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Intracardiac Leiomyomatosis: Diagnosis and Treatment

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Intracardiac leiomyomatosis is the presence of a benign smooth muscle tumor within a cardiac chamber reaching the heart by direct intravenous extension from an extracardiac source. After a case report and a review of the 13 previously reported cases, the clinical features, diagnostic considerations, differential diagnosis and treatment modalities of intracardiac leiomyomatosis are discussed.

Intravenous growth and extension of histologically benign leiomyoma emanating from the uterus was recognized and reported as early as 1903 (1). This phenomenon has been termed intravenous leiomyomatosis (2). Fewer than 100 cases of such intraluminal extension of benign smooth muscle tumors within uterine and pelvic veins have since been reported. Of these, 11 cases involved extension of the leiomyoma through the inferior vena cava and into the right atrium with varying degrees of caval and tricuspid obstruction. In addition, two cases of benign smooth muscle tumor arising from large veins with extension to the right atrium have been reported. Intracardiac leiomyomatosis is defined as the intravenous extension of a histologically benign smooth muscle tumor of extracardiac origin to the right side of the heart. The 13 previously reported cases meeting diagnostic criteria of intracardiac leiomyomatosis are reviewed and an additional case diagnosed by means of two-dimensional echocardiographic visualization is reported.

Case Report

A 46 year old woman with insulin-requiring diabetes mellitus was admitted to Booth Memorial Medical Center in a coma. The patient had been entirely well except for her diabetes until 6 months before admission when a large lower abdominal mass was discovered which was believed to represent uterine leiomyoma clinically. The patient refused further evaluation at that time. She remained asymptomatic until 5 days before admission when she noted the onset of ankle edema, dyspnea, fatigue and progressive lethargy.

Clinical findings. On admission, the patient was comatose and afebrile with a blood pressure of 150/80 mm Hg, a regular pulse of 100 beats/min and respirations of 40/min. Physical examination was otherwise significant for jugular venous distension, a grade 3/6 blowing pansystolic murmur heard with greatest intensity at the lower right sternal border and increasing with inspiration, an 8 × 8 cm mass in the left lower quadrant of the abdomen, an enlarged uterus and moderate leg edema. Laboratory examination revealed severe ketoacidosis and hyperglycemia. An electrocardiogram revealed sinus tachycardia with diphasic T waves in leads II, III and aVF. QRS complexes were of low voltage. On treatment of the ketoacidosis, the patient's mental status reverted to normal.

Noninvasive studies. M-mode echocardiography demonstrated a mass of echoes that entered the tricuspid orifice in early diastole (Fig. 1). Two-dimensional echocardiography showed a large (2 × 6 cm) elongated mass that filled the right atrium and moved in diastole across the tricuspid valve into the right ventricle (Fig. 2). The mass was not connected to the interatrial septum, but was seen to originate from within the lumen of the inferior vena cava. Pelvoabdominal ultrasonography and computed tomography demonstrated a solid pelvic and lower abdominal mass continuous with the uterus. Inferior vena cava venography showed a long continuous intraluminal mass extending to the right ventricle with partial obstruction of the upper inferior vena cava.

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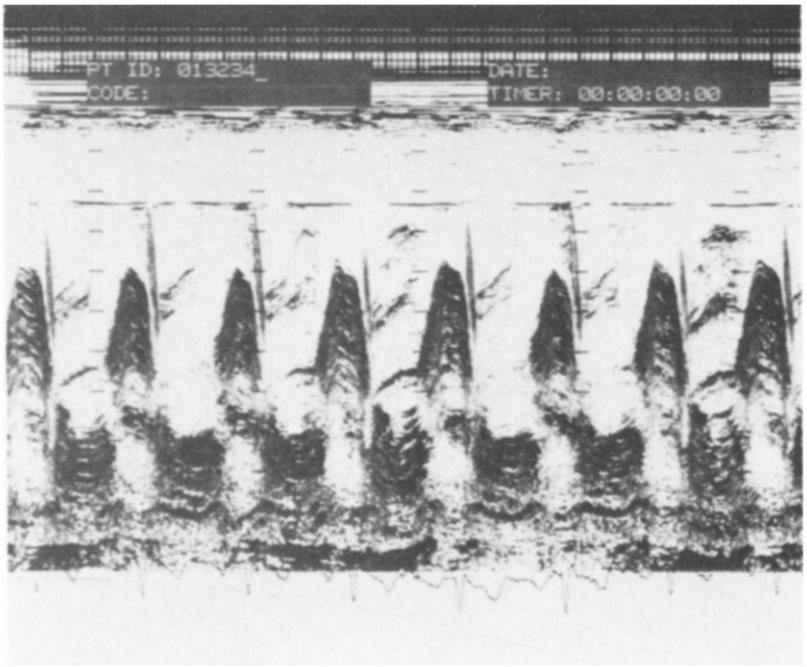

Figure 1. M-mode echocardiogram showing a large tumor mass in the tricuspic orifice in diastole.

Surgery and postoperative findings. The patient was transferred to New York University Medical Center where the intracardiac portion of the tumor was removed. The tumor was not adherent to the walls of the inferior vena cava or the right atrial endothelium. Pathologic examination showed a firm, light tan, smooth-surfaced, serpentine and roughly conical mass measuring 6 × 3 × 3 cm, conforming to the contour of a heart chamber (Fig. 3). Histologic sec-

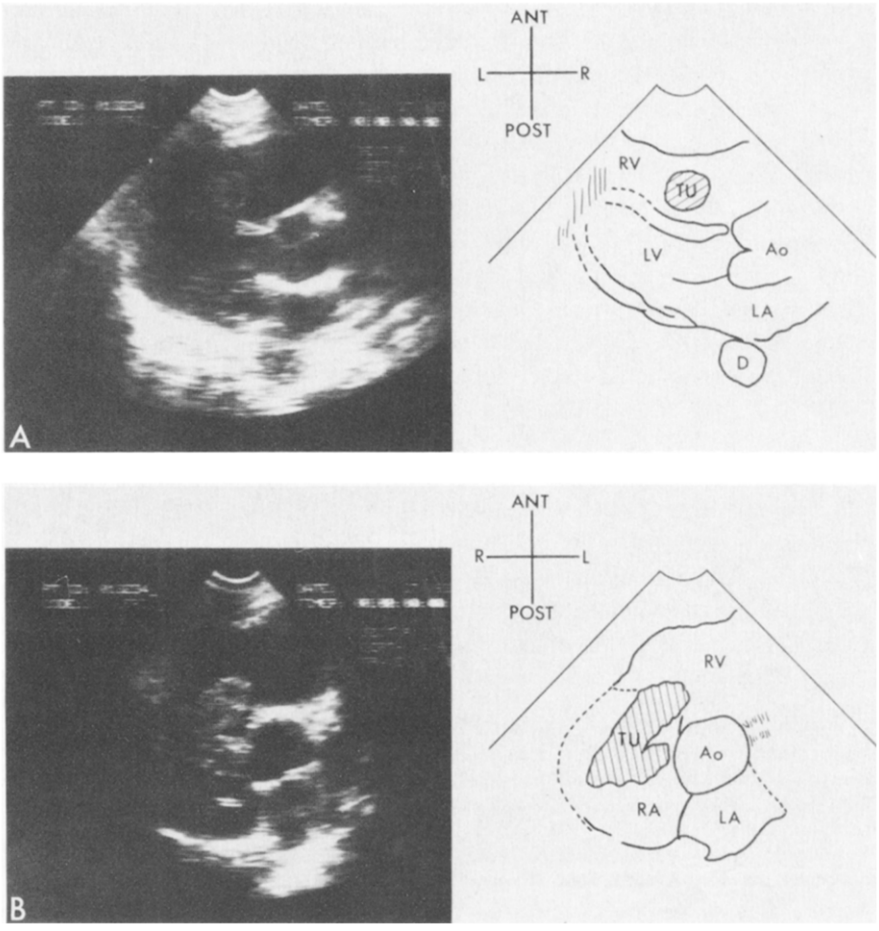

Figure 2. Two-dimensional echocardiogram. In the long-axis view **(A),** a round tumor mass (TU) is noted in the right ventricle (RV). In the short-axis view **(B),** the large tumor is seen filling the right atrium (RA) and crossing the tricuspid valve during diastole. ANT = anterior; Ao = aortic root; D = descending aorta; L = left; LA = left atrium; LV = left ventricle; POST = posterior; R = right; RA = right atrium.

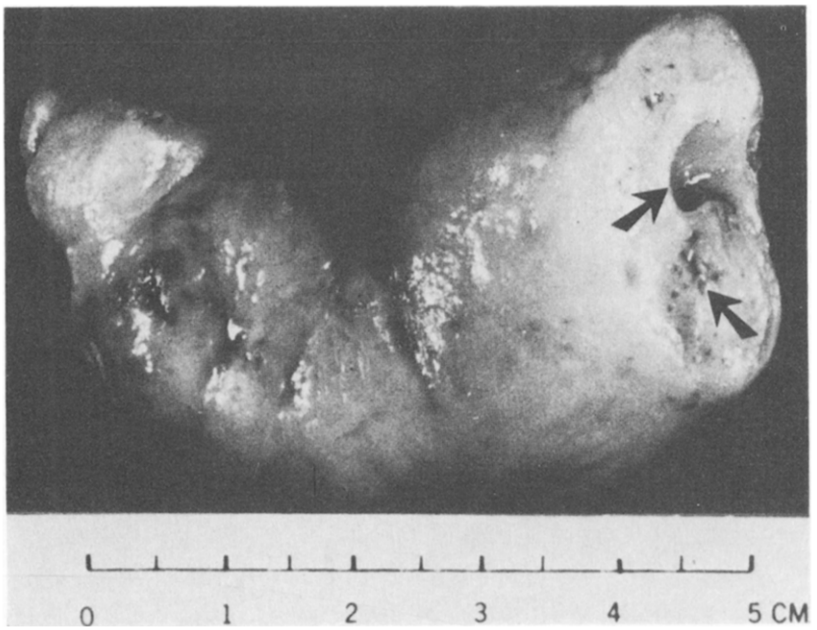

Figure 3. The surface of the tumor shows a firm, light tan, smooth mass conforming to the contour of a heart chamber. The cut section of the tumor shows the solid and cystic components, the latter corresponding to large intratumoral blood vessels **(arrows).**

tions showed bundles of uniform spindle-shaped tumor cells and many blood vessels in a dense collagenous stroma. The tumor cells had histochemical characteristics consistent with those of smooth muscle cells. Electron micrographs of tumor cells showed cytoplasmic myofilaments with associated dense bodies and pinocytotic vesicles, confirming that these were indeed smooth muscle cells.

The postoperative period was uneventful and the patient was discharged with plans for complete resection of the pelvoabdominal tumor in the future.

Review of Cases

We found 13 previous reports of cases of intracardiac leiomyomatosis. Clinical data are summarized in Table 1.

Prior histories. Eight of the 14 patients had a previous diagnosis of uterine leiomyoma that in 7 had been made histologically after uterine surgery. In five of the seven patients with prior uterine tumor excision, a histologic diagnosis of intravenous leiomyomatosis had been made 1 to 17 years before the diagnosis of intracardiac leiomyomatosis. Intravenous leiomyomatosis is a rare uterine neoplasm characterized by histologically benign smooth muscle growing within veins in worm-like projections that extend variable distances outside the boundaries of the primary tumor site (3).

Clinical findings at presentation. Symptoms attributable to the presence of an intracardiac tumor were reported in 13 patients, although 1 patient (Case 10) also had known rheumatic heart disease with mitral valve involvement. Signs of increased venous pressure were reported in 11 cases. Adventitious heart sounds were reported in eight patients, including systolic and diastolic murmurs, S_3 gallop and pericardial rub. Electrocardiogram revealing low voltage was reported in three patients (Cases 4, 8 and 14). Atrial flutter with 4:1 atrioventricular conduction was reported in one patient (Case 9) and atrial fibrillation was present in the patient with known mitral valve disease (Case 10).

Methods of diagnosis. The diagnosis of intracardiac leiomyomatosis was made postmortem in 4 of the 14 patients. The first antemortem diagnosis was made utilizing M-mode echocardiography and right heart catheterization in 1974 in Patient 4. Subsequent diagnoses were made utilizing catheterization alone in three patients (Cases 6, 7 and 12), inferior vena cava venography in a patient (Case 8) in whom the right atrium could not be visualized on M-mode or two-dimensional echocardiography, and with two-dimensional echocardiography in three (Cases 9, 10 and 14) of the six patients whose condition was diagnosed after 1982.

Pathologic findings. Right heart exploration was performed in all 10 patients in whom the diagnosis of right atrial tumor had been made antemortem. In two patients with intracardiac leiomyomatosis of nonuterine origin, the tumor was found to originate from the inferior vena cava at its entrance into the right atrium (Case 4) and from the right iliac vein (Case 13). These tumors were entirely resected in one operation. In one patient (Case 12), attempted removal of the tumor resulted in a massive fatal retroperitoneal hemorrhage. In the remaining seven patients, successful surgical excision of the right heart tumor was performed by sectioning the tumor from its stalk within the inferior vena cava. In six patients (Cases 4, 6, 7, 9, 12 and 14), the tumor occupied the right atrium and right ventricle, traversing the tricuspid valve. In one patient (Case 7), the

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Table 1. Clinical Data of 14 Patients With Intracardiac Leiomyomatosis

Case	Reference	Year Reported	Patient's Age (yr)	History of Leiomyoma	Presentation	Method of Diagnosis	Tumor Source	Intracardiac Extension	Therapy
1	10	1907	43	+	Death after total hysterectomy	Autopsy	Uterus	RA	–
2	11	1907	NA	NA	NA	Autopsy	Uterus	RA	–
3	12	1970	47	NA	Right-sided failure	Autopsy	Uterus	RA	–
4	8	1974	52	NA	Right-sided failure, cyanosis, polycythemia	M-mode echo and cath	IVC	RV	Surgical excision of tumor in toto
5	3	1975	55	NA	Right-sided failure	NA	Uterus	RA	Surgical excision of RA tumor; subsequent TAH
6	13	1978	41	+	Syncope, dyspnea, with prior pacemaker placement	Cath	Uterus	RV	Surgical excision of RA/RV tumor; subsequent residual tumor excision
7	7	1980	42	+, IVL	Right-sided failure	Cath	Uterus	RV	Surgical excision of RA/RV tumor, TVR, antiestrogen therapy
8	14	1980	46	+, IVL	Right-sided failure	IVC venogram	Uterus	RA	Surgical excision of RA tumor
9	15	1982	52	+, IVL	Right-sided failure, syncope	2D echo	Uterus	RV	Surgical excision of RA/RV tumor
10	16	1982	62	–	Rheumatic mitral valve disease, worsening failure	2D echo	Uterus	RA	Surgical excision of RA tumor, MVR, CABG; subsequent TAH
11	17	1982	66	+, IVL	Right-sided failure	Autopsy	Uterus	RA	–
12	17	1982	28	+, IVL	Signs of tricuspid stenosis	Cath	Uterus	RV	Operative death on attempted IVC/RA/RV tumor excision
13	9	1983	53	–	Right-sided failure	NA	Right iliac vein	RA	Surgical excision of tumor in toto
14	Present case	1984	46	+	Right-sided failure	2D echo	Uterus	RV	Surgical excision of RA tumor

+ = present; – = none; CABG = coronary artery bypass grafting; cath = cardiac catheterization; echo = echocardiography; IVC = inferior vena cava; IVL = intravenous leiomyomatosis; MVR = mitral valve replacement; NA = not available; RA = right atrium; RV = right ventricle; TAH = total abdominal hysterectomy; TVR = tricuspid valve replacement; 2D = two-dimensional.

tumor disruption of the tricuspid valve leaflets necessitated valve replacement. In another patient (Case 5), the tumor had ruptured several chordae tendineae, but no valve replacement was performed.

Clinical outcomes. After successful cardiac surgery, symptoms were universally lessened. Of the seven patients surviving surgery for intracardiac leiomyomatosis of uterine origin, three underwent subsequent laparotomy with total (Cases 6 and 10) or subtotal (Case 5) uterine and inferior vena cava tumor excision. One patient (Case 7) whose tumor was found to have estrogen receptors and was considered unresectable, was treated with antiestrogen agents in the hope of curtailing further extension from its site within the inferior vena cava. In all, eight of the nine patients in whom antemortem diagnostic evaluation disclosed a right-sided intracardiac mass extending from the inferior vena cava that proved to be benign leiomyoma had a favorable postoperative course.

Discussion

Definition. Intracardiac leiomyomatosis is the presence of intracavitary, histologically benign smooth muscle tumor of extracardiac origin reaching the heart by direct intravenous extension. A review of the reported cases and our additional case provides 14 cases for definitive delineation. The tumor of intracardiac leiomyomatosis may have its origin in either the smooth muscle walls of the veins or a rare form of uterine neoplasm, intravenous leiomyomatosis, in which there is intravenous growth of benign smooth muscle tissue. In both cases, there is direct extension of a tentacle-like leiomyoma through the inferior vena cava and into the right side of the heart. There is evidence for two theories of origin of intravenous leiomyomatosis: 1) intravenous leiomyoma arises from the smooth muscle wall of a vein within the myometrium, or 2) it results from unusual vascular invasion by a uterine leiomyoma (3).

Intracardiac leiomyomatosis, therefore, is a subset of leiomyomas originating from the walls of the veins and from the uterus in which there is intravenous extension of the tumor to the right heart chambers. Primary venous leiomyomas and intravenous leiomyomatosis are both rare entities, making intracardiac leiomyomatosis rare indeed.

Role of intravenous leiomyomatosis. Intravenous leiomyomatosis must be considered a precursor of intracardiac leiomyomatosis of uterine origin. In five of the seven patients who had prior uterine surgery for leiomyoma, a diagnosis of intravenous leiomyomatosis had been made 1 to 17 years before the diagnosis of intracardiac leiomyomatosis. The presence of intravenous leiomyomatosis in a uterine myomectomy specimen must raise suspicion that abdominal intravenous leiomyomatosis is present and that intracardiac extension of tumor is possible.

Clinical features. The clinical presentation of intracardiac leiomyomatosis is varied, ranging from lack of symptoms to sudden death. When symptoms and signs are present, they may resemble those of obstruction of the inferior vena cava or of the tricuspid valve orifice.

A tumor within the inferior vena cava may occupy varying degrees of lumen. Moreover, impeded blood flow through a partially obstructed lumen may lead to thrombosis and complete obstruction. Depending on the level of obstruction within the inferior vena cava, patients may present with signs of lower caval obstruction, renal vein obstruction or the Budd-Chiari syndrome.

Once the tentacle-like tumor reaches the heart, it tends to grow in all directions partially filling the right atrial cavity. Cardiac obstruction does not occur until right atrial outflow is impeded at the tricuspid valve orifice in a manner similar to that seen with right atrial myxoma. If there is a history of syncope, this may be an indication of intermittent severe cardiac obstruction distinguishing right atrial tumor from valvular tricuspid stenosis (4); in the latter, low cardiac output may cause generalized weakness, but not syncope (5).

The tumor may actually traverse the tricuspid orifice and enter the ventricle. If sufficiently tethered from its source, it may travel back and forth across the valve in and out of the ventricle through the cardiac cycle with concomitant tumor-produced adventitious heart sounds. In such cases, the persistent trauma of the valve apparatus may result in ruptured chordae tendineae, valve destruction and signs of tricuspid regurgitation.

Diagnostic considerations. Echocardiography, although not without limitations (6), is the method of choice for diagnosing the presence of intracardiac masses. As the right atrium is not well visualized by M-mode echocardiography and diagnosis by this method is dependent on pattern recognition, real time two-dimensional echocardiography is preferred. The differential diagnosis of a right atrial mass can be most facilitated by use of the apical four chamber view by visualizing the interatrial septum. First, if the mass is seen *not* to be attached to the interatrial septum, it is likely *not* to be a myxoma. Second, visualization of the mass emanating from the inferior vena cava proves its extracardiac origin.

Primary cardiac tumor thus being excluded, a search should be undertaken for the tumor's site of origin. Tumors that are most likely to invade the heart by direct intravenous extension include renal cell carcinoma, adrenal carcinoma, hepatoma and sarcomas of the retroperitoneum and large veins. Because one should suspect malignancy with the echocardiographic features of intracardiac leiomyomatosis, evaluation with pelvoabdominal computed tomography should be performed and a search for metastatic disease should be undertaken. Inferior vena cava venography will delineate the extent and perhaps the origin of the tumor.

Therapeutic considerations. The primary goal of therapy is to remove the intracardiac portion of the tumor to avoid tricuspid obstruction and tumor embolization and to obtain tissue for definitive diagnosis. In some cases, tricuspid valve replacement may be necessary. If the tissue proves to be benign leiomyoma, assay for cytoplasmic estrogen and progesterone receptors may be of value if the tumor cannot ultimately be totally removed, because smooth muscle tumors may be estrogen-dependent (7). In tumors originating in large veins, total excision may be achieved in one operation (8,9). Residual tumor removal in cases of uterine origin by subsequent laparotomy has been performed in three cases, but indications for this in the absence of caval obstruction and the Budd-Chiari syndrome are unclear. If estrogen receptors are shown to be present in the intracardiac specimen, treatment of the residual tumor with an antiestrogen agent may be tried (7).

Follow-up ultrasound examinations of the primary tumor site, the inferior vena cava and the heart should be performed at regular intervals to monitor tumor recurrence or growth and extension of residual tumor.

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