MALIGNANT HYPERTENSION IN CHILDHOOD

BY

JOHN CRAIG, M.B., M.R.C.P.

(From the Royal Aberdeen Hospital for Sick Children.)

Essential hypertension is predominantly a disease of the later years of life. It is uncommon under thirty years, and rare in childhood. Two forms or phases have been described, the benign \(^1\) - \(^7\) and the malignant. There seems to be unanimity of opinion among the writers on the subject regarding the clinical differentiation of the two forms, but the pathogenesis of the malignant type is still open to dispute. This type is usually seen in relatively young people, the average age being about forty.

Cases in children have been recorded by Keith, Wagener, and Kernohan \(^1\), by Amberg \(^2\), by Klemperer and Otani \(^3\), and by Murphy and Grill \(^4\).

In this article we describe the malignant hypertension syndrome and the autopsy findings in a girl of eight, who was observed over a period of eleven months.

Clinical report.

A. D., female, aged 8 years, was admitted to hospital on January 29th, 1930, in an unconscious condition. The evening before admission, she had gone to bed as usual about 7 p.m., but had wakened screaming at 10 p.m., and had cried off and on all night. At 7 a.m. she had complained of severe frontal headache, staring into space and complaining that she could not see anything. At 9 a.m. she had had a fit with jerking of the face and eye-balls, movements of the arms, and blueness of the face. The fit had lasted twenty minutes. Half an hour after this, she had had a second similar fit, and was then admitted to hospital.

She was born at full term, after a breech presentation and a prolonged labour. When two days old, she vomited blood, and also passed blood per rectum. This went on for several days and stopped without any special treatment. At the age of two, several days after her sister had been removed to hospital with scarlet fever, she had a sore throat of a dubious character and vomiting, but without any rash. She had whooping cough at three years, but never had measles. She was nearly two years old before she walked and talked.

She was never a strong child, and always seemed a little behind girls of her own age. 'Almost from the time she could speak' she had every other week a frontal headache, which was sometimes followed by vomiting. During the year previous to admission, the headaches came about twice a week, and during the previous week she had an attack every morning. The headaches were almost always in the morning, beginning about 7 a.m. and disappearing in the course of the forenoon. From time to time the child had attacks of inexplicable irritability. Nose bleeding had occurred a few times in the year before admission.

The father and mother, aged 48 and 39, are alive and well. The former had nephritis at the age of 14, but has now a normal blood pressure and no albuminuria. A sister aged 10, and two brothers aged 6 and 1\(\frac{1}{2}\) are well, and have no signs of vascular or renal disease. No history was forthcoming of any family tendency to vascular disease at an early age.

On admission the child had several short fits. She remained unconscious. She was pale and looked ill. There was no oedema. The heart was overacting, with the apex beat just outside the nipple line. The first sound at the mitral was loud. The second sound at all areas
was accentuated, and specially so at the aortic. The child looked like a case of meningitis. She lay with her back arched and her legs curled up and was restless and resisted handling. There was slight rigidity of the neck. There was hemiplegia of left arm and leg. The right plantar reflex was flexor, the left was extensor. No clonus was elicited. Both knee jerks were exaggerated, the left being greater than the right. On lumbar puncture, the cerebro-spinal fluid was under pressure, and showed an increase in globulin, and a fine coagulum developed on standing. The cells numbered 3 per c.mm., and no micro-organisms were found. The temperature was 102.8°, and the pulse rate 150. Nothing abnormal was found in the lungs or abdomen.

Course. — The following morning the child was quieter. The blood pressure was estimated, and found to be 160/120. The fundi of the eyes were examined and showed a hypertensive retinopathy. The report stated that the edges of the discs were blurred from slight swelling, the retinal arteries were tortuous, and the veins engorged. Several white woolly patches were seen in both eyes, and small white dots arranged in lines radiating from each macula. Numerous scattered small hemorrhages were seen in both eyes and in the right there were coarse flame hemorrhages among the superior temporal vessels, not far from the disc.

As the child was still unconscious hypertonic saline was given intravenously, after which she became less restless and began to take fluids by mouth. The temperature came down steadily, as did the pulse rate, and by the morning of the second day after admission the girl was conscious and could see, and had regained power in the left arm and leg. Thereafter she steadily improved. The urine contained rather more than a trace of albumin, no sugar, and a few pus cells, but no red blood cells and no casts. The albumin decreased to a mere trace within a fortnight. The specific gravity during the first month varied in different samples from 1010 to 1025. There was no upset of the normal day to night ratio, and no nocturnal frequency of micturition. The blood urea on February 4th, despite occasional vomiting and some dehydration, was only 46 mgm. per cent. Cerebrospinal fluid was again withdrawn on February 9th; it was not under pressure, and was normal as regards cells and protein. The urea of this fluid was 29 mgm. per cent.

The child weighed 33 lb. and was 44½ in. in height. She was thin and pale. There were no clinical or radiographic signs of rickets. The X-ray examination of the skull showed a normal sella turcica. The tonsils were ragged, and the tonsillar glands slightly enlarged. There was a catarrhal condition of the nose, but no chronic sinus suppuration. Throat and nose swabs gave only the usual catarrhal organisms. No diphtheria bacilli were found on repeated examination. The Wassermann reaction of the blood was negative.

The urine was kept alkaline with potassium citrate, given in five doses daily of 25 grn. each. The bowels were kept well open. On February 15th, the blood urea was 42 mgm. per cent. She went on improving for five weeks, although the blood pressure remained around 160/120. The urine remained as before, and there was morning headache from time to time.

Then in the first week of March came the next series of dramatic symptoms. Sickness and vomiting occurred every morning. On March 6th, the frontal headache was very severe in the morning, and the child was very sick. Later in the day she had four convulsions within an hour, and became unconscious. Lumbar puncture yielded fluid under great pressure. It was colourless, and the globulin was increased. The urea of the fluid was 50 mgm. per cent. The cells were not increased, and no micro-organisms were found. The temperature was normal. Hypertonic salines were given. She remained semi-conscious for forty-eight hours, and did not appear to see. She vomited often, and the temperature rose to 102°. It fell steadily to normal next day, and the child improved slowly. The urine contained albumin, but no blood and no casts. The systolic blood pressure was 160; it was impossible to estimate the diastolic pressure accurately. The interesting point was noted then that punctate hemorrhages were produced in the arm by the armlet of the sphygmomanometer. The blood urea on March 7th was 86 mgm. per cent. The eye report then read: 'Discs still show blurring of the edges. There are hemorrhages as before and radiating dots round the macula, but no woolly patches can be seen.' On March 10th the urine became red, and deposit showed red blood cells, a few pus cells, and blood casts for a few days.

Unfortunately, on March 12th virulent diphtheria bacilli were obtained from the nose and the child had to be transferred to a fever hospital, where she remained for five weeks. After this she remained at home for about two months, in fair health, but with frequent headaches and vomiting.
RE-ADMISSION.—On June 16th she was re-admitted to hospital. She was still pale, poorly nourished, and weighed 35 lb. The blood pressure was 210/150. The fundi of the eyes showed swelling of the discs, radiating dots around the macule, sclerosis of the vessels and a few small haemorrhages. The blood urea was 48 mgm. per cent. The urine varied in specific gravity from 1010 to 1020; it contained 0-1 to 0-2 per cent. of albumin, and the deposit showed a few red blood cells and pus cells, and B. coli, but no casts. The serum calcium was 10-2 mgm. per cent., and the plasma phosphates 4-2 mgm. per cent. The blood continued in the urine for a week. She continued to have, almost every morning, a severe headache, usually followed by vomiting, and for the next month was otherwise in fair health. Eye examination on July 17th showed the retinal haemorrhages to have disappeared, and the blurring of the discs to be less marked. The radiating dots at the macule remained.

On July 20th came the next alarming group of symptoms. Along with severe and continued headache came absolute loss of vision. After seven hours of this she had a convulsion and became unconscious. She remained so for 24 hours, and during this time had five fits of a generalized type. Lumbar puncture was done, and the fluid, which was under pressure, contained a moderate increase in globulin, but no increase in cells. The child improved steadily on the third day of this acute phase, the temperature became normal, consciousness returned, but it was only the following day that the child could see. On July 24th and 25th blood and a little mucus appeared in the stools, and no pathogenic micro-organisms were found.

The child continued to have headache and sickness every other day. On August 29th, the blood urea was 40 mgm. per cent. and the blood pressure 220/150. The daily amounts of urine during the illness varied from 17 to 42 oz., and the specific gravity from 1008 to 1024. There was no nocturnal frequency. A blood count on September 15th showed 90 per cent. haemoglobin, 4,600,000 red cells, and 7,200 white cells. There was nothing of note in the character of the cells.

A urea concentration test, after 10 grm. of urea, showed the following percentages of urea in the urine at hourly intervals:—0-9, 0-7, 1-0, and 0-9.

The next episode of note in the case came on September 27th, when complete paralysis of the external rectus muscle of the left eye was observed when the ward sister came on duty in the morning. At this time the nervous system was otherwise normal, and the eye report was: 'Retinal vessels are tortuous in places with here and there increased brightness of light reflex. Right optic disc is more blurred than it was six weeks previously. Small white spots are seen at nasal side of right disc, and at right macula. The superior temporal vessels disappear a short distance from the optic disc in a red grey region. The left optic disc is paler and clearer than the right. White spots are seen around the macula. No haemorrhages are seen in either eye.' The paralysis of the left external rectus muscle took about eight weeks to clear up.

Except for headaches the child remained fairly well during October and most of November, the systolic pressure being around 220 and the diastolic around 150. Then on November 24th she complained of loss of sight, became unconscious, and that day had six generalized convulsions. Lumbar puncture yielded a fluid under pressure, colourless, with a moderate increase in globulin, and no increase in cells. Its urea content was 57 mgm. per cent. The child remained semi-conscious for forty-eight hours, with staring eyes, and occasional vomiting. The systolic pressure during the attack was 230 to 240.

Improvement after this attack of unconsciousness was slow, and the headaches became more frequent. The urine albumin increased to 0-3 per cent., and during the first week of December the urine contained red blood cells, but no casts. Fresh haemorrhages were noted in the retina in December. The highest specific gravities in the 24-hour samples of urine in the twelve weeks preceding death were in order: 1012, 1022, 1015, 1018, 1020, 1022, 1020, 1022, 1018, 1015, 1012 and 1015.

On December 13th, she had what appeared to be an attack of angina pectoris, and after it said she could hardly breathe, as there was a weight pressing on her chest. On the 16th she became semi-conscious, and had a fit with movements of the right side of body, and nystagmoid jerking of the eyes to the right. Later that day she had two more fits, one generalized and one with movements of the left side. The systolic pressure was then 250, and the diastolic probably 150. She vomited food repeatedly. The cerebrospinal fluid was under pressure, its globulin was again increased, there were 12 cells per c.mm., and the urea content was 120 mgm. per cent. The apex beat of the heart was by this time half an inch outside the nipple line.
The child went steadily downhill after this last acute phase. She was never fully conscious, and was at times pale and collapsed. By the 19th December, the blood pressure had fallen to 170/140, and edema appeared in the legs. The tongue became foul and coated. That day breathing became laboured and signs of pneumonia appeared at the left base, and the temperature reached 101.6°. By the 24th the apex beat was 1½ in. outside the nipple line. There were tremors from time to time, but no convulsions, and no paralysis. Death took place on the 25th December, apparently from uraemia, pneumonia and cardiac failure.

Post-mortem report.

Post mortem on December 25th. Permission for abdominal incision only. The stomach was of normal size. Its mucosa was slightly inflamed and covered with a film of blood-stained mucus. No erosions or ulcers. Duodenum healthy. Small and large intestines normal. Appendix healthy. Mesentery of small intestine showed several small caseous glands. No naked eye alterations in the mesenteric vessels. Spleen weighed 105 grm. and showed no changes on surface or on section, and there were no visible changes in the vessels. Pancreas normal. Suprarenals were normal in size and appearance. Liver, pale, weighing 895 grm., showed fatty change, and no naked eye alterations in its vessels. Gall-bladder normal, and bile ducts patent. Uterus, tubes and ovaries healthy.

There was a moderate amount of fluid in the peritoneal cavity, and in both pleural cavities, but no excess in the pericardial sac.

Both lungs were congested. The lower lobe of the left lung was completely consolidated and showed the grey hepatization of lobar pneumonia. There were some petechial haemorrhages into the pleura over the consolidated lobe. The pericardium was healthy. The right auricle was dilated. There was slight dilatation and hypertrophy of the right ventricle. The tricuspid and pulmonary valves were healthy. The left auricle was very definitely hypertrophied. There was great hypertrophy and moderate dilatation of the left ventricle. There was some uniform arteriosclerotic thickening of all the larger branches of the coronary arteries. The mitral cusps were healthy, save for one or two superficial yellow flecks of early atheroma on the aortic aspect of the aortic leaflet of the valve. There was a trace of atheromatous thickening of the extreme bases of the aortic cusps. The ascending aorta was slightly dilated and showed a little superficial fatty change. There was some atheroma of the abdominal aorta, mostly localized to a strip, about an inch wide, involving the whole circumference at the middle of the aorta.

Kidneys.—Left kidney much reduced in size and weighing 34 grm. Very distorted contour, the kidney being much narrower opposite the hilum. Capsule not thickened and stripped fairly readily. Outer surface pale in colour, almost smooth, but on close examination showed a number of very fine red and evidently vascular depressions. The narrowed part opposite the hilum was smoothly depressed and had the appearance of vascular connective tissue. The cut surface showed extreme narrowing of the cortex, which in places, e.g., opposite the hilum, was little more than 1 mm. thick. Surface of cortex pale. At one point in cortex there was a small cyst 3 mm. in diameter. The medulla was deeply congested, reduced in size, and its demarcation from the cortex remained clear. The tips of the pyramids projected normally into the pelvis, but a few were flattened. The pelvis of the ureter was of normal size, but there were petechial haemorrhages into its mucosa. The tips of the pyramids were slightly haemorrhagic. There was no increase in the peri-pelvic fat.

Right kidney of about normal size, and weighed 84 grm. Capsule not thickened, and stripped readily, leaving a practically smooth, pale surface studded with numerous petechial haemorrhages. The cut surface showed a cortex of normal width and pale and blotchy in colour. At its upper pole was an irregular wedge of a dead-white colour and apparently partly necrotic. The medulla was well demarcated from the cortex. There was again a haemorrhagic condition of the tips of the pyramids.

In neither kidney was there obvious prominence of the vessels on the cut surface. The ureters were of normal calibre. There was no obstruction to the flow from either ureter into the bladder, nor in the urethra, and the bladder wall was not hypertrophied. There was no cystitis, but the trigone was congested and showed petechial haemorrhages.
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MICROSCOPIC EXAMINATION.—LEFT KIDNEY. (A). Section of depressed area opposite hilus. The vessels, medulla, and cortex will be described in order.

Vessels. The larger of the arteries in the section, middle-sized arteries, showed but one change, a hypertrophy of the media, sometimes slight, at other places considerable, but always present. There were no fatty or other degenerative changes, and no inflammatory change. The intima and adventitia were unaltered, and the elastic tissue was normal in distribution, there being only slight thickening of the internal and external lamina.

In the arterioles, and arteries of slightly larger calibre, diverse severe changes were found. Transitions between the different appearances found were so numerous and so close-set as to establish the view that they represented successive stages of the same lesion. Such changes were:—(1) Some vessels showed no more than a thickening of their wall, and narrowing of the lumen, due entirely to an extreme hypertrophy of the media. (2) In other vessels similar medial changes were present, but, in addition, a hyaline and fatty thickening of the intima, without cells, had taken place round a part or whole of the circumference. Adventitial changes were absent. (3) In many vessels, the lumen was completely closed by a marked acellular hyaline fatty thickening of the intima. Outside this, in the larger vessels of this group, there was a thinned internal elastic lamina, and the media consisted of just a few muscle-cells plastered over the thickened intima. This third type of change was generally more fully developed in the actual arterioles, and the severer grades were particularly common in atrophying areas of cortex.

The veins did not show appreciable alteration. The capillaries everywhere showed marked congestion and over-distension, the intertubular plexus, the capillaries in atrophied cortex, and capillaries in medulla. The walls showed no obvious pathological change, but extravasated red blood corpuscles could be found everywhere.

Medulla. The transitional epithelium covering the pelvis was normal in the portion shown in the section. The tips of the pyramids showed little beyond numerous extravasated red cells. The cells of the interstitium, as is normal here, were scanty, but there were occasional foci of small round cells. Capillaries were congested, and arterioles as above. The lower ends of some collecting tubules had been partly destroyed by the haemorrhage, and the lumina were filled with blood. Higher up in the pyramids, the collecting tubules were fairly normal, save that they were rather dilated and some contained homogeneous material.

Cortex. The site of entry of vessels between pyramids, and the inter-pyramidal cortex just above that, showed practically nothing but the leash of entering vessels and their branches,
along with a considerable increase of connective tissue with few cells. The number and variety of size of arterial vessels in this small area devoid of tubules, showed that it represented nevertheless most of the inter-pyramidal cortex which had been wiped out by the withering of the vascular tree. The vascular changes varied with the size of the arteries and have already been detailed.

The remainder of the cortex showed one of two appearances. First, part of it, a layer consisting mostly of the deeper part of the superficial cortex, was clearly hyperplastic. The convoluted tubules were enlarged, and lined by swollen epithelium, which was undergoing granular degeneration. There was only a trace of collagenous increase in the interstitium with no infiltrating cells. Many glomeruli were enlarged. Recent parietal capsular epithelial proliferation was present only in one or two tufts. Some glomeruli were partly adherent to their capsules, and one or two were necrotic. Secondly, the superficial layer of the superficial cortex was composed of atrophying parenchyma and glomeruli. The latter were small, hyaline, and close-set. Intimal changes were generally present in the arterioles. There was only a little increase of connective tissue separating the atrophied glomeruli and tubules, and only few cells.

FIG. 2. Section (high power) of glomerulus, showing sclerosis of afferent arteriole.

(B). Section at upper pole. This section showed a fairly thick cortical mantle. Description of the cortex:

Vessels. The types of change were identical with those described in the first section. No normal arteries or arterioles were seen, and as before, the changes varied with the size of the vessels.

Glomeruli. Only one or two scattered hyaline glomeruli were seen. Many of the remaining ones were enlarged. Hardly any were adherent to their capsules. Occasionally glomeruli were encountered in which the tuft tissue had undergone almost complete necrosis, the capsule containing numerous red cells, and also degenerating endothelial cells. There were no proofs of inflammatory factors in such necrosis.

Tubules. Some patches of convoluted tubules showed great hyperplasia, and granular degeneration. Some tubules were blocked by masses of desquamated cells; others were atrophied, with flat lining epithelium and varying degrees of dilatation of the lumen.

Interstitial. There was a very slight increase amid hyperplastic tubules, and a little more amid atrophied ones. Generally there were few cells in this increase. Capillaries were everywhere congested, and there was extravasation of a few red blood cells into the interstitium, and into a few of the tubules.
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RIGHT KIDNEY. (A). Section distant from the specially degenerated upper pole area. Vessels. These showed the same diversity of changes as in the other kidney. In particular, all the arterioles were seriously altered.

Medulla. Some tubules were fatty, but the most distinct changes were marked capillary and venous congestion, with capillary hemorrhages, and occasional round-celled infiltration.

Cortex. Only one or two glomeruli were hyaline. The majority were rather large, and showed no epithelial proliferation. A few whole tufts were completely necrotic. The majority of glomeruli showed only slight changes. Hyperplastic and degenerated convoluted tubules were predominant. Atrophied tubules, such as were described in the other kidney, were also present, but in small numbers. There was more fatty change than in the tubules of the other kidney. Some tubules were completely necrotic.

The interstitium showed practically no increase. The capillaries were again congested, and there were occasional capillary hemorrhages into the interstitium.

(B). Section of degenerated tissue at upper pole. The degenerative changes were marked in both glomeruli and tubules. About one-half of the glomeruli showed fatty or necrotic changes. Many of the hyperplastic tubules were fatty, most were necrotic.

LIVER.—There was no cellular infiltration of the portal tracts or under the capsule. Most of the arterioles showed a little medial hypertrophy but no further change. None showed appreciable intimal change. There was extensive parenchymatous fatty change, of irregular distribution, although chiefly peripheral and central.

ABDOMINAL AORTA.—The naked-eye changes seen were those of pure nodular atheroma.

SPLEEN.—The Malpighian bodies were of normal size. Practically every central artery and its arteriolar branches showed marked thickening and narrowing, often apparently amounting to closure. The thickening was usually entirely due to a hyaline thickening of intima. Slightly larger arteries in trabeculae sometimes showed a trace of similar intimal thickening, but the usual change was slight medial hypertrophy. The internal elastic lamina was not thickened.

HEART.—There were a few degenerate fibres, but most were healthy: no abnormal cellular infiltrations, and no fibroid changes. The coronary arteries showed medial hypertrophy. The descending branch of the left coronary showed some hypertrophy of the media, and also moderate uniform fibrous thickening of the intima with few cells and much elastic tissue. Slight medial hypertrophy of some arterioles, although most were healthy.

LEFT LUNG.—The lower lobe showed lobar pneumonia, early grey hepatization. No abnormalities of the vessels of the lung.

BLADDER.—The smallest arteries and arterioles, both in muscle and mucosa, showed medial hypertrophy, and in some arterioles slight hyaline thickening of the intima.

SUPRARENALS.—There was no change in the parenchyma of either cortex or medulla, but in the vessels there was a considerable hyaline thickening, sometimes leading almost to obliteration of the lumen. This was entirely an intimal thickening, the media having completely disappeared. The vessel walls were almost structureless.

HEAD OF PANCREAS.—The tissue of pancreas and islets was healthy. The arterioles practically all showed changes, hyaline thickening of intima with no great narrowing of lumen, slight hyalinization of media, and slight hypertrophy of media. The islets were over numerous(?).

CELIAC AXIS.—Hypertrophy of media: no intimal or adventitial change.

VOLUNTARY MUSCLE (left rectus abdominis).—Muscle fibres healthy. Minimal hyaline thickening of intims of some arterioles, others not altered. The arterioles in the fat within the muscle sheath showed slightly greater change, greater intimal thickening. The arteries had only medial hypertrophy.

Summary of autopsy—(a) The typical arteriolar changes of essential hypertension in all the organs examined, except the lungs. In order of severity of changes, the organs were kidneys, spleen, suprarenals, bladder, liver, voluntary and heart muscle. (b) Hypertrophy of large arteries, verified in coronaries, renal arteries and celiac axis. (c) Atheroma of aorta. (d) Secondary contraction of left kidney. Arteriolo-sclerotic ischaemic atrophies, degenerations and necroses in both kidneys. (e) No nephritic changes. (f) Lobar pneumonia.
Summary.

A case of malignant hypertension is described in a girl of eight years old. The autopsy findings are described in detail.

It will be noted that headaches had been complained of for a number of years, and had persisted to the end. The period of the malignant phase lasted at least a year, and was punctuated by bouts of alarming symptoms: convulsions, cerebral amaurosis, unconsciousness, transient hemiplegia, and paralysis of a sixth cranial nerve. Some renal impairment was present during the period under observation, but only at the very end did it become a pronounced feature. The specific gravity of the urine never became fixed. Blood was passed in the urine from time to time.

The blood pressure rose steadily, and was specially high in at least two of the series of acute exacerbations. The typical picture of hypertensive retinopathy was present all the time, with macular exudates, neuro-retinitis, sclerosis of retinal vessels, and haemorrhages, while woolly patches were not a feature except at the beginning of the observations. During the unconscious periods, the cerebrospinal fluid was under increased pressure, and on each occasion on which it was examined, it contained an increase in globulin with no increase in cells. In the intervals the fluid was normal.

The clinical diagnosis of malignant hypertension was confirmed at autopsy. This revealed the typical arteriolar changes of essential hypertension, and the renal arteriolo-sclerotic atrophies and necroses of the malignant phase of the disease.

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