Unexpected cure in metastatic rhabdomyosarcoma

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SUMMARY
A 3 year old boy presented with a presumably incurable form of rhabdomyosarcoma. Conventional treatment for advanced stage rhabdomyosarcoma (chemotherapy plus radiotherapy) was not used and intensive chemotherapy alone was given, resulting in an apparent cure. Our treatment rationale is discussed.

Case report
In March 1980 a 3 year old boy was referred to our hospital because of a progressive mass on the right side of his face and neck, and strabismus. Examination showed a firm mass in the right pre-auricular region, two palpable nodes in the subdigastic and submandibular region, right abducens paresis, and right tonsillar displacement. Computed tomography of the head and neck showed a large soft tissue mass extending from both sides of the ascending ramus of the mandible into the oropharynx, with partial destruction of the mandibular ramus, the pterygoid processus, the dorsal wall of the right maxillary sinus, and considerable widening of the foramen ovale.

An incisional biopsy of the tumour was performed, with excision of the submandibular node. On both specimens a histological diagnosis of embryonal rhabdomyosarcoma was made (Figure). Bone marrow aspiration and biopsy showed an extensive infiltration of tumour cells. Chest radiograph, bone scan, and spinal fluid cytology were normal.

Figure  Photomicrograph of the primary tumour specimen, showing a proliferation of tumour cells with irregular nuclei and little cytoplasm. Some cells are multinucleated (M) and two mitotic figures (m) are visible. (Ethyl-methacrylate embedding, H&E stain, × 350).
It was decided to treat the boy with cytostatic agents in a combination that should be as intensive as possible. For this purpose we chose a combination of vincristine, bleomycin, methotrexate, doxorubicin, actinomycin D, and cyclophosphamide. This combination has been reported for Ewing's sarcoma by investigators at Memorial Sloan Kettering Cancer Center. Because of the diffuse bone marrow infiltration by malignant cells and the intensive chemotherapy, a severe pancytopenia was anticipated and subsequently developed. A number of pancytopenia-related complications were successfully managed. After two months of treatment the child was judged to have no evidence of disease. Four months after diagnosis, tissues from the centre of the original tumour region were obtained by needle biopsies under computed tomographic guidance. No tumour cells could be found in multiple tissue samples. One year after diagnosis a complete reassessment of the disease status again failed to show any residual tumour. In view of the total doses of doxorubicin and bleomycin administered to the patient at that time, chemotherapy was altered. During the next year the patient was given vincristine, actinomycin D, and cyclophosphamide in a combination as used in the third rhabdomyosarcoma trial of the International Society of Pediatric Oncology. This prolonged course of chemotherapy was tolerated well and two years after diagnosis all treatment was stopped.

At the time of writing (in January 1985) 58 months after diagnosis, the patient is in good health and shows no evidence of disease. He is now aged 8 years, is doing well at school, and is growing according to the same centile as at the time of the diagnosis.

Discussion

At diagnosis, the presence of bone marrow and lymph node involvement in our patient warranted pessimism about the prognosis. Ruymann et al., reporting on the first Intergroup rhabdomyosarcoma study, mention that only two of 30 patients with initial bone marrow involvement were long term survivors. They stress that in both patients bone marrow was the sole metastatic site. Thus, among the patients in that study, no patient presenting with bone marrow metastases in association with another metastatic site survived.

In addition to the bone marrow and lymph node metastases, our patient also had symptoms of meningeal involvement. Cranial nerve palsies and lytic destruction of bone at the base of the brain, as present in our patient, meet criteria for meningeal involvement used in the first Intergroup rhabdomyosarcoma study. In the study experience spread to the central nervous system invariably meant a fatal outcome for the patient. According to conventional therapeutic programmes, as represented by Intergroup recommendations, craniospinal irradiation with a boost on the primary tumour would have been given in our patient. In young children, radiotherapy for head and neck rhabdomyosarcoma may cause growth retardation of facial bones, resulting in severe malformation of the face for long term survivors. It is probable that appropriate radiotherapy in this 3 year old child would also have caused hormonal disturbances, since the pituitary gland would have been in the radiation field. An additional objection to craniospinal irradiation was that it would interfere with the intended intensive chemotherapy. We, therefore, decided to treat this boy with chemotherapy only and to accept the risk of withholding radiotherapy.

The favourable outcome in this case shows that long term survival is possible in rhabdomyosarcoma, even with bone marrow metastases and lymph node and meningeal involvement. Relapse free survival is now more than 38 months. In childhood rhabdomyosarcoma a follow up period of three years from diagnosis is considered adequate. Therefore, we have reason to feel this child is cured. Although cytostatic agents, as used in our patient, may also have late sequelae, at this moment a small scar from the biopsy is the only noticeable local remnant of disease and treatment.

During the past two decades, there have been considerable improvements in chemotherapy for rhabdomyosarcoma. Like major pelvic surgery, radiation therapy in head and neck rhabdomyosarcoma may cause serious mutilation. In our opinion, studies aimed at elimination of radiotherapy in head and neck rhabdomyosarcoma, using more effective chemotherapy, are to be supported.

We thank our colleagues and other members of the paediatric oncology team who contributed to the care of this patient.

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References

Isolated myocarditis in the first year

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SUMMARY Over a period of nearly 40 years, 20 cases of isolated myocarditis were traced from 3086 necropsies. Seventeen occurred in infants less than 12 months of age, often with no antecedent clinical signs (sudden deaths) or with a short clinical history of less than 24 hours' duration.

A series of three infants dying from isolated myocarditis in a three month period prompted a review of the necropsy records of this hospital, tracing and comparing cases of 'isolated' and 'incidental' myocarditis.

Materials and methods

This hospital is the major referral centre in the province of Manitoba for children of all ages, and its pathology department performs most paediatric necropsies in the province.

The necropsy records and histological slides from 1945 onwards were searched for cases of myocarditis, and the histological slides were reviewed. Details of the sex, age, and heart weight of the accepted cases were abstracted and analysed. The clinical charts provided information on clinical details and results of any laboratory investigations. Where appropriate \( \chi^2 \) calculations using two by two tables were used to analyse the results.

Results

Thirty five confirmed cases of myocarditis were traced from the records of 3086 necropsies between January 1945 and June 1984. No difference in the sex ratios was discernible and the ages of the affected infants varied from 1 month to 14 years. Of the 35 affected cases, 21 were 12 months or less in age.

In 20 cases the heart was the primary organ affected and the only changes in other organs were due to cardiac failure ('isolated' myocarditis). In the remainder, myocarditis was part of a generalised infection and these cases were classified as examples of 'incidental' myocarditis (Table 1). Seventeen of the 20 cases of isolated myocarditis occurred in infants 12 months of age or less, whereas only three cases of isolated myocarditis occurred in older children. This difference in the incidence of isolated myocarditis between infants (12 months or less) and older children is highly significant (\( P<0.001 \)).

Due in part to a lack of suspicion of the underlying disease, appropriate cultures were submitted in only six of the 20 cases, who were later found to have isolated myocarditis on histologic examination. From one of these infants a Coxsackie B viral strain was isolated and an imported case of acute myocarditis due to \( T \) cruzi (Chagasic myocarditis) was identified histologically and ultrastructurally.

<table>
<thead>
<tr>
<th>Age</th>
<th>Cases of myocarditis</th>
<th>Total</th>
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<td>7-12 months</td>
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<td>&gt;12 months-14 years</td>
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*The difference in incidence between infants and older children is highly significant (\( P<0.001 \)).