Diagnosis: Carcinoid tumor of the thymus with extensive recent ischemic necrosis. Satellite tumor (probable lymph node metastasis).

Comment: Although focal necrosis is a common features of thymic carcinoid tumors, extensive infarction has not been described. Furthermore, necrosis was absent in the satellite tumor. It is probable that the infarction of the tumor resulted from vasoconstriction associated with smoking crack cocaine several hours before the chest pain developed.

Thymic Carcinoid Tumors

Classification: Thymic carcinoid tumors are rare tumors that most closely resemble well-differentiated neuroendocrine carcinomas (atypical carcinoid tumors) of the lung in their histologic appearance and behavior. In the thymus, they have a category of their own separate from thymic carcinoma, which includes small cell neuroendocrine carcinoma (table). It has been argued by some that carcinoid tumors should also be classified as a type of thymic carcinoma for the following reasons [1].

- They are not associated with paraneoplastic syndromes that are associated with thymoma
- They tend to metastasize to lymph nodes and extrathoracic organs as do thymic carcinomas
- The prognosis is similar to that of thymic carcinoma (1/3 alive at 5 y)
- A carcinoid component occurs occasionally in other types of thymic carcinomas

Table: Tumors of the Thymus [2]

Epithelial

Thymoma

Thymic carcinoma

Low grade

Well-differentiated squamous carcinoma

Well-differentiated mucoepidermoid carcinoma
Basaloid carcinoma

High-grade
Lymphoepithelioma-like
Small cell neuroendocrine carcinoma
Other: Adenocarcinoma, undifferentiated, sarcomatoid, and clear cell types

Other elements

Carcinoid tumor
Germ cell tumors
Lymphomas

Clinical features: Patients with thymic carcinoid tumors may present with symptoms related to compression of normal structures, or tumors may be found incidentally on chest radiographs (see table). The average age is 48.3 y, and the ratio of men to women is 4.3 to 1. About 10% of patients have Cushing's syndrome, and a similar fraction have a multiple endocrine neoplasia syndrome. Weight loss or the superior vena caval syndrome may be present. Other rare manifestations include Eaton-Lambert syndrome, the syndrome of inappropriate production of antidiuretic hormone, and hypertrophic osteoarthropathy [3]. An incidental thymic carcinoid tumor was described in a man with a thymoma that was associated with myasthenia gravis [4]. The carcinoid syndrome has not been described.

Differential diagnosis includes tumors of the thyroid or ectopic thyroid tissue, parathyroid tumors, paragangliomas, metastatic tumors, thymolipoma, soft tissue tumors, germ cell tumors, and the thymic tumors listed above. Carcinoid tumors metastatic to the thymus from another site are usually not occult, but search for an extrathymic primary site should be done before diagnosing a thymic carcinoid tumor [3].

Gross features: Tumors do not have a capsule and the cut surface is homogeneous rather than lobulated, as is characteristic of thymomas. The cut surfaces are usually firm and grey. Focal necrosis and hemorrhage are common [5].

Histologic features: Several variants include a usual form and diffuse, spindled, desmoplastic (fibrotic), and mucinous types, as well as a variant resembling medullary carcinoma of the thyroid [5]. A proliferation of pigmented thymic melanocytes darkened the gross appearance of one tumor [6].

- Usual: This type has islands or trabeculae of tumor separated by small, thin-walled vessels, as in other endocrine tumors. Nuclei are round to ovoid with finely-dispersed chromatin. N/C ratios are slightly increased. Nucleoli are small. Mitoses are usually fewer than 1-2 per high power field. Rosettes (cells arranged around a lumen) are common. A characteristic feature is the detachment of some nests from the adjacent stroma. There may be focal necrosis in the nests [5].
- Diffuse: Tumor grows in sheets interspersed with thin-walled vessels. These tumors may resemble lymphomas or germ cell tumors [5]
- Spindled [7]
- Desmoplastic: Stroma, which is prominent and densely fibrotic, isolates strands and nests of tumor cells [5]
- Mucinous: Abundant mucinous stroma makes the tumor resemble a mucinous adenocarcinoma [8]
- Medullary carcinoma of the thyroid-like: Intersecting bundles of spindled cells have focal stromal amyloid deposits [5]
- Pigmented: Cells within the tumor contain cytoplasmic pigment of melanin or ceroid [5,6]

Immunohistochemistry: Tumors react with antibodies to cytokeratin and chromogranin A, as well as other neuroendocrine markers including synaptophysin and Leu-7. Additionally, tumors may show reactivity for ACTH, serotonin, calcitonin, gastrin, cholecystokinin, or somatostatin, even if there is no clinical evidence of their presence. Parathyroid tumors can be distinguished by their staining with antibody to parathormone. Paragangliomas express neuroendocrine markers but do not react with cytokeratin. Lymphomas will show reactivity with leukocyte common antigen, and germ cell tumors will react with placental alkaline phosphatase [5].

Electron microscopy: Just as carcinoid tumors of the lung, thymic carcinoid tumors have neurosecretory granules. These range in size from 100 to 400 nm [5].

Treatment and outcome: Surgical excision is the preferred method of treatment with postoperative radiation and/or chemotherapy for tumors that cannot be removed completely [9,10]. Response to chemotherapy or radiation alone is poor. Embolic metastases occur in up to 3/4 of patients. Metastatic sites include mediastinal lymph nodes, but distant metastases (bone, liver, skin) occur in 30-40% of cases [3]. Five-year survival for cases without an associated endocrinopathy was about 70% and for those with an endocrinopathy was 35% in one report [3]. A more recent report indicated an overall survival of 31% at 5 years; all 14 patients were dead of disease by 109 months [1]. Late recurrence after 8 years has been reported [3].

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