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# Bone Metastasizing Renal Tumour of Childhood

## Histopathological and Clinical Review of 38 Cases

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**Summary.** The histopathological spectrum of a large series of a recently described tumour entity is presented. Seven diagnostic features which may be encountered are described and their frequency discussed. The most striking clinical feature was the marked male preponderance (M:F=7.6:1). It is suggested that an appreciation of the full histopathological spectrum is necessary to ensure adequate diagnosis.

**Key words:** Renal tumour – Childhood – Histopathology – Bone metastases.

### Introduction

The entity of a Bone Metastasizing Renal Tumour of Childhood (BMRTC) has been distinguished from Wilms' tumour both as regards pathological appearances and clinical behaviour (Marsden and Lawler 1978; Marsden et al. 1978; Lawler and Marsden 1979). Its relative rarity (approximately 4% of primary childhood renal tumours) makes it difficult for any one centre to acquire sufficient material for adequate histopathological study. The microscopic features may show considerable variation, not only between different tumours but also between different areas of individual tumours. Thirty-eight examples of this neoplasm, collected from various sources, have been studied, and a histological analysis is presented.

### Materials and Methods

The histological material was obtained from four sources: – the Manchester University Childrens' Tumour Registry (1954 to 1976 inclusive) – the First and Second Medical Research Council (MRC) Nephroblastoma Trials and the Oxford Childhood Cancer Study Group.

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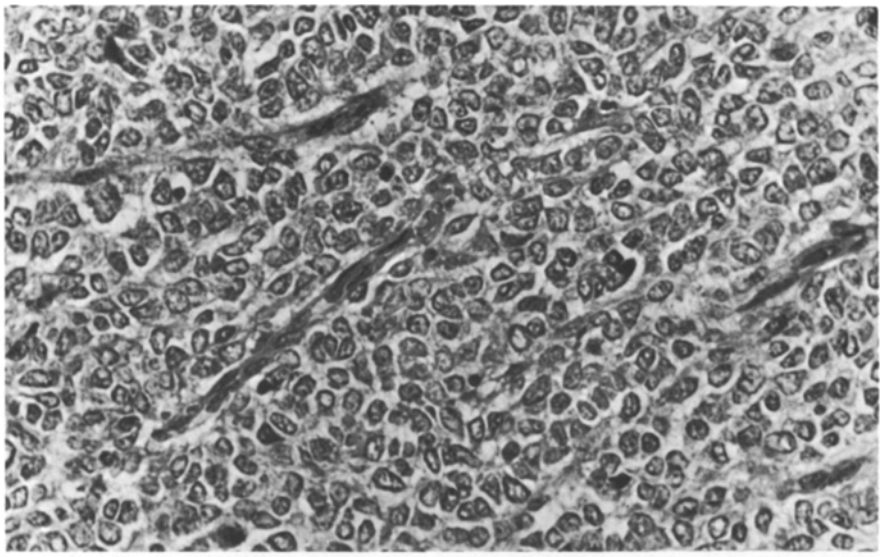

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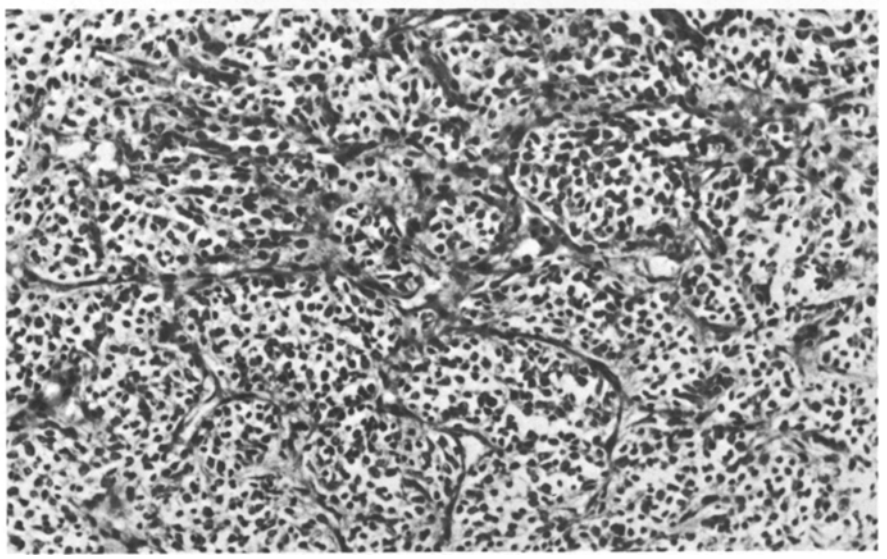

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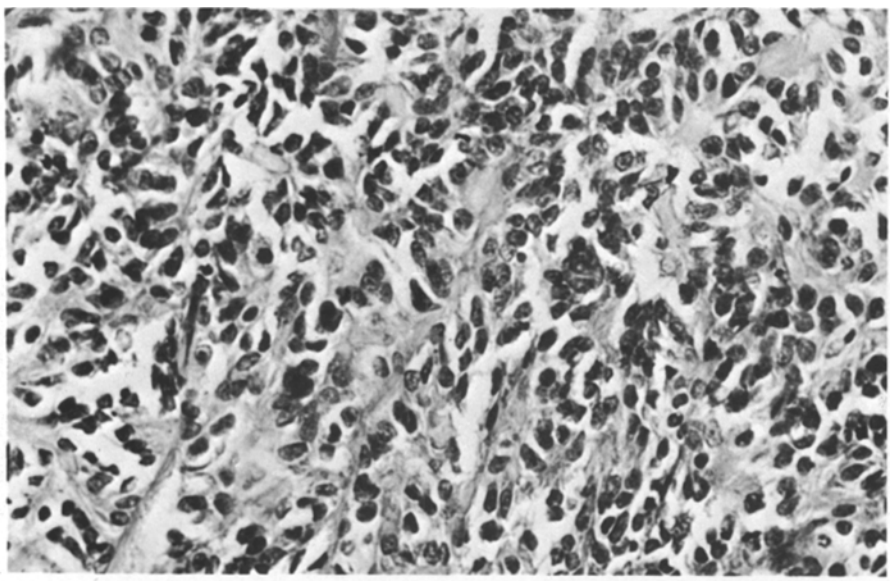
**Fig. 1.** "Classical" pattern showing ovoid and polygonal cells with delicate chromatin and intervening capillaries. H & E ×350

**Fig. 2.** Prominent capillary pattern separating groups of cells. H & E ×150

*Pathological Material*

In all cases, haematoxylin and eosin stained sections were available. In the majority, several sections from different parts of the tumour were obtained, but in a small number, only one section was provided. Whenever possible, other stains, particularly Alcian blue and PAS were used.

All the tumours were analysed for certain histological features which were assessed semiquantitatively as 0, +, ++ and +++. These features are listed below together with a brief description and illustration.



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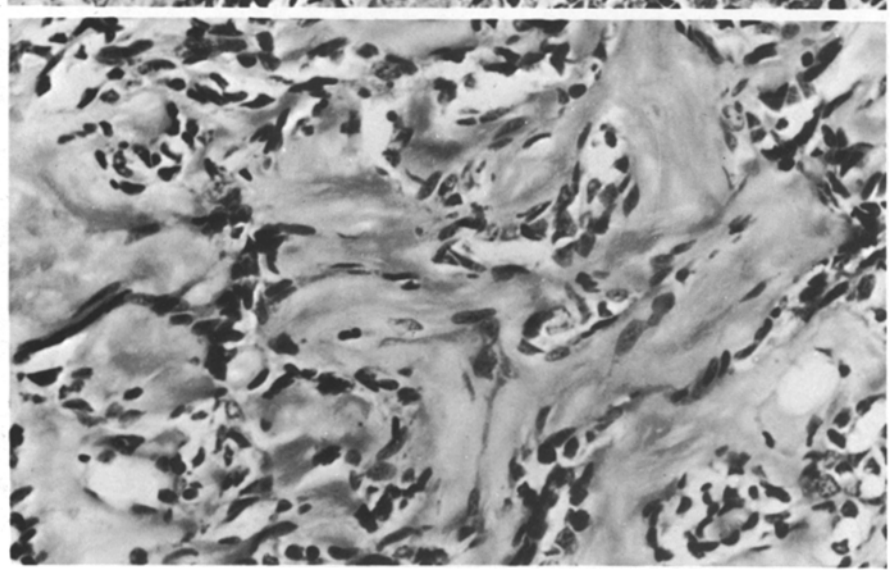

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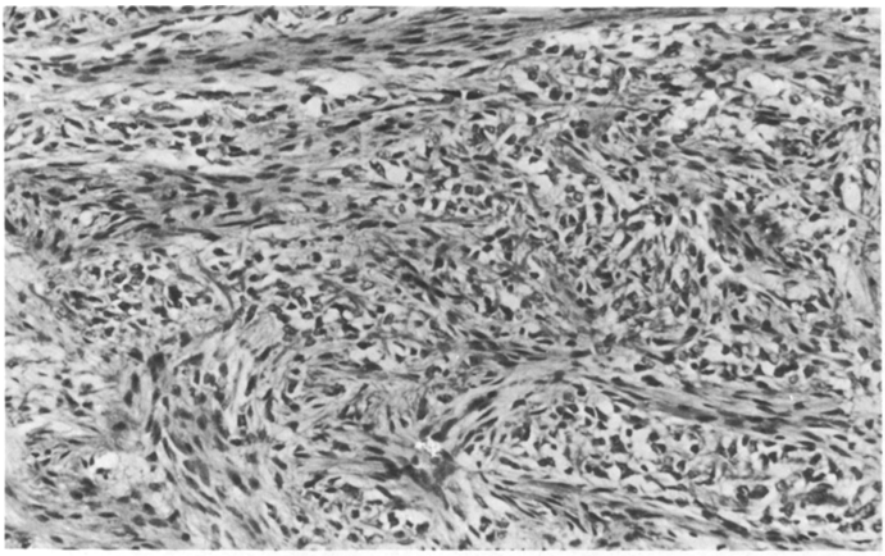
**Fig. 3.** Early sclerosis showing intercellular bands of collagen. H & E ×350

**Fig. 4.** Advanced sclerosis with broad collagenous bands. H & E ×350

*1. Polygonal Cell Areas ("Classical" Pattern).* The cells have a pale nucleus with a delicate chromatin pattern and groups of cells are separated by capillaries (Fig. 1).

*2. Capillaries.* The prominence of capillaries in the polygonal cell areas shows variation and was assessed separately (Fig. 2).



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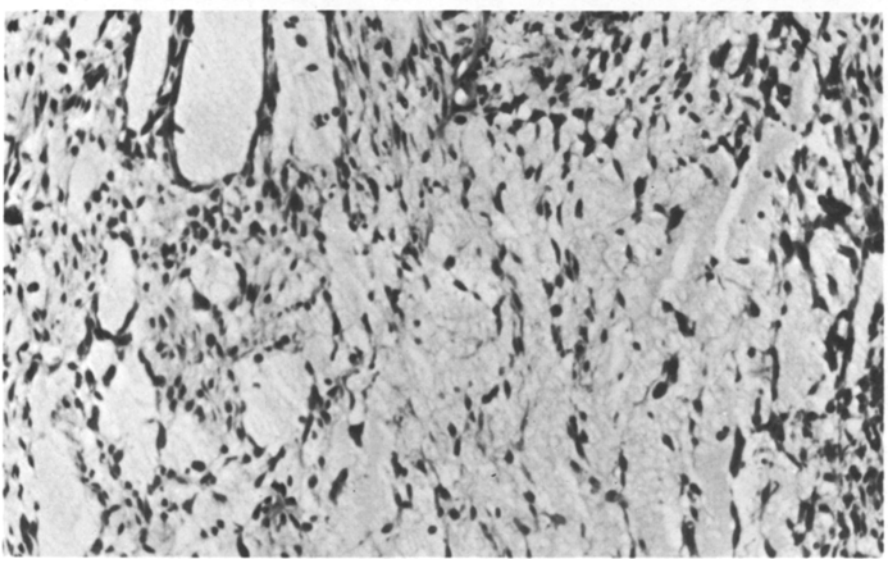

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**Fig. 5.** Fibrillary bands separating polygonal celled areas. H & E ×150

**Fig. 6.** Spongy areas of liquefaction with ill-defined margins and palely staining proteinaceous material. H & E ×150

*3. Sclerosis.* Eosinophilic collagenous fibres extend between the polygonal cells in some areas. There is considerable variation, ranging from a fine intercellular pattern to dense sclerotic bands which are sometimes the predominant feature of the tumour, and occasionally, early and advanced sclerosis are seen in the same neoplasm (Figs. 3 and 4).

*4. Fibrillary Component.* Fibrous tissue is seen in variable amounts, but more commonly as bands extending through the polygonal cell areas. Capillaries are sometimes encountered in these fibrous

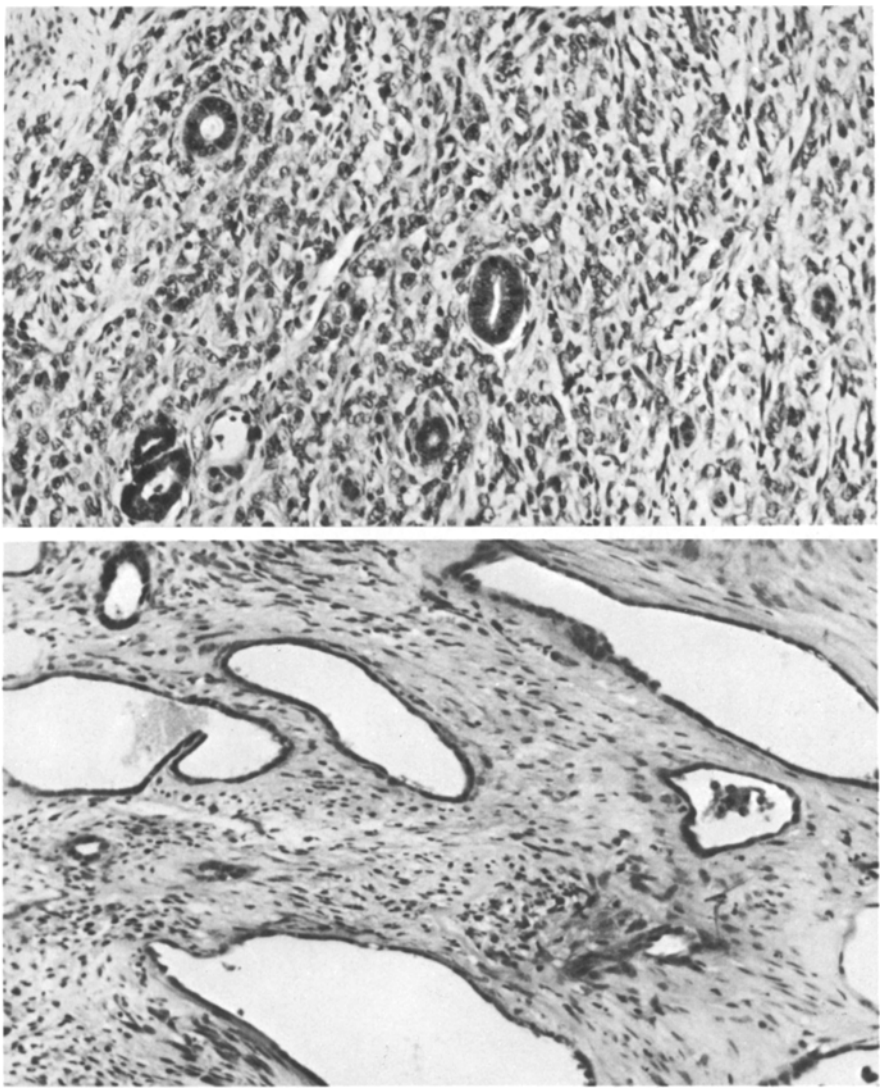

**Fig. 7.** Tubules lined by cuboidal and low columnar epithelium. H & E ×150

**Fig. 8.** Cysts with clearly defined flattened epithelial lining. H & E ×150

bands, but this is not a constant feature. The fibrillary component may be distinguished from sclerosis, not only by its distribution but also by the fibroblastic nature in which spindle-shaped nuclei are prominent (Fig. 5). Occasionally, the nuclei show alignment and create a palisaded appearance.

*5. Liquefaction.* In the hypocellular areas of the tumours, foci of liquefaction are sometimes noted. These vary between small intercellular foci producing a spongy appearance and large lakes of palely eosinophilic proteinaceous material (Fig. 6). This material has a high acid mucopolysaccharide content, staining positively with Alcian blue but negatively with PAS.

**Table 1.** Semiquantitative analysis of histopathological features of the 38 cases

| No | Name | Classical | Capillaries | Sclerosis | Fibrillary | Liquefaction | Tubules | Cysts |
|---|---|---|---|---|---|---|---|---|
| 1. | S.A. | 0 | + | +++ | + | + | +++ | +++ |
| 2. | C.R.B. | + | + | + | ++ | ++ | 0 | +++ |
| 3. | W.T.J. | 0 | + | ++ | + | ++ | + | + |
| 4. | K.S.L. | +++ | + | + | + | + | + | + |
| 5. | D.M. | +++ | +++ | + | + | 0 | ++ | + |
| 6. | P.J. | ++ | ++ | + | 0 | + | 0 | + |
| 7. | T.B. | ++ | ++ | +++ | +++ | + | + | + |
| 8. | R.S.B. | ++ | + | ++ | 0 | + | + | + |
| 9. | I.W. | +++ | ++ | + | + | 0 | + | + |
| 10. | L.C.D. | +++ | ++ | 0 | 0 | 0 | + | 0 |
| 11. | S.J.W. | + | + | ++ | + | 0 | 0 | 0 |
| 12. | C.J.T. | +++ | ++ | 0 | + | + | ++ | + |
| 13. | J.S.S. | ++ | ++ | 0 | + | ++ | + | ++ |
| 14. | K.P. | ++ | + | 0 | ++ | + | ++ | +++ |
| 15. | P.A.B. | ++ | ++ | + | 0 | 0 | 0 | 0 |
| 16. | J.F. | +++ | + | ++ | 0 | 0 | + | 0 |
| 17. | J.M. | 0 | + | 0 | ++ | + | +++ | +++ |
| 18. | J.A. | +++ | ++ | + | + | + | ++ | + |
| 19. | E.J. | +++ | ++ | 0 | + | + | + | + |
| 20. | M.H. | + | + | ++ | ++ | ++ | ++ | + |
| 21. | C.N. | + | ++ | +++ | 0 | 0 | ++ | ++ |
| 22. | S.R. | +++ | +++ | + | 0 | + | + | 0 |
| 23. | M.F. | +++ | ++ | 0 | 0 | 0 | + | 0 |
| 24. | T.McF. | ++ | + | 0 | + | + | 0 | 0 |
| 25. | D.S. | +++ | ++ | ++ | + | + | ++ | + |
| 26. | P.T. | ++ | + | + | ++ | ++ | 0 | ++ |
| 27. | R.W. | + | + | +++ | +++ | +++ | + | 0 |
| 28. | S.S. | ++ | ++ | + | 0 | + | + | + |
| 29. | A.E.G.S. | ++ | ++ | + | + | + | + | 0 |
| 30. | G.B. | +++ | +++ | 0 | + | 0 | 0 | +++ |
| 31. | A.McE. | +++ | ++ | +++ | +++ | 0 | + | 0 |
| 32. | M.C. | + | + | ++ | +++ | + | + | + |
| 33. | A.B. | +++ | ++ | + | ++ | + | ++ | + |
| 34. | K.B.M. | ++ | + | + | ++ | ++ | + | + |
| 35. | J.H. | +++ | + | 0 | 0 | + | 0 | 0 |
| 36. | J.W. | +++ | + | 0 | + | + | + | + |
| 37. | D.G. | ++ | +++ | 0 | +++ | + | ++ | + |
| 38. | B. | +++ | +++ | 0 | 0 | 0 | 0 | + |

*6. Tubules.* These are seen more commonly peripherally in the tumours and are often confirned to the extreme periphery. The epithelial lining is usually cuboidal, but occasionally more columnar and hyperchromatic. Lumina are always seen, with minor variations in luminal size and occasional branching (Fig. 7).

*7. Cysts.* These are dilated spaces lined by a clearly defined flattened epithelium. This is in contrast with the lakes of liquefaction where the margins are often ill defined and an epithelial lining is absent. In addition, Alcian blue positive material is not identified in the cysts (Fig. 8).

*Clinicopathological Features*

Brief clinical records of the 38 cases were available, and these were reviewed.

**Table 2.** Collations of semiquantitative analyses documented in Table 1

| | +++ | ++ | + | 0 |
|---|---|---|---|---|
| Classical | 17 | 12 | 6 | 3 |
| Capillaries | 5 | 16 | 17 | 0 |
| Sclerosis | 5 | 7 | 13 | 13 |
| Fibrillary | 5 | 7 | 15 | 11 |
| Liquefaction | 1 | 6 | 20 | 11 |
| Tubules | 2 | 9 | 18 | 9 |
| Cysts | 5 | 3 | 19 | 11 |

## Results

The results of the semiquantitative analyses of the pathological material are documented in Table 1 and collated in Table 2. In addition, necrosis was seen in 25 tumours, and small areas of haemorrhage in 10. The salient clinical features are summarized in Table 3.

## Discussion

In an earlier paper (Marsden et al. 1978), it was stated that the histological appearances of the BMRTC were uniform, with polygonal cell areas showing only minor variations, and because of this, the term "classical" has been used to describe this pattern with intervening capillaries. Subsequently, it has become apparent that a much wider variation of histological features may be encountered such that individual tumours may be difficult to classify as BMRTC unless the complete spectrum is appreciated. However, all the features described may be seen in varying degrees in different areas of the same tumour justifying the inclusion of all the tumours in the present series in one diagnostic group. Adequate sampling of the neoplasms is important in this context.

The classical pattern was clearly recognisable in 35 of the 38 tumours (Tables 1 and 2). In the 3 remaining neoplasms, capillaries were seen without polygonal cells, but other features, including cysts, sclerosis and liquefaction, consistent with a diagnosis of BMRTC were present. Capillaries provided a background in all tumours, and were relatively prominent in more than half. Sclerosis was not seen in 13; in the remainder, it was variable, and in 5, advanced and extensive sclerosis was noted. Widespread advanced sclerosis may obliterate the classical pattern. The fibrillary component was a relatively minor feature, with only 5 cases in the +++ group. Similarly, extensive liquefaction was rarely seen. Tubules were absent in 9 tumours and were numerous in only two examples. The presence or absence of cysts showed a similar pattern to the tubules – possibly suggesting a relationship between these two features.

The most significant clinical feature, as shown in Table 3, relates to sex incidence. Thirty-three of the 38 cases (86.8%) were boys, and this male predominance (M:F = 7.6:1) supports the findings in the smaller group of cases previous-

**Table 3.** Salient clinical features of the 38 cases of BMRTC

| No | Name | Age at Presentation | Sex | Side | Site of bone metastases | Other metastases | Age (survival or at death) | Comment |
|---|---|---|---|---|---|---|---|---|
| 1. | S.A. | 1 y 4 m | F | L | Multiple | None | 1 y 4 m (D) | |
| 2. | C.R.B. | 3 y 5 m | M | L | Skull | Liver, scalp | 3 y 6 m (D) | |
| 3. | W.T.J. | 2 y 2 m | M | R | Multiple | Lungs | 2 y 2 m (D) | |
| 4. | K.S.L. | 2 y 10 m | M | R | Multiple | None | 4 y 5 m (D) | |
| 5. | D.M. | 1 y 8 m | M | L | Multiple | None | 6 y 4 m (D) | |
| 6. | P.J. | 3 y 3 m | M | R | Multiple | Liver | 5 y 5 m (D) | |
| 7. | T.B. | 5 y | M | L | Multiple | Lung | 7 y (D) | |
| 8. | R.S.B. | 2 y 4 m | M | L | Multiple | Liver | 3 y 3 m (D) | |
| 9. | I.W. | 1 y 1 m | M | L | Skull | None | 1 y 8 m (D) | |
| 10. | L.C.D. | 1 y 4 m | F | R | Skull | Lungs | 2 y 8 m (D) | |
| 11. | S.J.W. | 5 y 2 m | F | L | Skull | Scalp, lung | 6 y 8 m (D) | |
| 12. | C.J.T. | 1 y 1 m | M | R | Skull | None | 2 y 1 m (D) | Local recurrence |
| 13. | J.S.S. | 1 y 11 m | M | L | Skull | Lung | 2 y 7 m (D) | Local recurrence |
| 14. | K.P. | 2 y 5 m | M | R | Shoulder | Testis | 3 y 7 m (D) | Local recurrence |
| 15. | P.A.B. | 1 y 1 m | M | L | None | Brain | 2 y 3 m (D) | Local recurrence |
| 16. | J.F. | 5 y 5 m | M | R | Vertebra | None | 7 y 6 m (D) | |
| 17. | J.M. | 2 y | M | R | Multiple | Lung | 3 y 3 m (D) | |
| 18. | J.A. | 2 y | M | L | Multiple | Lung | 5 y 9 m (D) | |
| 19. | E.J. | 1 y 9 m | M | R | Skull | None | 2 y 6 m (D) | Local recurrence |
| 20. | M.H. | 3 y | M | L | Multiple | Soft palate lung | 5 y (D) | Local recurrence |
| 21. | C.N. | 4 y 6 m | M | L | Multiple | None | 8 y (D) | |
| 22. | S.R. | 1 y 11 m | M | R | Multiple | None | 3 y (D) | |
| 23. | M.F. | 2 y | M | R | Multiple | None | 2 y 6 m (D) | |
| 24. | T.McF. | 14 y 10 m | M | L | cervical vertebra | Lungs | 16 y 7 m (D) | |
| 25. | D.S. | 6 y 7 m | M | R | None | None | 10 y 6 m (A) | Removed osteoma |
| 26. | P.T. | 2 y 6 m | M | R | None | Lung | 4 y 6 m (A) | |
| 27. | R.W. | 1 y | M | R | None | Lung, Liver | 3 y 6 m (D) | |
| 28. | S.S. | 1 y 6 m | M | R | Multiple | None | 2 y 9 m (D) | |
| 29. | A.E.G.S. | 2 y 10 m | M | L | Rib | None | 11 y (A) | |
| 30. | G.B. | 4 y 2 m | M | L | None | None | 4 y 2 m (D) | Post-op death |
| 31. | A.McE | 13 y | M | R | Multiple | Extradural | 17 y 7 m (A) | |
| 32. | M.C. | 1 y 5 m | M | L | Multiple | None | 5 y 10 m (A) | Local recurrence |
| 33. | A.B. | 3 y 10 m | M | R | None | None | 6 y 2 m (A) | |
| 34. | K.B.M. | 4 y 11 m | M | L | Rib | None | 9 y (A) | |
| 35. | J.H. | 10 y | M | R | None | None | 10 y (D) | Post-op death (cerebral tumour embolus) |
| 36. | J.W. | 1 y 2 m | F | L | C2/3 vertebrae | Lung | 2 y 10 m (D) | |
| 37. | D.G. | 1 y 6 m | F | L | None | None | 1 y 6½ m (D) | Post-op death |
| 38. | B. | 4 y | M | R | None | None | 4 y 3 m (A) | |

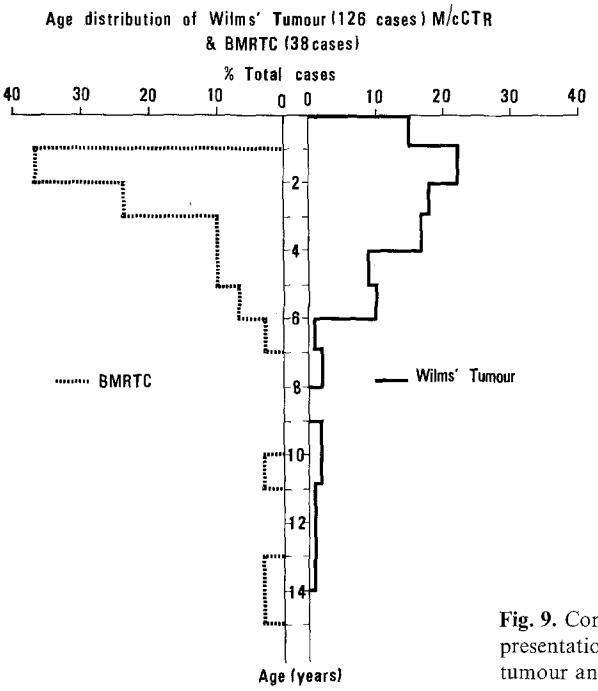


**Fig. 9.** Comparison of ages at presentation between Wilms' tumour and BMRTC

ly published (Marsden and Lawler 1978). The age at presentation was similar to that seen in Wilms' tumours (Fig. 9) with the exception that the BMRTC was not found in children under one year of age. However, although two thirds of the cases were obtained from general population studies, the remainder were derived from the MRC Nephroblastoma Trials in which patients under one year of age were excluded.

There was no difference between the incidence of right and left sided tumours, and there were no bilateral tumours.

Bone metastases developed in 29 cases, although half the cases were obtained through the Oxford Childhood Cancer Study Group in an analysis of children with primary renal tumours who developed bone metastases (Marsden et al. 1980). Of the remaining 9, three died postoperatively, and one has only been followed up for a short time. In 16 cases, bone metastases were multiple, often widespread and sometimes there was extensive skeletal involvement. In the 13 patients with single bone deposits, the skull was involved in 7. In 18 cases, non-osseous metastases developed, and in three of these there were no bone secondaries. In 7 cases, local recurrence of the tumour was documented.

Eight of the patients are still alive, and all but one of these have been followed up for two to eight years. There were three postoperative deaths, and the other fatal cases survived for less than one month to 4 years 8 months.

From our examination of the literature, the tumour described in the present paper has been reported from two other centres (Beckwith and Palmer 1978;

Morgan and Kidd 1978). The terms "clear cell sarcoma" and "undifferentiated sarcoma of the kidney" respectively were applied by these authors. Cells with "water clear" cytoplasm are not a feature in our material, and this aspect was not stressed by Morgan and Kidd (1978). Furthermore, in the absence of definitive features, the term "sarcoma" is considered to be inappropriate at the present time. Both Beckwith and Palmer (1978) and Morgan and Kidd (1978) classified the neoplasm as a variant of Wilms' tumour with different clinicopathological behaviour from the usual nephroblastoma, although Morgan and Kidd (1978) emphasized its distinct characteristics. We feel that this tumour has sufficient distinguishing features, both pathological and clinical, to justify designation as a separate entity.

Both the publications from other centres described the polygonal cell (classical) pattern, and Beckwith and Palmer (1978) showed the fibrillary and sclerosing components in addition. In our initial publication on this entity (Marsden et al. 1978), classical and fibrillary features were documented, whilst in a later paper (Marsden and Lawler 1978), a more comprehensive picture was presented. The full spectrum has only been appreciated following study of a relatively large number of cases.

Recently, Penchansky and Gallo (1979) reported seven cases of rhabdomyosarcoma of the kidney in children, four of whom developed bone metastases. These authors regarded their tumours as identical to the BMRTC. There are, however, several differences, notably the complete absence of rhabdomyoblastic differentiation in the latter.

The two clinical features stressed in our earlier reports on the BMRTC are the frequency of bone metastases and the male predominance. It is not possible to assess the true incidence of bone metastases from the present material, but this tendency is clearly shown and is apparent in the reports from the other two centres (Beckwith and Palmer 1978; Morgan and Kidd 1978). The sex incidence of this tumour is not given by Beckwith and Palmer (1978), and there were 5 boys and 4 girls in the series of Morgan and Kidd (1978). However, in the present report, 33 of the 38 cases (86.8%) were boys.

## Conclusion

An attempt has been made to identify the histological features of a tumour entity which is regarded as distinct from nephroblastoma. The importance of establishing the correct diagnosis of this neoplasm is shown by its different clinical behaviour, which may necessitate more intensive chemotherapeutic regimes.

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