Pazopanib-induced regression of metastatic cardiac tumor from uterine leiomyosarcoma evaluated by cardiac computed tomography

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A woman in her seventies with a large uterine mass underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy. The pathological diagnosis was uterine leiomyosarcoma (ULMS) (Fig. S1). She presented with transient syncope 2 months after surgery. Transthoracic echocardiography showed an intracardiac mass extending from the right ventricle (RV) to the main pulmonary artery (PA) (Fig. S2A, B). Electrocardiography-gated cardiac computed tomography (CCT) demonstrated a mass of 33 mm by 23 mm in diameter involving the right ventricular wall with a highly mobile pedunculated acinous component that extended through the pulmonary valve.
into the PA, resulting in multiple pulmonary embolism (Fig. 1A, B). Cardiac and lung metastasis of ULMS was diagnosed. Pazopanib administration at 400 mg/day was started. CCT re-examination 6 weeks after pazopanib treatment showed prominent regression of cardiac and lung metastasis (Fig. 1C, D). The right ventricular mass was 17 mm by 9 mm in diameter. Cardiac and lung metastasis regression continued after five months of pazopanib treatment, but gradually enlarged afterward. After eight months of treatment, pazopanib administration was discontinued because of disease progression. The patient died four months after cessation of pazopanib.

Uterine leiomyosarcoma is a rare tumor subtype that accounts for approximately 1% to 2% of all uterine malignancies. Compared with other types of uterine malignancies, ULMS is a biologically aggressive tumor, as evidenced by high rates of progression, recurrence, and mortality. Uterine leiomyosarcoma favors vascular invasion and has a high propensity for hematogenous spread, most commonly to the lungs. However, metastasis to the heart is rare. The only treatment effective for ULMS is complete early resection. Chemotherapy plays a major role in managing unresectable, advanced, or recurrent ULMS. Pazopanib is an orally active multi-targeted tyrosine kinase inhibitor of vascular endothelial growth factor receptors, platelet-derived growth factor receptors and stem cell factor receptors, thereby blocking angiogenesis and thus inhibiting subsequent tumor growth. Pazopanib has been tested in patients with metastatic non-adipocytic soft-tissue sarcoma after failure of standard chemotherapy and was shown to prolong median progression-free survival by three months relative to placebo [1]. In 2012 the Food and Drug Administration approved pazopanib for treating advanced soft-tissue sarcoma in patients failing prior chemotherapy. Previous reports have shown the clinically relevant efficacy of pazopanib with metastatic ULMS, but did
not include patients with cardiac metastasis [2]. Therefore, its efficacy for cardiac metastasis of ULMS is unknown. Compared with tumors in other organs, cardiac tumors are difficult to measure precisely by non-electrocardiography-gated contrast-enhanced computed tomography due to cardiac motion artifacts. Delineation of the whole extent of cardiac tumors is difficult with echocardiography due to the limited echo angles, making it difficult to evaluate drug-induced cardiac tumor size reduction. In contrast, CCT can visualize the whole extent of intracardiac masses with few cardiac motion artifacts and few dead angles. In this case, we could examine CCT before and after pazopanib monotherapy and demonstrate obvious cardiac tumor regression. This is the first report to clearly show the effectiveness of pazopanib in a cardiac metastatic lesion of ULMS.

**Article informations and declarations**

**Conflict of interest**

Author declares no conflict of interest.

**Supplementary material**

Figures S1, S2.

**REFERENCES**


**Figure 1A, B.** Electrocardiography-gated cardiac computed tomography (C {A?}. Axial view; D {B?}. Coronal view) before pazopanib treatment showing a mass involving the right ventricular wall (arrows) with a pedunculated component (red arrowheads) that extended into the pulmonary artery (PA). White arrowheads indicate the right lung metastasis of the uterine leiomyosarcoma; C, D. Electrocardiography-gated cardiac computed tomography (C. Axial view; D. Coronal view) 6 weeks after pazopanib treatment; Aao — ascending aorta; LA — left atrium; LV — left ventricle; RA — right atrium; RV — right ventricle
Supplementary material

Figure S1. A. Sagittal image of T2-weighted pelvic magnetic resonance imaging showing heterogeneous uterine mass with lesions of high and low signal intensity with maximum diameter of 17.9 cm; B. Gross specimen of surgically resected uterine mass; C. Microscopic findings of the resected uterine mass on hematoxylin and eosin staining showing spindled tumor cells with marked nuclear pleomorphism and brisk mitotic activity
Figure S2. A, B. Transthoracic echocardiography (A. Parasternal long axis view; B. Parasternal short axis view) showing an intracardiac mass (arrows) extending from the right ventricle (RV) to the main pulmonary artery (PA); Aao — ascending aorta; AV — aortic valve; LA — left atrium; LV — left ventricle; RA — right atrium