The Children's Tumour Clinic in Port Elizabeth*

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SUMMARY

A children's tumour clinic in Port Elizabeth is described, and the need for such an organization outlined. A very broad outline of treatment and results in 66 cases is given.

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The concept of 'combined clinics' consisting of representatives of the various disciplines in the practice of medicine is now commonplace, and an accepted standard at most medical schools. It is perhaps unusual in centres not endowed with the benefits of teaching institutions. It may even be argued that such clinics are impracticable and probably serve no useful purpose as reliance has to be placed on non-teaching, part-time hospital consultant staff.

Notwithstanding this, the need for such a clinic to guide the management of malignancy in childhood has long been felt here and so the Children's Tumour Clinic in Port Elizabeth was started in January 1969 to study the incidence of malignancy in childhood in this area and analyse the types encountered. It was also felt that any epidemiological peculiarities, should they exist, could be investigated and compared with other centres in South Africa or, for that matter, other countries, or other ethnic groups. Finally, this would provide the opportunity to evaluate various modalities in therapy of different tumours.

Where the common ground is radiation and chemotherapy of tumours, physician, surgeon, therapist and pathologist are drawn together, pitted against the knowns and unknowns of malignant disease in childhood. The inevitable benefit to the sufferers and their parents is obvious: a certain confidence and hope is derived from this gathering of forces.

The volume of such pathology in the Eastern Cape seemed to warrant the establishment of a Registry for Children's Tumours. It would reflect the past, and provide a glimpse of the future in regard to the mortality of malignancy in childhood. There has hitherto been a widespread attitude of pessimism regarding malignant disease, particularly in childhood, and this is probably justified by previous records. Moreover, the approach to childhood malignancy appears to have been negative, despite the fact that it is with children—because of the nature of the patient as well as the tumour—that one's efforts could be most rewarding, and provide lessons which could prove beneficial regarding oncology generally.

In a sophisticated society, where malnutrition and its associated ravages are uncommon, malignancy and road accidents vie for a place at the top of the list of causes of death in childhood.[1] But the prevalence of malnutrition in this area cannot be allowed to blind us to the importance of other aspects of paediatrics. The life expectancy of children compared with adults, makes attention to malignancy vital.

Where treatment of a single disease varies in the hands of different practitioners, no individual method can be singled out as giving the best prognosis. Encouraged by the remarkable improvement in results in collaborative studies elsewhere,[2-10] and stimulated by the evident need for a positive approach to malignancy in childhood, it was decided to collect, channel, and co-ordinate management of children's tumours by means of the Combined Children's Tumour Clinic and the Children's Tumour Registry. This follows the lines of a number of adult combined clinics in Port Elizabeth.

We are now able to obtain information for incidence studies, ensure a life-time follow-up of all patients and, through these studies, decide on treatment policies.

METHOD

Details of histories taken include the usual age, sex, place of birth and family history. Rural Bantu are difficult to trace, so the locality of the dwelling, the names of the headman of the kraal, and the nearest or accustomed trading-store are noted. In addition, information about the mother's pregnancy, gestation and delivery, are sought. Full clinical details of treatment and/or operation are recorded, together with comments from the panel at each attendance.

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The basic structure of this panel provides for a radiotherapist, two paediatricians, two paediatric surgeons with part-time hospital appointments, and a pathologist. At least 3, usually 4 of the 6 always attend meetings.

All practitioners, both private and full-time, are invited to attend and refer to the clinic all cases of childhood malignancy found. In this way the case is registered and progress followed up. Should a practitioner wish to retain responsibility for the management of his case, comments and recommendations from the clinic are forwarded to him and he is at liberty to accept or reject the advice offered. He is requested to inform the clinic of progress and outcome.

These circumstances, however, seldom obtain. Usually definitive treatment is prescribed by the clinic and the members become responsible for the treatment of the patient. Following registration and decision about treatment, each child attends the clinic subsequently, and is hospitalized, when necessary at the Provincial or Livingstone Hospitals.

The combined clinic is held fortnightly in the Department of Radiotherapy, Provincial Hospital, Port Elizabeth, where children of all races are seen.

The policies on the management of individual malignancies are based largely on those of a similar clinic held at Groote Schuur and Red Cross Children's Memorial Hospitals, Cape Town, under the chairmanship of Professor J. H. Louw.

The radiotherapist in attendance at the Port Elizabeth Clinic has his headquarters at Groote Schuur Hospital. Thus, the Port Elizabeth Children's Tumour Clinic enjoys the great advantage of liaison with the University of Cape Town Medical School. Moreover, when a sophisticated form of therapy, e.g. cobalt 60 is required, the patient is transferred to Cape Town for treatment with the minimum of delay.

Histopathology and haematology are carried out by the staff of the Port Elizabeth branch of the South African Institute for Medical Research. If doubt arises, they refer to their headquarters in Johannesburg. In addition, copies of histology and some haematological slides are sent to the University of Cape Town Medical School's Department of Pathology for registration and record purposes.

MANAGEMENT

In general, a unified system of management for each group of tumours is prescribed. It is not within the compass of this paper to discuss details of treatment, but the broad outlines for some of the common tumours are as follows:

Wilm's Tumour

Investigations consist of haematology, serology including alkaline phosphatase and SGOT, urine analyses, and radiology. If this tumour is suspected, abdominal palpation and handling of the child is prohibited unless special circumstances warrant it. Where doubt exists, further investigations are carried out, e.g. bone marrow, VMA estimation, skeletal surveys and, in older children, renal angiograms.

Staging of the tumours is helpful in assessing the value of treatment. Stage I indicates that the tumour is limited within the capsule and the entire tumour is resected. Stage II tumours extend beyond the renal capsule, but are completely resected. Where local spread renders some tumour remnants non-resectable, but there is no evidence of distant (haematogenous) metastases, the growth is classified as Stage III. Stage IV is diagnosed when there are distant metastases. If both kidneys are involved, it is a Stage V tumour.

Treatment is pre-operative irradiation and nephrectomy within 2 weeks of the radiotherapy. Actinomycin D, 15 μg/kg body weight, is given on the day of operation and for 4 daily doses thereafter.

At operation, after removal of the tumour the area occupied by the growth is marked with silver clips. These are also used to indicate the site of any residual tumour if it is gross and not resectable. Within a week of operation, irradiation is recommenced and continued for 3 - 4 weeks. The child is carefully monitored throughout this time for evidence of intolerance to chemotherapy or irradiation.

Follow-up is all-important. The policy is to readmit every 5 weeks for a week, over the ensuing 18 months. During this week of hospitalization all investigations, which may include pyelograms, are repeated and a 5-day course of actinomycin D is administered. The child is also seen at the Clinic when not hospitalized. After the intermittent chemotherapy has ceased patients attend less frequently, depending on presence or absence of metastases, and after 5 years, they attend annually. If metastases appear, additional chemotherapy may be instituted, e.g. vincristine 0·05 mg/kg weekly for 5 weeks, as well as actinomycin D every 6 weeks, the drugs being used alternately. Pulmonary metastases are irradiated or even resected. Follow-up should be for life, and include eventual offspring.

Neuroblastoma

When this diagnosis is suspected, investigations are along the same lines as for nephroblastoma. In addition, liver scan, skeletal surveys and VMA estimations are carried out. If necessary, exploration of the suprarenals to identify the primary tumour is carried out under cytotoxic cover, using Endoxan. The tumour is removed, if possible, whether or not it is the primary growth.

Radiotherapy is given to residual tumour mass if localized. If widespread, chemotherapy is instituted, using Endoxan and vincristine as a weekly 'cocktail' for 6 doses, then bi-weekly until there is complete regression or the tumour 'escapes'.

Lymphomata

Diagnosis in this group is often difficult. There are 4 main groups: lymphosarcoma, reticulum-cell sarcoma, Hodgkin's disease and giant follicular lymphoma. Staging depends on the number of lymphatic chains involved, and whether above or below the diaphragm, or both. Stage IV

indicates visceral or CNS involvement, or activity in the bone marrow. Cognizance is taken of the symptomatology in assessing severity and advancement of the disease.

Investigations are the same as for the above-mentioned tumours. Node biopsy is also performed and chemical analyses of the urine. Tuberculosis must be excluded, the Heaf test will aid in this. Where doubt still exists, a lymphogram is indicated.

Treatment is radiotherapy using cobalt 60, and chemotherapy. If palliation only can be achieved, chemotherapy alone is employed. The exception is Hodgkin's disease, when chemotherapy and steroid therapy may be alternated with irradiation; immunotherapy may be of help, but is usually used as a last resort.

Acute Leukaemia

As the main aim is to establish the diagnosis beyond doubt, a bone-marrow examination is mandatory. General management involves correction of anaemia and thrombocytopenia, and the control of possible infections, which are common.

Specific treatment is directed toward inducing remission, and then maintaining it. It is often impossible to follow a routine with steroid and chemotherapy, since the response varies from case to case. Usually initial treatment is prednisone combined with vincristine or 6 mercaptopurine. Subsequent therapy depends on response and the time taken to remit. Drugs used to maintain remission are ever increasing. The ones in common use are 6 mercaptopurine, vincristine (in combination with 6 mercaptopurine), methotrexate, and cyclophosphamide. Rubidomycin and cytosine arabinosine are also occasionally employed; and where all else fails, possibly immunotherapy.

During therapy, a rapid response may lead to hyperuricaemia and possibly renal failure as a result of excessive DNA breakdown. Precautions against this may require the administration of allopurinol and urine alkalinization. Adequate urine output must be ensured.

Retinoblastoma

Surprisingly, this tumour is not commonly encountered at the clinic (Table I). Usually, besides general supportive measures, the initial step is enucleation of the eye. Two weeks later radiotherapy is commenced, and continued over a period of 4 weeks. The irradiation may be combined with cytotoxics.

Careful follow-up is essential, with, of course, particular attention to the remaining eye. Frequent examinations under anaesthesia are desirable. Should the remaining eye become involved, irradiation is employed with care to try to avoid the lens.

A life-time follow-up is extended to the patient's offspring.

Rhabdomyosarcoma

This has so far not been seen at the clinic in Port Elizabeth. Management would follow lines similar to those for nephroblastoma.

Intracranial Tumours

These fall in the province of the neurosurgeon, with whom close liaison should be maintained. Depending on the tumour, treatment may be by surgery only (e.g. grade I astrocytoma) or operation followed by irradiation by means of the cobalt unit.

RESULTS

Since the inception of the Children's Tumour Clinic in Port Elizabeth in January 1969, 66 cases have been registered and treated. An analysis of these cases is shown in Table I.

The majority of cases (51) have occurred in non-White patients. Apart from the benign tumours (10)—which included giant haemangioma, papilloma and polyps of rectum, etc.—the best prognosis in the clinic has been for Wilm's tumours and lymphomata. There have been only 2 each of cases of teratoma and osteogenic sarcoma, and the patients are alive and well with no evidence of active disease at present. Among some of the rarer tumours have been xeroderma pigmentosa, ependymoma, granulosa-cell ovarian tumour, hepatoblastoma, synovioma, and chondromyxofibroma.

The 66 cases have been found among a total local population of 385 000. Of these, 260 000 are non-Whites.

TABLE I. ANALYSIS OF CASES

Tumour	Total	No. of deaths	Duration before death (months)	Longest living (months)
Wilm's	11	2	2 & 14	24
Neuroblastoma	6	5	16, 6, ?, ?, 3	3
Leukaemia	11	6	21, 1 day, 8, 2, 2 wks, 1 day	14
Lymphoma	11	3	7, 4, ?	29 (excl. Hodgkin's)
(Hodgkin's)	(4)	(1)	(1)	(30)
Retinoblastoma	2	2	6, 6,	—
Teratoma	3	1	?	12
Osteogenic sarcoma	2	—	—	17, 15
Others	11			
Benign	10			

DISCUSSION

While still in its early days, it is nevertheless felt that the clinic has fully justified its existence. It is already becoming possible to formulate opinion and modify treatment in some forms of malignancy, and so perhaps improve on some results.

Pitfalls in therapy have been experienced, and measures to counter these devised. When problems arise, they are seen from the aspects of the various disciplines in medicine, and an over-all picture obtained. Only in this way has it been possible to endeavour to overcome them. The pooled experience of a number of workers interested in children's tumours has been invaluable, and much knowledge and experience gained through the collaborative guidance from our visiting colleagues from the University of Cape Town Medical School.

It would have been desirable to have had the benefit of the attendance of more paediatricians and pathologists on the panel since the help given by the few faithfuls has proved immeasurable. Private practice and part-time (as opposed to full-time) appointments are no bar to the successful organization of the meetings. It must be admitted that the king-pin of the Clinic is the radiotherapist from Groote Schuur Hospital, Cape Town, who visits Port Elizabeth weekly.

Such a clinic should be possible, and is desirable, in most of the larger non-medical-school hospital centres.

The Port Elizabeth Children's Tumour Clinic was the brain-child of Dr I. Bhettay, formerly of Livingstone Hospital, and he, together with Dr R. Sealy and Dr E. Mills, Department of Radiotherapy, Groote Schuur Hospital, and Dr J. M. Wynne, Port Elizabeth, have comprised the clinic team, under the chairmanship of the author. Their regular and devoted attendance have made this venture not only a possibility, but a success.

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