TUMOURS OF THE SYMPATHETIC NERVOUS SYSTEM IN CHILDREN

A STUDY OF TWENTY-FIVE CASES

BY

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Pepper⁸, in 1901, in his paper entitled 'A study of malignant suprarenal tumours in children' described six cases, all of which proved fatal during the first three months of life. In each there was a massive infiltration of the liver with metastases, the source of which was a growth in one of the suprarenal bodies. This combination of primary suprarenal tumour and secondary deposit in the liver has since come to be known as the Pepper syndrome. The first reference to bony metastases arising from a primary suprarenal tumour in a child was by Cohn⁴ who reported a child who died at the age of nine months. The autopsy revealed a large tumour of the left suprarenal and metastases in the skull, ribs, liver, kidney and ovary. But it was not until 1907 that a clear account of this syndrome was given by Robert Hutchison⁶ in his paper entitled 'On suprarenal sarcoma in children with metastases in the skull.' He regarded the tumours arising from the suprarenals as sarcomata. Four years later Frew⁵ published a further series of twenty-nine cases, thirteen of which were patients in the Hospital for Sick Children, Great Ormond Street. Since then no further contribution to the literature on this subject has appeared from this hospital and as we have been able to verify pathologically twenty-five cases* the results seem worthy of record.

Although Wright¹⁴ in 1910 pointed out that these tumours originated from nervous tissue and were not sarcomata, it is only during the last two decades that advances in technical methods have permitted their more exact

* Two cases were reported in the Proc. Roy. Soc. Med. (Children's Section), both by R. Lightwood, case 14 in 1932 and case 12 in 1933.

histological differentiation. Many cases of 'retroperitoneal sarcoma' have thus been identified as tumours of the sympathetic nervous system. Several of the present series, for example, were originally given this diagnosis and only more detailed investigation of the material revealed their true nature.

As Scott, Oliver and Oliver⁹ have recently reviewed the literature and have analyzed 158 cases it is proposed to refer only to some of the more important papers. The most exhaustive study made within the last few years in this country is that of Blacklock³, who reported on eighteen tumours of the sympathetic system in children, twelve of which were examined pathologically. Sixteen were derived from the adrenal (nine from the right, seven from the left), one from the abdominal sympathetic ganglia, and one which arose in the left superior cervical ganglion. Blacklock maintained that pathologically there was no justification for the division of these tumours into the Pepper and Hutchison types, though as a clinical syndrome Hutchison's description should stand. The conclusions Blacklock came to regarding their pathology will be discussed later. In the series of seventeen cases reported by Askin and Geschickter¹, there were several in which secondary deposits were found in the bones as well as in the liver and other abdominal viscera. Such a combination of the Hutchison and Pepper syndromes was also found in the case reported by Sturtevant and Kelly¹². Lewis and Geschickter⁷ studied forty cases, of which eight were ganglioneuromata. Half of these forty cases were in children under the age of three years. The Hutchison type occurred in the older children whose average age was six years.

General remarks

The series of twenty-five cases described in this paper covered a period of sixteen years (1921 to 1936 inclusive). Six of the autopsies were performed by one of us (G. H. N.). The rest were found in the post-mortem records often under other names. These twenty-five cases represented 0.9 per cent. of the total autopsies during this period.

Fifteen were males and ten females. The age incidence is given in table 1. From this it is seen that all but two of the girls were under the age of two whereas in the boys the highest incidence was in the third to fifth year. Four of the twenty-five patients were over the age of five at death; three of these were males.

Twenty-four of the tumours were abdominal. One arose from sympathetic tissue in the thorax. In view of its rarity a separate description of this tumour will be given.

An analysis of the early symptoms is as follows:—

Enlargement of the abdomen	9 cases.
Pain in the legs or limping	8 cases.
Pallor, wasting, listlessness	4 cases.
(apart from other symptoms)	
Swelling on the head	3 cases.

These were the symptoms that brought the child to hospital. In no case did proptosis of an eye occur early in the disease though it often appeared later. It is interesting to note that pain in the legs or limping

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occurred almost as frequently as the enlargement of the abdomen from the rapidly growing intra-abdominal tumour. In the former group there was one patient who had a swelling in the upper part of the right thigh; in the others no clinical sign of a secondary deposit was present. Half of these eight patients were x-rayed and in these there were metastases in one or other of the long bones in the lower limbs. Tidswell and Sear¹³ remarked on the frequency of this symptom of pain in the lower limbs, for it was present in every one of their eight cases.

Metastases are always more advanced in the lower than in the upper limbs. But the pain is probably caused not by deposits in the medulla of the bone but by elevation of the periosteum by tumour cells (see fig. 8). The same kind of sub-periosteal infiltration may occur in leukaemia. (A good description of the x-ray appearances and pathology was given by

TABLE 1
AGE AND SEX INCIDENCE

	0-1 YR.	1-2 YR.	2-3 YR.	3-4 YR.	4-5 YR.	5-6 YR.	6-7 YR.	7-8 YR.
Males	3	1	2	3	3	1	1	1
Females	3	5	0	1	0	0	1	0
Total	6	6	2	4	3	1	2	1

Snelling, Brown and Erb¹¹.) The pain and tenderness in one of the present series of cases was so severe that a diagnosis of acute osteomyelitis was made.

In eight cases there was proptosis of one or both eyeballs at some time during the course of the disease and in eleven there were tumours on the head. This may be compared with the autopsy findings which showed that thirteen of the cases had bony metastases (only five of these were examples of the 'pure' Hutchison syndrome).

In eleven patients the liver was enlarged, in some very greatly. In only three of these were there swellings on the head.

A moderate degree of fever was present in three-quarters of the patients. In a third of the total number it was periodic in type, the temperature being raised for a few days at a time. In one the periods resembled the Pel-Ebstein curve sometimes seen in lymphadenoma.

In twelve patients the blood was examined. A moderate anaemia was present in nine of these; in the remaining three, the anaemia was severe, one having a red cell count of 1,400,000 per c.mm. and haemoglobin of 20 per cent. In seven of the anaemic patients the colour index was considerably below one. Of the remaining two, one had a colour index slightly above and the other slightly below unity. Three patients had a raised reticulocyte count—3 to 5 per cent., and one had many normoblasts and megaloblasts in the circulating blood. In none were there any significant changes in the

leucocytes nor were there any immature leucocytic cells in the peripheral blood.

Anaemia is commonly associated with malignant growths but in the neuroblastomata an important factor is the extensive haemorrhages into the tumours which so often occurs. A leuco-erythroblastic anaemia is occasionally met with. In these patients immature leucocytes and red cells appear in the peripheral blood. One of the patients in this series had a decided erythroblastosis. No bony changes were visible in the x-rays of this patient; nor were any to be seen in the case shown by Hart* at the Royal Society of Medicine, Children's Section in May, 1937, although there was a severe anaemia with large numbers of immature white and red cells in the blood. The cause of this leuco-erythroblastosis could not be a massive infiltration of the bone-marrow with secondary deposits as it is in carcinomatosis of bones. It is probably caused by a generalized cellular infiltration of the bone-marrow with malignant cells. If this were so x-ray changes would not be expected. The normal bone-marrow cells would, however, be stimulated excessively and many immature cells would appear in the circulating blood.

When metastases are present in the skull the x-ray shows diffuse mottling and separation of the sutures. These changes are well seen in fig. 10. The same mottled appearance also occurs in the long bones. In these there may be a characteristic elevation of the periosteum resembling what is sometimes seen in leukaemia (fig. 9). It is due to subperiosteal infiltration with tumour cells and is probably the cause of the limb pains which occur in both these diseases. Occasionally in the skull and long bones a striking spiculation may be observed (fig. 9). Less than a third of the present patients were x-rayed and in only the more recent ones were the long bones included. The skull was normal in most cases x-rayed but two showed well-marked mottling. In four there were secondary deposits in the bones of the lower limbs.

The prognosis is hopeless, for by the time the patient comes under observation the tumour is inoperable, either by reason of its great size or because of the presence of secondary deposits. The course of the disease is a relatively short one. Only two patients survived for more than six months from the onset of the symptoms, ten lived from three to six months and twelve died in less than three months from the first symptom. Askin and Geschickter¹ found that the average duration of symptoms before observation in their series was six months, though in half of the patients it was one month or less.

Many cases of neuroblastoma are only recognized at autopsy and even then their true nature may be missed. In the present series they have been found under other diagnoses such as retroperitoneal sarcoma, Wilms' tumour and sarcoma of the liver. The incidence of neuroblastoma and Wilms' tumour is about the same. The former, however,

* Reported in the *Lancet*, 1937, i, 1458.

remains localized for a long time. Metastases appear late and spare the bones. When, therefore, an abdominal tumour is found in early life in association with a tumour on the head or secondary deposits in the long bones it is almost certainly a neuroblastoma. In young babies, the disease often takes the form of an extreme enlargement of the liver. Such cases, frequently diagnosed as sarcoma of the liver, are in reality sympathetic suprarenal tumours of the Pepper type, the primary growth being small and the liver massively infiltrated with metastases (see fig. 4).

Morbid anatomy

It has already been mentioned that some of these cases had been misdiagnosed as retroperitoneal sarcomata, the reason being that the tumour occupied the whole of the posterior part of the abdomen, and did not seem to be arising from either suprarenal. An analysis of the cases showed that this variety is by no means uncommon. In four cases, despite the presence of an enormous mass, neither suprarenal was involved macroscopically or microscopically in the growth. We assumed that in these cases the origin of the tumour was not from the suprarenal but from the abdominal sympathetic chain. In others, one or other suprarenal was definitely included in the tumour mass the origin of which was probably from the sympathetic tissue of that organ (fig. 1).

It is customary to classify these tumours into the Hutchison and Pepper types, but Scott et al.⁹, Blacklock³, Askin and Geschickter¹ and others have pointed out that in many cases no such clear distinction can be drawn. This is borne out by the present figures. While five of the cases presented solely the features which Hutchison described, and five those of the Pepper syndrome, in no less than nine there were both bony and visceral metastases. In four cases only the kidney and the adjacent lymph glands were involved, and in one of the two ganglioneuromata there were no metastases.

Lewis and Geschickter⁷ stated that the Hutchison syndrome was commoner in older children, the average age in their series being over six years. It was found, however, in the present series that there was little difference in age distribution between the Hutchison and Pepper types, the average age for the former being three-and-a-half years and for the latter slightly under two-and-a-half years. Whilst, generally speaking, bony metastases occurred in older children yet they were found frequently in the very young child. The average age for the 'mixed' type was two years and eight months.

Scott et al. in their analysis of 158 cases did not discover any predilection of the growth for one side, nor could they demonstrate any relationship between the side of origin and the site of metastases. This series confirms these observations. The tumours arose with equal frequency from the two sides, eight arising from the right suprarenal and eight from the left. In three, both suprarenals were involved; in one the state of the suprarenals was not mentioned.

FIG. 1.

CASE 2.—Large retroperitoneal mass. The right kidney is almost completely replaced by growth. A few small secondary deposits are present in the liver.

FIG. 2.

CASE 7.—The tumour shows cystic degeneration. The kidney is pressed on but not invaded.

FIG. 3.

CASE 4.—Anterior half of tumour showing primary growth in right suprarenal. Left suprarenal normal. Note the large mass between the kidneys and the hydronephrosis of the right kidney due to obstruction of the ureter.

FIG. 4.

CASE 10.—Large growth in right suprarenal, and a smaller one in the left. The liver is studded with metastases (Pepper syndrome).

FIG. 5.

CASE 15.—Thoracic tumour. The arrow points to the place where the cord is compressed by the growth.

FIG. 6.

CASE 15.—Thoracic tumour. A. The main part of the tumour. B. The compressed right upper lobe. C. The right lower lobe which was invaded by growth.

FIG. 7.

CASE 5.—Large secondary deposit in the femur. The x-ray of the same case at an earlier stage is shown in fig. 9.

FIG. 8.

CASE 7.—Humerus showing raising of the periosteum. Deposits are also present in the bone marrow.

FIG. 9.

CASE 5.—Elevation of the periosteum of both femora. Spiculation is indicated by the arrow.

FIG. 10.

CASE 14.—The x-ray shows diffuse mottling of the skull and separation of the sutures.

Distribution of visceral metastases

Besides the metastases which were present in the liver in thirteen cases, macroscopic deposits were found in many other viscera. In five cases intrapulmonary metastases were seen, but the pleura was not involved. This contrasts with Blacklock's findings, for in two out of four of his cases with thoracic deposits, there was a malignant pleurisy with a haemorrhagic effusion. Blacklock also found a surprisingly large number of metastases in the pancreas—in seven out of eleven cases. We were able to trace only two such metastases in the present series of twenty-five. It is generally recognized that the kidney is pressed upon rather than invaded and we were surprised to find that in a third of the cases a spread to the kidney had occurred (see fig. 1). Rare sites for metastases were the intestine (two cases—one in the caecum and the other in the colon) and the ovary (one case only). There was one example of a metastasis in the brain. This was

in the parietal lobe adjacent to a large haemorrhagic deposit in the dura (case 5).

Histology

Although the characteristic structure of tumours of the sympathetic system arising from the adrenal medulla had been recognized as long ago as 1864 by Virchow, it was not until 1910 that Wright¹⁴, by comparison with the adrenals of embryos, was able to show the resemblance between the arrangement of the tumour cells and that of foetal adrenal medulla and sympathetic ganglia. He was therefore the pioneer of a classification for these tumours based on their histology. Since then, a number of classifications, with many sub-divisions, most of them complicated and unwieldy, have been devised. These are not quoted as they are given in detail in the historical review of Scott et al⁹. Whilst it is desirable that a terminology should be used by which tumours consisting of a primitive type of cell can be distinguished from those in which mature cell types predominate, pure cell types occur only rarely in these tumours and the cellular form may vary greatly from one part of the tumour to the other. Consequently it is strongly felt that unwieldy and complicated classifications should be abandoned in favour of a simplified one which embraces the main cellular types encountered. A brief description of the essential features of the sympathetic nervous system is necessary in order to present the simple classification which Bielschowsky² evolved and which we have adopted here.

FIG. 11.

General view of section from case 20 to show cells arranged in columns separated by strands of fibrous tissue.
Stain: haematoxylin and Van Gieson. $\times 100$.

FIG. 12.

Low-power photograph of section from case 22. Four pseudo-rosettes are seen, two of them adjacent to each other. There is much variation in the size and shape of the cells.
Stain: haematoxylin and eosin. $\times 100$.

FIG. 13.

High-power view of pseudo-rosette (case 23). The fibrillar material in the centre of the rosette is formed by processes arising from the cytoplasm of the innermost layer of cells.
Stain: haematoxylin and eosin. $\times 400$.

FIG. 14.

Section of ganglioneuroma (case 16). Three large cells resembling sympathetic nerve cells are present in the field. Smaller, less differentiated cells are also to be seen.
Stain: haematoxylin and eosin. $\times 400$.

The parent cell of the sympathetic nervous system is the sympathogonia, a small rounded cell resembling a lymphocyte, with a densely staining nucleus and only a small ring of cytoplasm in which no processes can be identified. This cell is multipotential and gives rise to both ganglion cells and to the chromaffin cells. The next stage in development is the sympathoblast, a larger, more polygonal shaped cell possessing a considerable amount of cytoplasm in which fine fibrils may be seen. The cytoplasm is prolonged at one end of the cell body into a short process. The nucleus is large and the chromatin is finely divided, giving a vesicular appearance to the nucleus. The adult multipolar ganglion cell with intracellular fibrils and Nissl granules in the cytoplasm represents the final stage in development. Corresponding approximately to these three stages in development, though often no arbitrary line can be drawn, there may occur three varieties of tumour of the sympathetic system and on this basis the simplest classification would be:—

1. Tumours consisting of completely undifferentiated cells. (Sympathogoniomata.)
2. Tumours in which the predominating cell resembles a sympathoblast. (Sympathoblastoma.)

(This tumour is extremely rare. Bielschowsky² was able to find only one example in the literature.)

3. Tumours which contain mature ganglion cells. (Ganglioneuromata.)

It is common to find cells resembling both sympathogoniomas and sympathoblasts in one tumour and it is this intermediate group which has caused such confusion in nomenclature. No name for it has received general acceptance. According to the above classification the accurate term for it would be 'sympathogonioblastoma' and this is the term which we propose to adopt.

In the present series there were six examples of sympathogoniomata, sixteen of the 'mixed' type of tumour, the sympathogonioblastoma, none of a true sympathoblastoma, and two ganglioneuromata. In one case no sections were available for study. Two of the sympathogoniomata occurred in the youngest children in the series, aged three and five months respectively. This was not surprising as it is generally accepted that the most primitive cellular types occur more frequently in younger children. Nevertheless, one example of this type of tumour was in one of the oldest children in the series, aged three-and-a-half years (case 14).

Although the individual cells in the sympathogoniomata all showed the same characteristics, namely, densely staining nuclei, little cytoplasm and many mitotic figures, their arrangement varied considerably. In some cases the cells were closely packed together in dense masses with no connective tissue separating them, giving a picture resembling a small round-celled sarcoma. In others there was a definite alveolar arrangement, the cells being grouped into alveoli, separated from each other by strands of firm fibrous tissue (fig. 11). In none of the sympathogoniomata were any pseudo-rosettes observed. These were found only in the slightly more differentiated sympathogonioblastomata of which there were sixteen examples. The microscopical picture of these tumours varied greatly. Haemorrhage was a feature of nearly every case and in some there was difficulty in making out the histological details. When autopsy material was available, as in the more recent cases, fresh sections were made from less haemorrhagic and degenerated parts of the tumours. In some sections in this group the cells contained much cytoplasm and were arranged in alveolar formation with strands of fibrous tissue separating the alveoli. In others, in which the cellular types were intimately mixed the cells were loosely packed, showed no orderly arrangement, but had strands of connective tissue between irregular masses of cells. We were able to demonstrate rosettes in ten cases, though usually many sections had to be examined before a few rosettes were discovered. We were unable to demonstrate fibrils in the centre of the rosettes by Gros's silver method, but they were easily identifiable by van Gieson's counterstain, with which they stained a buff colour, and by Mallory's phosphotungstic acid haematoxylin (fig. 13). A perivascular arrangement of the cells was not uncommon, giving rise to another variety of 'pseudo-rosette.' The amount of fibrous stroma was variable, but as might have been expected in a tumour with more differentiated cells, it was greater than in the sympathogoniomata. It was

surprising to find that the two cases of ganglioneuromata occurred in young children. These patients were aged fourteen months and nineteen months respectively (cases 15 and 20). Whilst many mature nerve cells were present, sympathoblasts were also seen. A section from case 15 is seen in fig. 14.

Description of thoracic growth (fig. 5 and 6)

The patient was a girl age seven years who had a flaccid paralysis of both legs and loss of sensation up to the level of the sixth dorsal segment. The shadow of the tumour could be seen in an x-ray of the chest. At autopsy a large growth was found occupying the posterior mediastinum. It could not be separated from the bodies of the vertebrae or the posterior parts of the ribs. The aorta was stretched out over the front of the mass and the upper lobe of the right lung was displaced forwards. The lower lobe was invaded by growth. Large secondaries were present in both pleurae. The tumour had infiltrated the epidural space and compressed the spinal cord. The liver and both suprarenals were normal. Histologically the tumour was a sympathogonioblastoma and it must have arisen from the thoracic sympathetic chain.

Discussion

Although this study adds nothing original to the well-defined clinical description of these sympathetic tumours, certain features not hitherto generally recognized attracted special attention and deserve mention. The first is the frequency with which pain in the limbs occurs as an early or even as the only presenting symptom. In no less than eight of the patients, one-third of the total number, the initial complaint was of pain in the legs or limping. Only four of these eight patients had x-rays taken of the long bones, but in these, metastases were visible. A tumour of the sympathetic system must therefore be considered when a child complains of persistent pain in the legs for which there is no obvious cause. Attacks of periodic fever were present in one-third of the cases. Whilst slight fever is often associated with the occurrence of malignant growths, particularly in the thorax, the periodicity of these attacks was striking, and in one abdominal case the fever resembled the true Pel-Ebstein type. The age incidence was different from that recorded in other series. Scott et al. found that in thirty-eight cases of the Hutchison type the tumour occurred at an average age of 8.5 years when originating in the left adrenal and at 3.5 years when originating in the right, whilst the Pepper type (thirty cases) occurred at an average age of 2.5 months when primary in the right adrenal, 15.5 months when in the left. In the present series the average age for the Hutchison type was 3.5 years, for the Pepper type 2.3 years. Nine tumours of the 'mixed' type had an average age incidence of 2.7 years. In view of the high proportion of cases in which there were both bony and visceral metastases and the slight difference in age incidence between the 'Hutchison' and 'Pepper' types, it is considered, as Blacklock has already intimated, that the only justification

for separating these two types is clinical convenience; there is no etiological or pathological distinction. Bony metastases may occur at an early age (case 4, one year old) and older children may have only visceral deposits (cases 19 and 6, 5·8 and 3·5 years respectively).

Pathologically one of the chief points of interest was the incidence of the two cases of ganglioneuroma in children aged fourteen months (case 15) and nineteen months (case 20). Certainly in case 20 the tumour was more malignant than is usual in a simple ganglioneuroma as it had invaded the kidney. No other metastases were present, and microscopically the tumour contained many well-formed ganglion cells. These tumours are rare in children, and particularly in infants. Scott et al. could trace only four arising in the adrenal medulla in children; in two of these the ages were between four and five years (in the other two the age was not stated). Two out of the eight cases of ganglioneuromata recorded by Lewis and Geschickter occurred in children aged four and ten years respectively, but Blacklock's patient was an infant of one year and ten months.

An unusual feature of the morbid anatomy was the high incidence of metastases in the lung. These were present in five cases and formed obvious intrapulmonary masses, the pleura being unaffected. Metastases in the brain are rare enough to be noteworthy. In case 5 there was a definite tumour mass present in the parietal lobe underlying the bone which was the site of a large deposit. The tumour had extended through both tables of the bone and had penetrated through the dura, invading the brain by direct extension.

As regards the histological structure of the tumours, we reached the same conclusion as other observers, namely, that these sympathetic growths nearly always contain cells in different stages of development; in some parts of a very immature type of cell and in others a more differentiated type of cell predominates. Even in the two examples of a fully differentiated tumour (ganglioneuroma) encountered the tumour did not consist entirely of ganglion cells. In view of this fact it seems purposeless to elaborate a complex and confusing terminology based on slight differences in the morphology of the component cells. In spite of the advances which have been made in the identification of sympathetic cells in various stages of development, for practical purposes it is sufficient to differentiate the main types corresponding to the main developmental cells. We therefore consider it wise to adopt the simple terminology of Bielschowsky² which has been used in the description of the histology of the present cases. As a general term for the group of sympathetic tumours as a whole, the name 'sympathoblastomata' is suggested in preference to the commonly employed 'neuroblastomata.' The latter term affords no indication of the sympathetic origin of the tumours besides being the name given to a tumour occurring in the central nervous system,

TABLE 2

No.	Sex	Age in years	Adrenal involved	Kidney involved	Liver metastasis	Lung metastasis	Bone metastasis	Other metastases	Histological classification
1	M.	2½	Left	Yes	No	No	R. orbit and 9th r. rib	Head of pancreas	Sympatho- gonioblastoma
2	F.	2	R. incorporated with tumour	Yes	Yes	No. Primary tub. focus in l. lower lobe	Both tables of r. frontal and parietal bones 8th r. rib	—	Sympatho- gonioblastoma
3	F.	11½	L. incorporated with tumour	No; L. kidney completely sur- rounded but not invaded	No	No	Both tables of r. frontal	—	Sympathogonioma
4	F.	1	Right	Yes	No	No	R. frontal and parietal bones; base of skull, spinal column and ribs	Submucous and muscular coats of caecum	Sympatho- gonioblastoma
5	M.	6½	Left	No	No	No	Frontal bones; femur, humerus, ribs	Small degenerating deposit in parietal lobe and dura	Sympatho- gonioblastoma
6	F.	3½	Right	No	Yes	Yes	No	—	Sympatho- gonioblastoma
7	M.	5	Right	No	Yes	No	Humerus; ribs, tibia	—	No sections available
8	M.	10 1½	Right	Yes	No	No	No	—	Sympatho- gonioblastoma
9	M.	3 1½	Both	No	Yes	Yes	Many cranial bones	Dura mater	Sympathogonioma
10	F.	5 1½	Both	No	Yes	No	No	—	Sympathogonioma
11	M.	3½	Neither	Yes	Yes	Not mentioned	Cranial bones	Dura mater	Sympatho- gonioblastoma
12	M.	1½	Not mentioned	No	Yes	Yes	No	—	Sympathogonioma

TABLE 2—*continued*

No.	SEX	AGE IN YEARS	ADRENAL INVOLVED	KIDNEY INVOLVED	LIVER METASTASIS	LUNG METASTASIS	BONE METASTASIS	OTHER METASTASES	HISTOLOGICAL CLASSIFICATION
13	M.	2 $\frac{6}{12}$	Left	Yes; micro- scopically only	No	No	No	—	Sympathogonioma
14	M.	3 $\frac{1}{2}$	Neither	No	No	No	Cranial bones, ribs, long bones	—	Sympathogonioma
15	F.	7	Neither	No	No	Yes Thoracic tumour	No	—	Sympatho- gonioblastoma
16	F.	1 $\frac{4}{12}$	Right	No	No	No	No	—	(Ganglioneuroma
17	M.	3 $\frac{10}{12}$	Left	Yes	Yes	Yes—extensive	Skull, ribs	—	Sympatho- gonioblastoma
18	M.	4 $\frac{1}{2}$	Left	No	No	No	Skull	—	Sympatho- gonioblastoma
19	M.	1 $\frac{1}{2}$	Right	No	Yes	Yes	No	—	Sympatho- gonioblastoma
20	M.	5 $\frac{10}{12}$	Neither	No	Yes	No	No	—	Sympatho- gonioblastoma
21	F.	1 $\frac{9}{12}$	Right	Yes	No	No	No	—	Ganglioneuroma
22	F.	1 $\frac{1}{2}$	Left	No	Yes	No	Skull	Dura mater	Sympatho- gonioblastoma
23	F.	2	Neither	Yes	No	No	Ribs, skull	Intestine (duodenum and colon), ovaries	Sympatho- gonioblastoma
24	M.	8	Both	Yes	No	No	No	Many mesenteric and preaortic glands	Sympatho- gonioblastoma
25	M.	4 $\frac{1}{2}$	Left	No	Yes	No	Skull; ribs	Head of pancreas	Sympatho- gonioblastoma

Summary

1. A study has been made of twenty-five cases of sympathetic nerve tumours. Twenty-four were in the abdomen. Because of its rarity, the thoracic case is described in greater detail.

2. Two-thirds were in males and one-third in females. The average age of the Hutchison group was three-and-a-half years, of the Pepper group two-and-a-half years, and of the children with bony and visceral metastases two years and eight months. The average age of the patients with the Hutchison syndrome was lower and of those with the Pepper syndrome higher than that of other series described in the literature.

3. In many cases the tumours formed large retroperitoneal masses. In a small proportion of these the suprarenals were normal and the tumour must have arisen from the abdominal sympathetic chain.

4. The tumours arose from either side with equal frequency. There was no relation between the side of origin and the situation of the metastases.

5. Metastases were found in the kidneys, lung, pancreas, intestine, ovary and brain, as well as in the liver and bones.

6. The commonest early symptoms were pain in the lower limbs with limping and abdominal swelling. Periodic fever was a common feature. Hypochromic anaemia, partly due to large haemorrhages into the tumour, was present in half the cases.

7. The presence of metastases in bones distinguishes the tumour from Wilms embryoma, the other common malignant growth of early childhood.

8. The histological structure of the tumours is described and a simplified classification proposed. The name sympathoblastoma is suggested as a general term for this class of tumours.

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