

Breast Malignancy in Children

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● In 25 years, 18 patients with breast cancer were treated at St Jude Children's Research Hospital, 16 were female and 2 were male. The patients presented with primary malignancy (2), metastatic disease (13), or secondary malignancy (3). One of the females with primary breast malignancy had alveolar rhabdomyosarcoma. She was treated with wide excision and is currently receiving chemotherapy. The other patient presented with non-Hodgkin's lymphoma of the right breast. After biopsy, she was treated with chemotherapy. Of 13 patients with metastatic disease, the primary lesion was rhabdomyosarcoma in nine. One patient each had non-Hodgkin's lymphoma, Hodgkin's lymphoma, neuroblastoma, and signet-cell adenocarcinoma. All patients with metastatic disease to the breast died of the disease. Three females presented with invasive ductal carcinoma of the breast after treatment for Hodgkin's disease. Two underwent mastectomy and are alive without evidence of disease. One patient refused therapy and died of the second malignancy. We conclude that (1) breast malignancies had three distinctly different presentations in our patients, (2) the breasts of pediatric oncology patients should be carefully and routinely examined for metastatic disease, and (3) metastatic disease in the breast of a child is a manifestation of disseminated disease and is associated with an extremely poor prognosis. Copyright © 1994 by W.B. Saunders Company

INDEX WORDS: Breast, malignancy, children.

MALIGNANCY of the breast is rare in children. The purpose of this report is to describe the cases of breast cancer treated at an institution that specializes in the care of pediatric oncology patients.

MATERIALS AND METHODS

Patients with malignancies of the breast were identified, and their charts were reviewed. Information was gathered regarding patient demographics and the details of management. This included an analysis of the role of chemotherapy, radiation, and surgery. The complete medical records of patients with second malignancies were obtained from the hospital at which they were treated.

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RESULTS

Eighteen patients were identified—16 females and two males. There were three distinct patient groups.

Primary Malignancy Group

There were two patients in this group. The first was a 14-year-old girl who presented with a painless, gradually enlarging mass in the upper inner quadrant of the right breast. A mammogram was obtained, and a biopsy was performed. When the histological diagnosis of alveolar rhabdomyosarcoma was made, computed tomography (CT) scans of the neck, abdomen, and pelvis were obtained. All the results were normal. The chest CT scan showed only the residual primary lesion. Proctoscopy, cystoscopy, and a pelvic examination (with the patient under anesthesia) showed no other evidence of disease. The patient underwent wide local excision and is currently receiving multi-agent chemotherapy on the current prospective St Jude protocol for rhabdomyosarcoma. Because the margin of resection was negative, radiation therapy was not used.

The second patient was a 14-year-old girl who presented with an 8- × 7-cm mass in the subareolar mass, with a single enlarged axillary node. A biopsy of the breast mass was performed, which showed lymphoblastic-type non-Hodgkin's lymphoma. A CT scan showed pulmonary involvement. She was treated with chemotherapy, and the breast mass and axillary adenopathy resolved. She is currently in complete remission.

Metastatic Disease Group

Thirteen patients had metastatic disease in the breast (Table 1). The primary was rhabdomyosarcoma in nine patients, and we have seen one case each of breast involvement with Hodgkin's lymphoma, non-Hodgkin's lymphoma, neuroblastoma, and adenocarcinoma. Seven cases of metastatic rhabdomyosarcoma of the breast have been reported previously.¹ We discovered two other cases of metastatic rhabdomyosarcoma of the breast (in adolescent girls). In one, the rhabdomyosarcoma occurred as a relapse; when the breast mass was discovered, there was also evidence of pulmonary metastatic disease. The patient was treated with chemotherapy but died of progressive disease. The other patient had a breast mass that was excised at the time of presentation;

Table 1. Profiles of Patients With Metastatic Disease of the Breast

Patient No./Sex	Age	Primary Site	Histology	Interval to Metastasis	Treatment of Metastasis	Outcome
2/F	12 yr 1 mo	Perineum	Alveolar rhabdomyosarcoma	15 mo	S, C	Died at 9 mo, progressive disease
3/F	16 yr	Arm	Primitive rhabdomyosarcoma	Presentation	S, C	Died, progressive disease
4/F	17 yr	NA	Hodgkin's lymphoma	16 mo	R, S, C	Developed AML, underwent bone marrow transplantation, no evidence of disease
5/F	14 yr 6 mo	Adrenal	Neuroblastoma	8 mo	None	Died at 1 mo, progressive disease
6/F	13 yr 11 mo	NA	Non-Hodgkin's lymphoma	Presentation	C	Died at 7 mo, progressive disease
7/F	15 yr	Unknown	Adenocarcinoma, signet-ring cell	Presentation	C	Died, progressive disease

Abbreviations: S, surgery; C, chemotherapy; R, radiation therapy; AML, acute myelogenous leukemia.

however, metastatic disease was found in a rib. She was treated with multiagent chemotherapy but died of progressive disease.

Of the four patients with diseases other than rhabdomyosarcoma, two had metastatic disease in the breast and died of progressive disease. Two developed a breast mass subsequent to treatment of the primary malignancy. Eight months after the original diagnosis, patient no. 5 presented with bilateral breast nodules and metastatic disease in the gingiva. She died of progressive disease. Patient no. 4 presented with a mass in the left breast 16 months after conclusion of her therapy for Hodgkin's lymphoma. The impression at the time of excision was that the mass was a fibroadenoma, but the final diagnosis was recurrent Hodgkin's lymphoma of an anterior axillary node. She was treated with additional chemotherapy and radiation therapy, and currently has no evidence of disease.

Secondary Malignancy Group

Three patients with nodular sclerosing Hodgkin's lymphoma subsequently had infiltrating ductal carcinoma of the breast (Table 2). All three received

mantle irradiation, and two had multiagent chemotherapy. The patients presented with an early-stage breast malignancy 12, 16, and 19 years after therapy for Hodgkin's lymphoma. Two of the patients who underwent modified mastectomy are alive; one is currently receiving chemotherapy. The third patient refused further therapy and represented with metastatic disease. She was treated with chemotherapy but died of progressive disease.

DISCUSSION

The overwhelming majority of masses that occur in the breasts of children and adolescents are benign.²⁻⁴ This is true at our pediatric oncology center as well. During the 25 years in which the 18 cases of malignancy were treated, there were 21 cases of documented benign masses. The most common diagnosis in these cases was fibrocystic change. There are relatively few reports of malignancies involving the breast in children and adolescents. In our experience we identified three distinct clinical presentations:

Table 2. Profiles of Patients With Breast Cancer Occurring as a Second Malignancy

Patient No./Sex	Age (yr)	First Malignancy			Age (yr)	Second Malignancy				
		Histology	Chemotherapy	Radiation Therapy		Histology	Surgery	Radiation Therapy	Chemotherapy	Outcome
8/F	24	Hodgkin's lymphoma (nodular sclerosing, stage IIIA)		Cobalt Mantle 35 Gy L neck 2.9 Gy	43	Poorly differentiated infiltrating ductal carcinoma, T1N0 M0	Mastectomy	None	Adriamycin, Cytoxan	Alive without disease, receiving chemotherapy
9/F	13	Hodgkin's lymphoma (nodular sclerosing, stage IIB)	CCNU, Adriamycin, Velban	Cobalt Pelvis 35 Gy Sacrum 2.5 Gy Abd 35 Gy Neck 35 Gy Mantle 35 Gy Femur 35 Gy (relapse)	29	Infiltrating ductal carcinoma, T1N0 M0	Biopsy	None	Vinblastine	Died at 8 mo, progressive disease
10/F	16	Hodgkin's lymphoma (nodular sclerosing, stage IIA)	Vincristine, cyclophosphamide (for relapse)	6 MEV Mantle 37 Gy L neck 2 Gy Paraortic 32 Gy	28	Infiltrating ductal carcinoma, T1N0 M0	Mastectomy	None	None	Alive at 4 yr, without disease

primary malignancy, metastatic involvement, and secondary malignancy.

Primary malignancy of the breast is extremely rare in children, but carcinomas,⁵⁻¹⁰ sarcomas,^{11,12} and lymphomas¹¹ have been reported. Carcinomas should be managed as in the adult. The option of breast-conserving procedures for early-stage carcinoma for children has not been addressed but should be dependent on the patient's age and breast size. Cystosarcoma phyllodes is the most common sarcoma of the breast in this age group. It can be managed by wide local excision without axillary dissection.^{13,14}

Primary rhabdomyosarcoma of the breast is extremely rare. This prompted the extensive search for a primary lesion in our patient. Treatment of this lesion is governed by the principles used for rhabdomyosarcoma, which include wide local excision of the primary lesion, and use of multiagent chemotherapy.^{15,16} The location of the tumor in the breast parenchyma in our patient was favorable in that it permitted a wide excision and an acceptable cosmetic result.

Non-Hodgkin's lymphoma can occur as a primary process in the breast,¹¹ as it did in our patient, or the breast may be involved as a site of metastasis. In both presentations, surgical therapy is limited to an adequate biopsy.

The second presentation of malignancy of the breast is metastatic involvement. The two new cases of rhabdomyosarcoma described in this report are similar to those reported previously.^{1,17-19} Specifically,

metastatic disease in the breast is generally associated with metastatic disease elsewhere, and ultimately with a very poor prognosis. This is also true of other forms of metastatic disease in the breast. If a patient undergoing treatment for a childhood malignancy presents with a breast mass, we advocate fine needle aspiration before incisional or excisional biopsy. A complete metastatic workup should also be performed. The role of further surgical therapy in these patients is limited.

It has been reported that carcinoma of the breast can occur as a second malignancy in patients treated for other malignancies during childhood.²⁰⁻²³ The contribution of the management of the primary childhood malignancy to the subsequent development of breast cancer is not clear, although both multiagent chemotherapy and radiation therapy have been implicated as increasing the risk for this second malignancy.^{20,21}

It is doubtful that a pediatric surgeon will treat these patients because the second malignancy generally occurs in adulthood. The primary involvement of the physicians caring for the patient during childhood includes maintaining a complete medical record. Chemotherapeutic regimens and radiation ports may impact on the subsequent management of the patients' breast malignancy. For example, previous irradiation to the mediastinum and axilla may preclude lumpectomy and radiation therapy as options in the treatment of breast cancer. Similarly, toxicity from chemotherapy may affect the chemotherapeutic options.

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