

# RESECTION OF METASTASES IN WILMS' TUMOR: A REPORT OF THREE CASES CURED OF PULMONARY AND HEPATIC METASTASES

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**ABSTRACT.** Three cases of Wilms' tumor metastatic to both the lungs and liver are described. The first case had pulmonary metastases on three occasions. The initial episode was treated with radiation, the second by excision, and the third by combined chemotherapy. The second case also had three recurrences of pulmonary metastases; the first two were treated by excision and the third was treated by radiation followed by excision of residual tumor. Pulmonary involvement occurred only once in the third case and was treated by combined radiation and actinomycin D.

All three cases had hepatic metastases. Hepatic lobectomy was employed in two cases and radia-

tion was used in a third. The apparent cure of these cases emphasizes the importance of vigorously applying the therapeutic modalities currently available.

The frequent use of surgical excision in these cases was based upon three advantages of this modality: minimal damage to normal tissues, undiminished effectiveness on repeated use, and ability to discover metastases otherwise undetectable. The indications for resection for pulmonary metastases are discussed. Hepatic lobectomy, previously unreported in Wilms' tumor, would appear to merit more extensive use. *Pediatrics*, 41:446, 1968, NEPHROBLASTOMA, HEPATECTOMY.

**E**XCISION of pulmonary metastases of Wilms' tumor with apparent cure has been previously reported (Table I). Encouraged by these reports, we have placed increased emphasis upon the use of metastasectomy in addition to the usual modalities of radiation and chemotherapy in suitable cases of Wilms' tumor. The present report of three cases serves to reassert the useful therapeutic role metastasectomy can play in the management of both pulmonary and hepatic metastases. The discussion centers on the advantages of this mode of therapy and the indications for its use.

## CASE REPORTS

### Case 1

In June 1961 a 5-year-old boy had a left nephrectomy and postoperative cobalt radiation (2150 R/t)\* for Wilms' tumor. Multiple pulmonary radio-

\* R/t = minimum tumor dose in roentgens.

densities were treated with cobalt radiation (dose range—1130 R/t to 1520 R/t). The pulmonary metastases, which prior to treatment had increased in size and number, disappeared completely.

**FIRST RECURRENCE:** In October 1961 the liver became enlarged. An easily palpable mass was present on its surface. An I<sup>131</sup> Rose Bengal scan of the liver revealed an 8 cm defect in the right lobe. A 5-day course of 5-fluorouracil (15 mg/kg/day I.V.) reduced the size of the defect on liver scan but did not eliminate it. Therefore, in November, cobalt radiation (460 R/t) was applied. Within a month the liver scan had returned to normal.

**SECOND RECURRENCE:** In June 1962 a pulmonary metastasis in the superior segment of the right lower lobe was resected. During thoracic exploration, palpation through the diaphragm revealed a nodule on the superior surface of the liver. On July 3, a 3 cm tumor nodule in the right lobe of the liver was excised by a right hepatic lobectomy.

**THIRD RECURRENCE:** In September 1962 a chest x-ray revealed multiple metastases throughout both lung fields. A 3-week course of combined chemotherapy (methotrexate, 2.5 mg orally/day; chlorambucil 0.2 mg/kg/day orally, and actinomycin

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D 50  $\mu\text{g}/\text{kg}$  I.V. once a week) produced complete disappearance of the metastases.

He has remained well and free of disease for the subsequent 5½ years.

### Case 2

A 26-month-old girl had a left nephrectomy and postoperative radiation in July 1961 for Wilms' tumor. No metastases were present at that time.

**FIRST RECURRENCE:** In May 1962 a nodule in the right lower lobe was visualized (Fig. 1). At thoracotomy this 1 cm tumor nodule in the right lower lobe was removed by wedge resection. A superficial nodule noted in the right upper lobe was also excised, but on microscopic examination it proved to be only hematoma formation.

**SECOND RECURRENCE:** In October 1962 a 6 cm nodule (Fig. 2) was removed by resection of the apical and posterior segment of the right upper lobe. A liver scan was normal.

**THIRD RECURRENCE:** In February 1963 a small nodule was noted in the incision line and a large mass in the right hilus was seen (Fig. 3). Liver scan revealed hepatic enlargement and a diffuse filling defect in the superior border. Cobalt radiation (3000 R/t) was administered to the right lower chest and right upper abdomen over the period from February 19 to March 16. Some decrease in the size of the chest lesion was noted by March 7 (Fig. 4), but none thereafter. Repeat liver scan revealed persistence of the filling defect.

When it became apparent that total resolution would not be achieved by radiation, surgical intervention was undertaken. Thoracotomy on April 24 revealed a 6 cm mass lying on the anterior and right lateral pericardium extending laterally to the mid portion of the right anterior diaphragm. The tumor was excised in continuity with a portion of the pericardium and right diaphragm. In addition, separate tumor nodules were removed from the wall of the inferior vena cava, the right lower lobe, and the old incision.

No further therapy was used. The postoperative lung changes gradually cleared. The liver scan became normal. She has been subsequently free of disease for 4 years. There are some residual pleural changes in the right costophrenic angle and a chest deformity secondary to the resection of ribs 4 through 6 is present (Fig. 5).

### Case 3

In July 1964 a 10-month-old boy had a left nephrectomy for Wilms' tumor. The tumor was encapsulated. Resected abdominal nodes were free of tumor.

**FIRST RECURRENCE:** In March 1965 a grapefruit-sized subxiphoid mass was noted. Liver scan revealed uneven uptake in the left lobe of the liver. Several large tumor nodules were removed by a

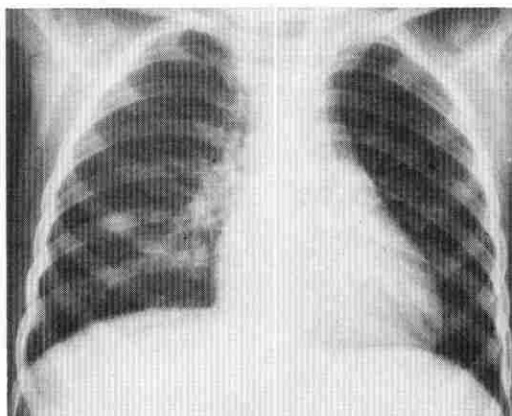


FIG. 1. Case 2. Twenty-six-month-old girl, left nephrectomy for Wilms' tumor July 1961. Solitary nodule in right mid lung field excised May 1962.

left hepatic lobectomy. The remaining liver was free of tumor on gross inspection. Fluoroscopy of the chest 2 days postoperatively revealed a suspicious lesion in the left hilus which had not been recognized on plain chest films. He therefore received a 5-day course of actinomycin D (15 mg/kg/day I.V.) together with cobalt radiation to both lung fields (1400 R/t) and the left upper abdomen (300 R/t).

He is well and free of disease 2 years post hepatic lobectomy.

### COMMENT

Metastatic Wilms' tumor can no longer be considered incurable. In addition to numerous individual case reports, there are several series of cases<sup>1,2</sup> which indicate that

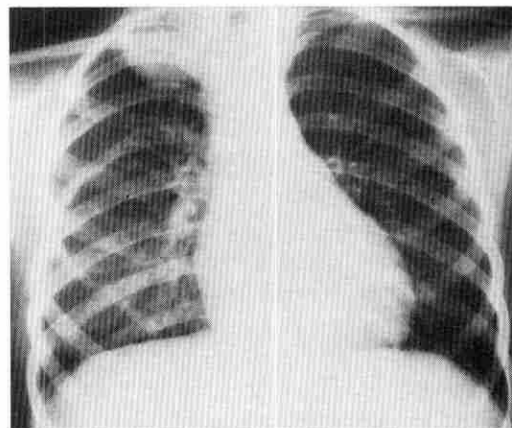


FIG. 2. Solitary metastasis in apex of right lung excised October 1962.

TABLE I  
SUMMARY OF ALL REPORTED CASES OF PULMONARY METASTASECTOMY IN WILMS' TUMOR

Reference	Number of Cases Reported	Age at Nephrectomy	Interval Until Metastasectomy*	Results†	Comments
12	1	4 yr	17 yr	Alive 18 mo	Chest x-ray negative at 14 yr of age.
18	1	5 yr	9 mo	Died 7 mo	
19	1	—	7 mo	Alive 42 mo	Tabular data only
20	1	—	—	Died 23 mo	Tabular data only
21	1	3½ yr	2¼ yr	Died 13 mo	
22	2	2½ yr	10 mo	Alive 49 mo	Metastasis appeared after 2 mo., treated with x-ray, recurred; at 10 mo lobectomy done.
13	1	6 yr 5 yr	7 mo 5 yr	Mediastinal recurrence 11 mo Died 6¼ yr	Abdominal recurrence, no pulmonary disease.
14	1	6 yr	13 mo	Alive 6 yr	
23	1	—	—	Alive	"Patient has not lived long enough (for survival) to be evaluated."
24	1	—	—	—	Tabular data only.
15	1 (Case 6)	3 yr	8 mo	Alive 20 mo	
25	17	—	—	14 alive—13 over 2 yr and 4 alive for over 5 yr	
11	1	21 mo	13 mo	Alive 10 yr	
26	1	33 yr	81 mo	Died 30 mo	
1	7 cases, all of whom had failed actinomycin D and radiation	—	—	3 alive after 4½ to 5 yr 1 died of liver metastases after 6 mo 1 died of radiation nephritis 4 yr after resection 1 died pulmonary recurrence 1 died cerebral metastasis without pulmonary residual	
2	11	—	—	Results not stated; at least one survivor	2 operated on twice
27	2	6½ yr 2½ yr	24 wk 9 mo	Alive 61 mo Alive 47 mo	Metastases appeared after three courses of actinomycin D, responded poorly to radiation, ? had three courses of actinomycin D. postmetastasectomy. Cyclophosphamide for 28 da after nephrectomy
3	4	—	—	Alive 33 mo Died Died Died	Actinomycin D, vincristine and radiation given 2 mo prior to pneumonectomy "resection could not be achieved" "shock during the operation" Developed bilateral Wilms' tumor

\* From date of nephrectomy.

† From date of metastasectomy.

a substantial proportion of patients with pulmonary metastases may be successfully treated. The three cases in this paper further indicate that not only extensive and recurrent pulmonary metastases, but also hepatic metastases, can respond to the unrelenting application of the diagnostic and therapeutic methods currently available.

These results are achieved by taking advantage of two favorable characteristics of Wilms' tumor. The first is that metastases in Wilms' tumor tend to be localized to the lungs.<sup>2-4</sup> When more than one site in the body is involved, the lungs have usually

been the first organ affected.<sup>2</sup> This predilection for the lungs permits early detection and objective evaluation of response to therapy. The liver is the next most common site of metastasis.<sup>2-4</sup> Isotopic scanning techniques have improved our diagnostic ability in this area. Other sites such as brain and bone are infrequently involved.<sup>2-4</sup>

The second favorable characteristic of metastatic Wilms' tumor is its responsiveness, not only to surgical excision, but also to radiation and chemotherapy. This responsiveness is well illustrated in our cases, where radiation and chemotherapy were

major factors in the therapeutic management. The use and curative potential of these two modalities have been discussed extensively elsewhere.<sup>5,6</sup> We will, therefore, confine our discussion to the role of metastasectomy in the treatment of Wilms' tumor.

The surgical excision of metastases in Wilms' tumor has the following advantages.

#### **Metastasectomy Is Diagnostic as Well as Therapeutic**

Lee<sup>7</sup> has shown that nodules too small to be visualized roentgenographically are detectable by direct examination of the lung. This is illustrated in Case 2 where a small nodule was discovered during exploration. Schweisguth and Bamberger<sup>2</sup> have reported three similar cases. In one of our cases not reported here, a nodule was seen on chest x-ray and excised. The nodule was found to be benign, thus sparing the child any further therapy. The discovery of hepatic metastases during pulmonary surgery was important in the management of Case 1.

#### **Metastasectomy Produces Minimal Damage to Normal Tissues**

Deformity of the chest secondary to rib resection has been slight, except in Case 2 where three ribs had to be removed. Little or no functional impairment is to be expected in patients undergoing resection of a portion of one lung. Removal of 80% of the liver is not attended by any serious deficit in hepatic function.<sup>8</sup> Radiation and chemotherapy, by comparison, have in the past produced pulmonary fibrosis, lung cysts, hyperlucent lung, muscle deformities, abnormalities of bone growth, scoliosis, hepatitis, nephritis, telangiectasia, and secondary induction of malignancy.<sup>9,10</sup> Much of this was, however, associated with relatively high dose radiotherapy with orthovoltage equipment. The use of more advanced technique has eliminated much of this morbidity. The occurrence of these complications at higher dosage does, however, set an upper limit on the total amount of radiation and chemotherapy which may be applied.

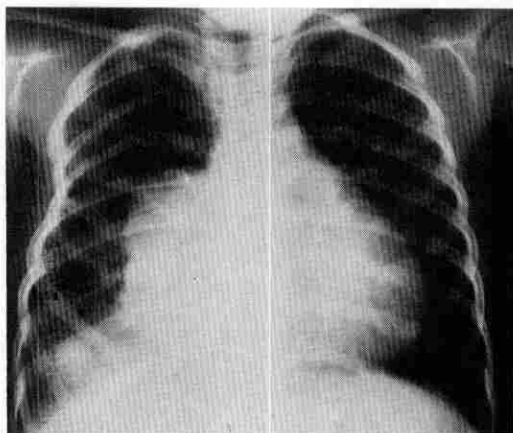


FIG. 3. Large mediastinal mass extending over right diaphragm irradiated February 19 to March 16, 1963.

#### **Metastasectomy May be Performed Repeatedly Without Loss of Effectiveness**

Cellular resistance, which may develop against radiation and chemotherapy, obviously does not occur with surgical removal.

In the treatment of pulmonary metastases surgical excision is usually reserved for the "solitary lesion" or a few metastases localized to a lobe or smaller subdivision of the lung. Generalized metastases remain in the province of radiation and/or chemotherapy. If, however, radiation and chemo-

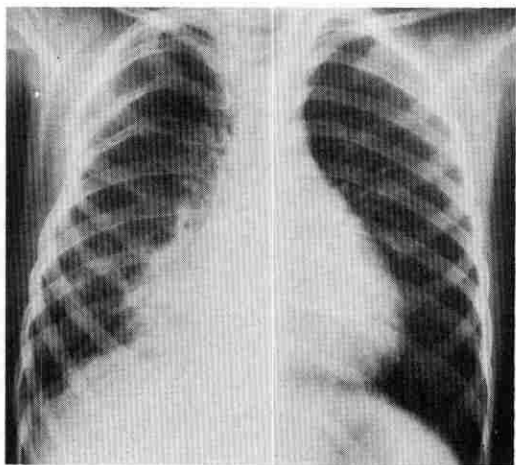


FIG. 4. Size of mediastinal mass prior to surgical removal on April 24, 1963.



FIG. 5. Recent chest film showing residual scarring and rib deformity. Child is well.

therapy have failed, pneumonectomy<sup>3</sup> and bilateral excisions<sup>2</sup> have been used.

The treatment of the solitary pulmonary metastasis, when it happens to be the first metastasis to develop, is a matter of debate. Since the first appearance of pulmonary metastases is usually multiple, many authors believe that the "solitary metastasis," in lungs previously untreated, is seldom truly solitary, but rather is merely the only detectable metastasis. Cases, such as our Case 2, which recur after local treatment would further support this belief. Therefore, some would favor the primary use of radiation and/or chemotherapy to clear the lungs of the undetectable metastases. Any solitary recurrence or residual tumor would then have a greater chance of being truly solitary and amenable to cure by excision.

On the other hand, successful use of metastasectomy as the first and only treatment of a pulmonary metastasis has been reported<sup>11-15</sup> indicating that pulmonary metastases are not always multiple. Schweisguth and Bamberger<sup>2</sup> have advocated the combined use of actinomycin D and surgical excision as the primary treatment of the solitary metastasis.

We have found that an extensive search is required before a conclusion can be

reached regarding the actual number and distribution of metastases. Our routine includes skeletal survey, chest films including the apical lordotic and both oblique projections, laminography of the chest, and isotopic scanning of the liver. This information is essential to the intelligent selection of the therapy most appropriate for a particular patient.

With regard to hepatic metastases, there has been only one cure reported in the literature. This 4-year-old boy, reported by Schweisguth and Bamberger,<sup>2</sup> was cured of an hepatic metastasis by radiation (2100 R) and actinomycin D. He was reported free of disease 42 months following his last treatment. These same authors treated 12 other cases similarly without success. In our Case 2, some question can be raised as to whether the isotopic liver scans were conclusive evidence of hepatic involvement. The defect in the superior border may have been caused by pressure of the adjacent mediastinal tumor. On the other hand, there was definite enlargement of the liver compared to a previous scan, and following radiation there was a decrease in liver size. The scans were interpreted at the time as unequivocally indicative of metastatic involvement. If this evidence is accepted, our Case 2 would be the second reported cure of hepatic metastases by radiation.

Our Cases 1 and 3 are the first reported cases of surgical cure of hepatic metastases of Wilms' tumor. They are the only two in which the diagnosis was confirmed by microscopic examination. Although partial hepatectomy has become a well established procedure for many other tumors metastatic to the liver,<sup>8,16</sup> its use has been reported only twice in Wilms' tumor. Sutow, *et al.*<sup>17</sup> reported a case free of disease 8½ months following a left hepatic lobectomy. Silva-Sosa and Gonzales-Cerna<sup>3</sup> performed a right hepatic lobectomy for a metastasis noted during nephrectomy. No follow-up was given for this child. The excellent result obtained in our two cases would encourage the more frequent use of hepatic lobectomy in metastatic Wilms' tumor.



## SUMMARY

Three cases of Wilms' tumor with hepatic and pulmonary metastases are presented. Their apparent cure emphasizes the need for aggressive treatment, even in the face of a seemingly hopeless situation. Metastasectomy has played a prominent role in all three cases. The advantages of metastasectomy are outlined and the indications for its use are discussed.

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