologie der Nebennierencysten. Frankfurt. Z. Path. **66**, 153—160 (1955).

KAUFMANN, E.: Lehrbuch der speziellen pathologischen Anatomie, 9. Aufl., Bd. 1, S. 893. Berlin u. Leipzig: W. de Gruyter & Co. 1931.

KUSKE, H.-J.: Vergleichende Untersuchung über Bau und Pathogenese von Leber- und Hautkavernom. Frankfurt. Z. Path. **51**, 131—149 (1937).

LUCKSCH, F.: Untersuchungen über die Nebennieren. Beitr. path. Anat. **62**, 204—226 (1916).

MARDEN jr., H. E., W. J. HOPKINS and W. W. SCOTT: Lack of conversion in *vivo* of Δ_4 androstenedione-3, 17 to a more active androgen by passage through the liver. J. Urol. (Baltimore) **77**, 315—317 (1957).

MARK, J.: Inactivation of desoxycorticosterone acetate. Endocrinology **31**, 582—585 (1942).

MARTEN, M. E., and L. M. MEYER: Hemangioblastoma of the adrenal. Amer. J. Cancer **48**, 485—487 (1940).

MENON, T. B., and D. R. ANNAMALEI: A hemangioblastoma of the adrenal gland. J. Path. Bact. **39**, 591—594 (1934).

MOORE, R. A.: A textbook of pathology, edit. 2, p. 151. Philadelphia: W. B. Saunders Company 1951.

MÜLLER-STÜLER jr., M.: Doppelseitiges, kavernöses Hämangiom der Nebennieren. Virchows Arch. path. Anat. **290**, 177—181 (1933).

PACK, G. T., and T. R. MILLER: Hemangiomas; classification, diagnosis and treatment. Angiology **1**, 405—426 (1950).

POTTER, EDITH L.: Personal communication.

RIBBERT, H.: Über Bau, Wachstum und Genese der Angiome. Virchows Arch. path. Anat. **151**, 384—401 (1898).

RIGDON, R. H., J. WALKER and A. H. TEDDLIE: Hemangioma. An experimental study in the duck. Cancer (Philad.) **9**, 1107—1115 (1956).

STRAUSS, L.: Personal communication.

TAVERNARI, A.: Emoangioma cavernoso della surrenale. Arch. ital. Urol. **13**, 481—488 (1936).

VÉLICAN, C.: Le barrage vasculaire cortico-médullaire de la surrénale de l'homme. Ann. Endocr. (Paris) **8**, 495—502 (1947).

VIRCHOW, R.: Über kavernöse (erektile) Geschwülste und Telangiektasien. Virchows Arch. path. Anat. **6**, 525—554 (1854).

VOLKMUTH, W.: Über Angiome der Nebennieren. Diss. Bonn 1919.

ALFRED PLAUT, M.D.,
Armed Forces Institute of Pathology,
Washington 25, D.C./U.S.A.