Residual Abdominal Masses after Chemotherapy for Nonseminomatous Testicular Cancer: Correlation of CT and Histology

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Computed tomographic (CT) characteristics of 45 residual masses in 30 patients with disseminated nonseminomatous testicular cancer treated with chemotherapy were correlated with histologic findings at surgery. Thirty-one masses were studied serially on pre- and postchemotherapy scans. At the time of tumor-reductive surgery, all patients had normal serum tumor markers (alpha-fetoprotein and human chorionic gonadotropin). Residual malignancy was found in 27% of patients, teratoma in 33%, and fibrosis or necrosis in 40%. The CT appearance of the masses—size, qualitative density, and change noted during the course of treatment—was insufficient to exclude the presence of residual malignancy or teratoma. An enlarging mass of psoas density occurred only once in this series; it contained malignancy. Other CT characteristics of residual masses had no greater than 50% correlation with the presence of malignancy. Histologic evaluation of residual masses remains necessary to guide further patient management.

Although testicular cancer accounts for only 19% of all cancer deaths and affects only 2.1–2.2 males per 100,000 in the U.S. annually, it is the most common malignancy in men aged 20–34 years. About 95% of testicular cancers are germ-cell tumors; 60% are nonseminomatous, with or without seminoma, and 40% are pure seminoma [1]. Before multiagent chemotherapy was used in conjunction with surgery, patients with metastatic disease had a mortality rate of 80%–90% [2]. Combination chemotherapy (cisplatin, vinblastine sulfate, and bleomycin sulfate) has produced complete response rates of 70% [3, 4]. This regimen followed by tumor-reductive surgery has rendered 60%–83% of patients disease free for 3–4 years after treatment [4, 5]. Ultimate cure depends on the achievement of a complete remission.

The role of CT and serum tumor-marker assays in the posttreatment evaluation of metastatic testicular cancer has been described in several reports [5–9]. Specifically, the potential use of CT to differentiate between residual masses of malignancy, teratoma, and fibrosis or necrosis has been addressed by Husband et al. [10] and Scatarige et al. [11]. In our series, all patients had nonseminomatous germ-cell tumors and had been treated with both chemotherapy and surgery at the Dana-Farber Cancer Institute and the Brigham and Women's Hospital in Boston. Our series of CT scans and histologic evaluations was undertaken to further define the role and accuracy of CT in this setting.

Materials and Methods

Seventy-four abdominal and pelvic CT scans obtained between 1979 and 1985 were reviewed. The study group consisted of 30 patients with disseminated nonseminomatous testicular cancer who underwent tumor-reductive surgery for persistent masses (45 masses) after four cycles of vinblastine, bleomycin, and cisplatin. Patient selection depended on availability of CT scans. Patient median age was 26 years (range, 20–45 years). The original histologic diagnosis was made by inguinal orchiectomy in each patient. Of the group, 70% had mixed germ-cell tumors (embryonal, teratoma, choriocarcinoma, and/or yolk sac) with or

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without seminoma; in 30%, embryonal-cell carcinoma was the preponderant tumor type. Associated abdominal masses were not biopsied before chemotherapy but were presumed to be metastatic.

Tumor-reductive surgery was performed within 3 weeks of post-chemotherapy CT scans in all patients. Serial scans taken both before or after treatment were available on 20 patients (31 masses). Most of the scans were performed at the Brigham and Women's Hospital on an Ohio Nuclear Delta 2020 scanner; others were obtained elsewhere. Scans were obtained at 1-cm intervals (1-cm-thick slices) after the administration of oral and intravenous contrast medium. Masses were categorized according to size and density on the CT scans. Size was described as the single greatest dimension in any plane. Density was determined by visual inspection of the scans and categorized as psoas density (equal to that of the psoas muscle), uniform low attenuation (less dense than the psoas muscle with a homogeneous or thin-walled "cystic" appearance), and mixed (low attenuation with solid or septate components).

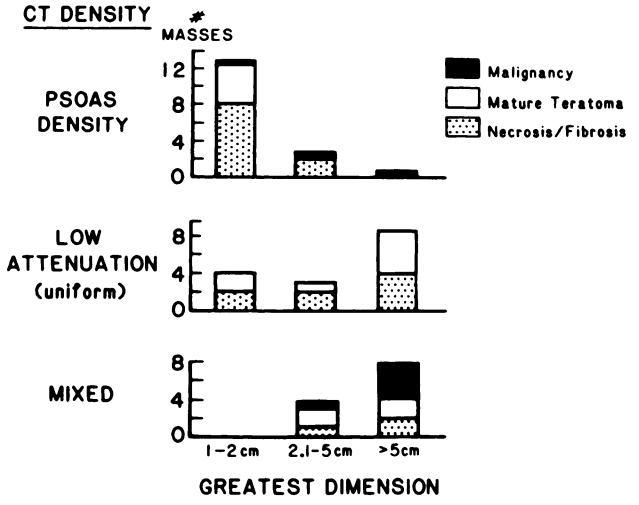


Fig. 1.—Greatest CT dimension and histologic diagnosis of residual masses.

For all patients in this study, surgery was performed on the basis of two criteria: (1) the presence of a single residual mass greater than 1.5 cm in diameter or of multiple masses greater than 1 cm; (2) normal levels of serum tumor markers (alpha-fetoprotein [AFP] and human chorionic gonadotropin [HCG]). The location and histology of residual masses were obtained from surgical and surgical pathology reports and diagrams. Histology was categorized as malignant if any component of malignancy was present and as teratoma if there was no evidence of malignancy but a component of teratoma. All others were categorized as necrosis and/or fibrosis.

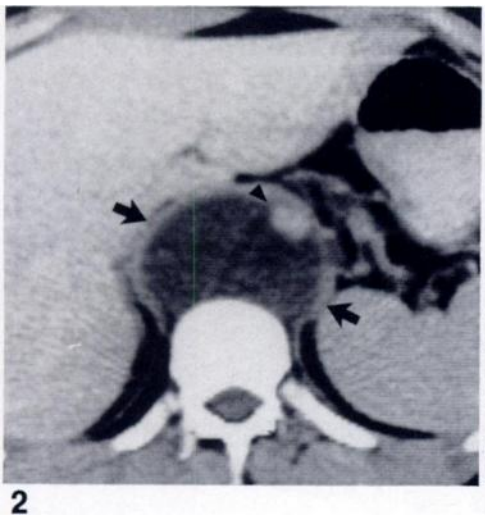
Results

Eight (27%) of 30 patients had residual malignancy. Ten patients (33%) had teratoma without evidence of malignancy, and 12 (40%) had fibrosis and/or necrosis only. Of 45 residual masses in 30 patients, eight (18%) were categorized as malignant, 17 (38%) as teratoma, and 20 (44%) as fibrosis and/or necrosis.

Correlation of CT Density and Histology

Seventeen residual masses exhibited uniform CT density equal to that of the psoas muscle. Three (18%) contained malignancy, four (23%) were teratoma, and 10 (59%) consisted of fibrosis and/or necrosis (fig. 1). In 16 other masses that showed uniform low attenuation, there was no evidence of malignancy. Eight (50%) were teratoma and eight (50%) necrotic material (fig. 2). The remaining 12 masses were of mixed density. Each of the five masses (42%) in this group that contained malignancy consisted predominately of gross areas of necrosis associated with a small or microscopic malignant component. Five (42%) were teratoma and two (16%) represented necrotic material only (fig. 3). Histologically, low-attenuation regions in this series of masses corresponded to areas of necrosis with lipid-laden macrophages, regions of prior hemorrhage in several cases containing choriocarcinoma, and epithelial-lined cystic spaces of teratoma.

Of the 31 masses that were studied before and after



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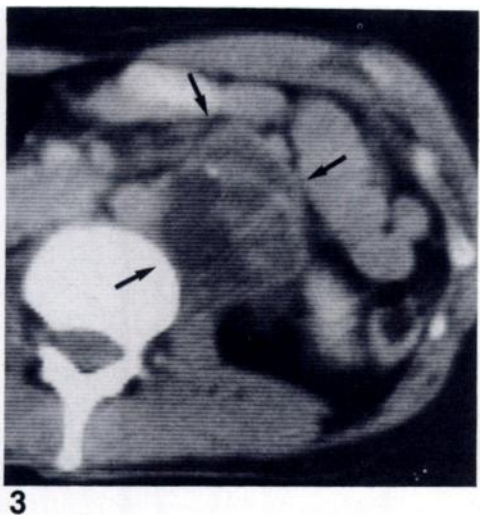

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Fig. 2.—Postchemotherapy scan. Enlarging, 8-cm low-attenuation retrocrural mass (*arrows*). Aorta is displaced anteriorly (*arrowhead*). Histology: cystic teratoma without active malignancy.

Fig. 3.—Postchemotherapy scan. Mixed-density, 6-cm left paraaortic mass (*arrows*), which had identical appearance on prechemotherapy scan. Histology: large area of necrosis containing small focus of malignancy.

chemotherapy, only three underwent a change in density that was appreciable by visual analysis. A psoas-density mass developed areas of low attenuation (mixed), and histologic evaluation demonstrated mature teratoma. A mixed-density mass and a uniform low-attenuation mass both decreased in size during the course of therapy and assumed a uniform psoas density. On histologic examination, both proved to contain fibrosis. Density of the remaining masses did not change appreciably during the course of treatment.

Correlation of CT Size and Histology

Seventeen residual masses measured 1–2 cm in greatest dimension, and one of these contained active malignancy. (This represented one of six patients who had only masses of 2 cm or less.) Six masses contained teratoma, and 10 represented fibrosis. Of 10 masses measuring 2.1–5 cm, two were malignant and three were teratomas; of the 18 larger than 5 cm in greatest dimension, five contained malignancy and seven contained teratoma.

Ten of 31 masses evaluated on serial scans demonstrated a reduction in greatest dimension of more than 70% during therapy (fig. 4). Two contained persistent malignancy and one contained teratoma; the rest were fibrosis (fig. 5). Two of 14 masses that decreased less than 70% during therapy contained malignancy, and four contained teratoma. The rest represented fibrosis. Four masses that remained the same size during therapy contained fibrosis. One of the three masses that grew represented malignancy; two were teratomas.

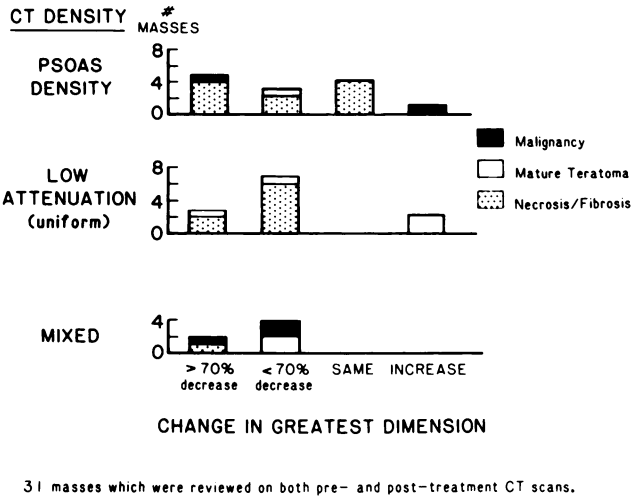

Fig. 4.—Serial change of greatest CT dimension and histologic diagnosis of residual masses.

Discussion

CT in conjunction with serum tumor markers (AFP and HCG) offers the best noninvasive means to assess the response of metastatic nonseminomatous testicular germ-cell cancer to therapy. Earlier studies correlating CT findings and postchemotherapy lymph-node dissection have demonstrated lack of active malignancy in those cases where the lymph-node size has returned to normal limits by strict CT criteria (less than 1.5 cm diameter or 20 ml volume) [5, 10, 12]. Thus, patients with negative serum markers and complete tumor remission by CT scan did not undergo surgery during the period of this study but are being followed closely. The incidence of malignancy in patients with residual masses has been reported to be 32%–37%, as compared to 27% in this study group [5, 9, 13]. The ideal role of noninvasive testing would be accurate differentiation of postchemotherapy residual masses containing malignancy, necrosis, or the teratomas unique to this disease. Further treatment options at present would then include additional chemotherapy for residual malignant masses and follow-up for necrotic or fibrotic masses. Adequate surgical resection is recommended for teratoma

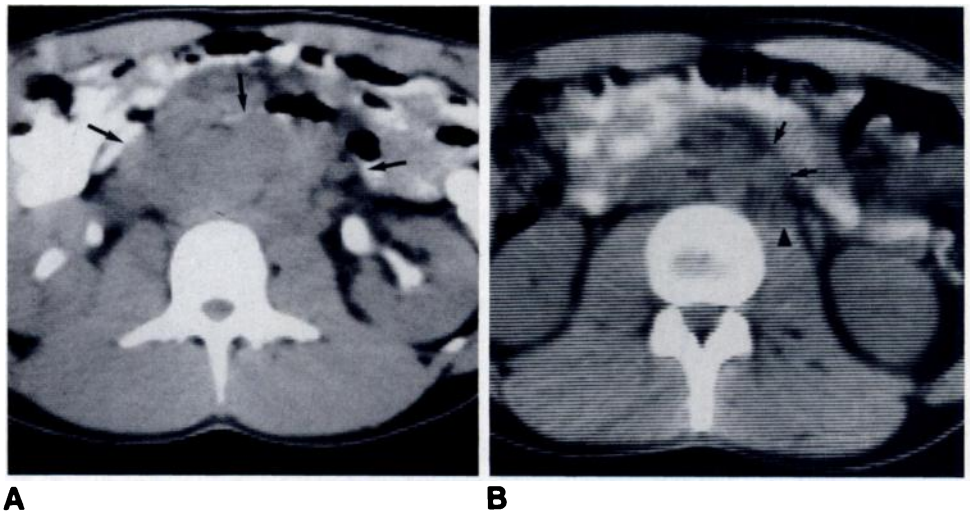

Fig. 5.—**A**, Prechemotherapy scan. Psoas-density, 20-cm retroperitoneal nodal mass extends from upper abdomen through pelvis. **B**, Postchemotherapy scan. Psoas-density, 1.5-cm left paraaortic mass (*arrows*), 1-cm node adjacent to left psoas muscle (*arrowhead*), and several nodes measuring 1 cm or less on other sections are only evidence of residual mass. Histology: 1.5-cm left paraaortic node contained active malignancy. Several smaller nodes were fibrotic.

due to the potential for local growth and uncertain malignant potential [5, 14].

Various CT appearances of nodal metastases and several examples of overlap in the appearance of benign and malignant residual masses were described by Soo et al. [15] and Zingas et al. [16]. Husband et al. [10] correlated histology with mean CT attenuation numbers and volumetric measurements in 36 patients with nonseminomatous germ-cell tumors who had residual masses after chemotherapy. Twenty-six patients were examined both before and after chemotherapy. For residual masses greater than 20 ml, no correlation was observed between residual tumor volume or change in volume during therapy and the presence or absence of malignancy. Residual masses with a density greater than 30 H that demonstrated stable or increased density during the course of therapy correlated with active malignancy. No masses of low attenuation contained malignancy. Scatarige et al. [11] later reported three patients with low-attenuation masses after chemotherapy. Each had extensive necrosis, but two also had persistent malignancy within the mass.

Our experience again demonstrates no correlation between the size or change in size during treatment of a residual mass and the histology. Masses that grew during therapy contained malignancy or teratoma. Masses that markedly diminished contained malignancy, teratoma, or fibrosis.

In this study, there was poor correlation between CT density of the residual masses and histologic findings. The presence of a small or microscopic focus of malignancy in a larger necrotic mixed-density mass was seen in five of eight malignant masses and could not be differentiated on the CT image. No malignancy was found in masses of uniform low attenuation in this series. At present, surgical excision of these masses will continue to be performed because of the unknown malignant potential of the teratomas and lack of differentiation from necrotic masses. Eight of these masses were present on prechemotherapy scans included in this study and may have represented components of teratoma or necrosis originally. The biology of teratomatous transformation in this disease is still under investigation. Since many of our patients received serial studies on scanners of different models, qualitative rather than quantitative (attenuation number) assessment of serial change in density was performed. The 26% incidence of inhomogeneous (mixed-density) masses in our series might have created a problem of sampling error with regard to a quantitative density measurement of a particular mass on serial scans.

The lack of appreciable density change in 28 of 31 masses including seven malignant masses in this study demonstrates that assessment of serial change in CT density in this manner will be of no value in most patients. However, note that the single case that exhibited an enlarging mass of psoas density during therapy contained malignancy. As suggested by Husband et al. [10], this finding, although rare in our experience, may suggest a greater risk of persistent malignancy. If a rather uniform distribution of malignancy within this enlarging mass is assumed, percutaneous needle biopsy of this small subgroup of masses could provide a histologic diagnosis of malignancy and preempt surgery in lieu of further chemotherapy in these patients. Other patients will continue to undergo surgical excision of residual masses to assess the response to chemotherapy and remove malignant tissue and teratoma.

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