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CASE REPORT

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# Cardiac interventricular septum hemangioma in a colon cancer patient treated with Capecitabine: A case report and review of literature

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**Key Clinical Message**

We report a case of a 21-year-old male with stage IIIB sigmoid colon adenocarcinoma who experienced atypical chest pain post-adjuvant chemotherapy with Capecitabine (5-FU prodrug). Evaluation revealed an unexpectedly detected interventricular septum hemangioma. Due to the vasospasm effect of chemotherapy presenting with semi-ischemia, conservative management was chosen for atypical presentation.

**KEYWORDS**

cardiac hemangioma, chemotherapy, colon cancer, interventricular septum, intraventricular neoplasm

## 1 | INTRODUCTION

Cardiac hemangiomas (CHs) are exceptionally uncommon primary cardiac tumors characterized by the aberrant growth of blood vessels within the heart. Their occurrence spans both infancies, frequently linked with Kasabach–Merritt syndrome, and adulthood, constituting approximately 2.8%–5% of all primary cardiac tumors.[1] Despite their benign nature, CHs represent a noteworthy proportion of heart tumors, comprising 1%–2% of all cardiac neoplasms.[2] Frequently asymptomatic, they are often incidentally discovered during diagnostic imaging procedures.[3,4] However, symptomatic presentations can encompass a spectrum of manifestations, including atypical chest pain, dyspnea, palpitations, and arrhythmias.[3] Despite their benign nature, these tumors can precipitate serious complications such as heart failure, vascular obstruction, valvular dysfunction, arrhythmias, and in rare instances, cardiac tamponade.[5]

Echocardiography, cardiac Magnetic Resonance (CMR) Imaging, and Computed Tomography (CT) are essential modalities for assessing the size, location, and extracardiac involvement of CH.[4,6] Moreover, coronary angiography aids in evaluating tumor vascularity and blushes.[4] The

optimal management of CH remains contentious; while some clinicians advocate for conservative therapy due to the benign nature of the tumor, others advocate for surgical intervention to mitigate risks such as embolism, rupture, and sudden death.[4]

To date, very few cases of concurrent CHs and cancer or metastases in various organs have been reported. Although its etiology is uncertain, studies suggest that some inflammatory and infectious causes (such as endocarditis and rheumatism) may predispose to its development.[2,7] Here, we report another case diagnosed with colon cancer, referred due to chest pain, and unexpectedly found to have an intraventricular hemangioma undergoing treatment.

## 2 | CASE PRESENTATION

A 21-year-old male, previously diagnosed with stage IIIB sigmoid colon adenocarcinoma with microsatellite instability-high in March 2023, underwent adjuvant chemotherapy. The treatment regimen included XELOX (Oxaliplatin 130 mg/m$^2$ IV on Day 1 and Capecitabine 1000 mg/m$^2$ orally twice daily on Days 1–14), administered over eight sessions at 21-day intervals. On November 2023, following the final chemotherapy session, the patient presented with atypical chest pain and shortness of breath, and referred to our hospital for further evaluation.

### 2.1 | Clinical findings

Upon examination, the patient exhibited tachypnea with a respiratory rate of 24 breaths per minute. Blood pressure was elevated at 150/90 mmHg, and heart rate was elevated at 108 bpm. Oxygen saturation was 93% on room air. Auscultation of the chest revealed decreased breath sounds bilaterally. A grade II systolic ejection murmur was heard at the left sternal border, characterized by medium intensity and crescendo-decrescendo sound during systole. No peripheral edema or jugular venous distention was observed. Electrocardiogram showed sinus tachycardia with non-specific ST-T wave changes. Troponin levels were within normal limits.

### 2.2 | Diagnostic assessments

Transthoracic echocardiography (TTE) revealed a mass in the interventricular septum (IVS), extending from the base to the mid-septum, measuring 2.7 × 4.7 cm. The mass had irregular borders and a hyperechoic appearance. Ventricular function decreased to 35% (Figure 1), and contrast echocardiography along with flash echo imaging represented a well-defined vascular mass within the IVS. CMR Imaging confirmed the presence of a localized, irregularly bordered intramyocardial mass in the basal to mid-septal wall of the left ventricle, measuring 2.5 × 3.8 cm. The mass appeared iso-intense on T1-weighted images and hyperintense on T2-weighted fat-saturated images. It exhibited hypervascularity in perfusion scans and enhancement in late gadolinium enhancement (LGE) images, indicative of a hemangioma (Figure 2A–D).

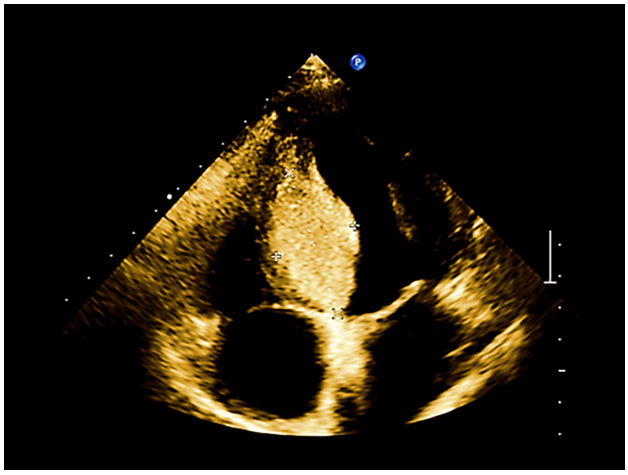

FIGURE 1 Transthoracic echocardiography of a patient with IVS hemangioma. Large hyperechoic and well-defined mass (2.7 × 4.7 cm) in the basal to mid-septal wall of the Left Ventricle. Left ventricle ejection fraction = 35%. IVS, Interventricular septum.

Additionally, the prompt troponin level was elevated at 0.12 ng/mL, indicating myocardial injury. Additionally, the NT-proBNP level was markedly elevated at 2500 pg/mL, reflecting significant cardiac strain and heart failure. Other laboratory tests, including CBC, LFTs, RFTs, and electrolytes, were within normal limits.

### 2.3 | Treatment and outcome

Upon admission, the patient's management focused on stabilizing his condition and addressing potential complications related to his presenting symptoms. Supplemental oxygen therapy was administered to maintain oxygen saturation above 95%. Sublingual nitroglycerin was initiated to alleviate chest pain and reduce myocardial oxygen demand. Enoxaparin was administered for suspected pulmonary embolism due to clinical signs of tachypnea and elevated D-dimer levels. Chest CT angiography ruled out pulmonary embolism but revealed mild to moderate bilateral pleural effusions with associated compressive atelectasis. A diagnostic

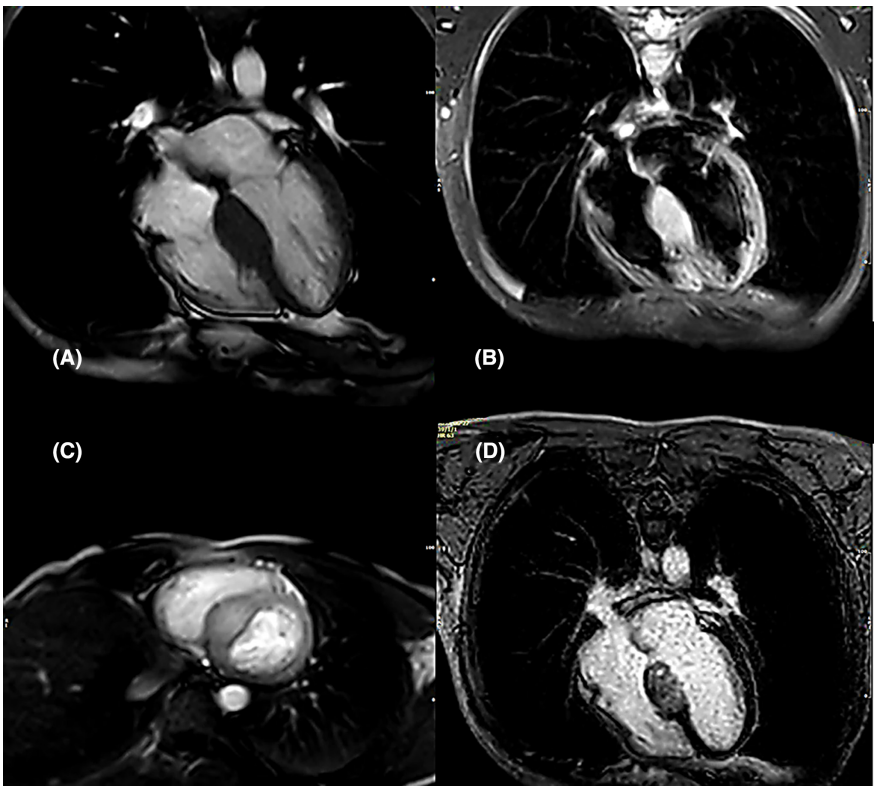


**FIGURE 2** Cardiac Magnetic Resonance Imaging Findings in a patient with IVS hemangioma. (A) The SSFP image on a 4-CH view shows localized thickening of the IVS with well-defined borders, indicative of the presence of a mass. (B) A T2-weighted STIR image highlights a hypersignal intensity mass within the IVS. (C) A first-pass perfusion image captures the septal mass, revealing remarkable perfusion that distinguishes the hemangioma from surrounding cardiac tissue. (D) LGE imaging in a 4-CH view demonstrates hyperenhancement of the septal mass post-contrast administration, confirming its vascular nature and differentiating it from myocardial tissue. 4-CH, four-chamber; IVS, interventricular septum; LGE, late gadolinium enhancement; SSFP, steady-state free precession; STIR, short tau inversion recovery.

thoracentesis was performed, yielding serosanguinous fluid with no evidence of malignancy on cytological analysis (transudate). Intravenous diuretic therapy with furosemide was initiated to alleviate symptoms of dyspnea secondary to pleural effusions. Fluid status was closely monitored, and adjustments in diuretic therapy were made to achieve euvolemia.

### 2.4 | Multidisciplinary collaboration and follow-up

A multidisciplinary team comprising cardiologists, oncologists, and cardiothoracic surgeons collaborated to formulate a comprehensive management plan. Surgical resection of the intramyocardial mass was deemed unnecessary at this stage, given the patient's age and the benign nature of the mass.

Close surveillance with serial echocardiograms and CMR Imaging was recommended to monitor the intramyocardial mass's size and characteristics over time. The patient was discharged with stable hemodynamic (BP = 130/80 mmHg, HR = 86 beats/min), and with instructions for close outpatient follow-up with the cardiology and oncology departments for ongoing monitoring and management. On April 2024, 5 months after discharge, the patient's hemodynamics were stable, and have not experienced recurrent episodes of sharp pain.

## 3 | MATERIALS AND METHODS

A comprehensive search was conducted using PubMed and Google Scholar databases to identify relevant case reports focusing on the association between heart ventricles or ventricular septum and hemangioma. The search strategy utilized the following keywords: "Heart Ventricles" or "Ventricular Septum" and "Hemangioma." All English-language case reports published up to the present (March 2024) were included in the search.

## 4 | RESULTS

Our search identified another nine articles on intramyocardial hemangioma. Along with the report of our study, patients, mainly male, had an average age of $28.15 \pm 23.88$ years. Initial symptoms ranged from chest pain and palpitations to cutaneous hemangioma. The diagnostic modalities utilized also included nonspecific changes in ECG along with findings from TTE, TEE, CMR, and CAG. Additionally, in the case of pediatric and neonatal hemangiomas, prenatal ultrasound screening demonstrated the diagnosis of intramyocardial mass. Treatment primarily involved open-heart surgery (60%), or non-invasive follow-up approach (30%). Nevertheless, intramyocardial hemangioma led to mortality in only one case (10%). A comprehensive demographic of all relevant studies is described in Table 1.

**TABLE 1** Demographic table of case reports of cardiac hemangioma with interventricular septal involvement.

| Study | Patient profile | Symptoms and signs | Imaging and cardiac findings | Treatment strategy and follow-up |
|---|---|---|---|---|
| Our case | 21-year-old male | • Atypical chest pain<br>• Shortness of breath<br>• Tachypnea<br>• High BP: 150/90 mmHg | • ECG: Sinus tachycardia with non-specific ST-T wave changes<br>• TTE: a 2.7 × 4.7 cm hyperechoic mass in IVS<br>• CMR: a 2.5 × 3.8 cm intramyocardial mass in the basal to mid-septal wall of the left ventricle | • Periodic follow-up |
| Bangal et al.[8] | 3-year-old male | Worsening dyspnea on exertion | • Pregnancy ultrasound: intramyocardial mass<br>• TTE: hypertrophied IVS, severe RVOT obstruction, LVOT narrowing<br>• TEE: Echogenic Mass (4.6 cm × 2.4 cm) in the basal, mid, and anteroseptal regions of the IVS and anterior RV wall<br>• CMR: enhancing (4.2 cm × 2.6 cm × 4.4 cm) lesion involving the basal, mid, and anteroseptal regions of the IVS and the anterior wall of the RV. Isointense on T1W and mildly hyperintense on T2W/STIR sequences | • Open heart surgery |
| Gilbert et al.[9] | 38-year-old male | • Atypical chest pain<br>• Palpitations | • CXR: NL<br>• ECG: NSR<br>• TTE: Homogenously echo-dense mass measuring 4 × 2 cm in the left ventricular cavity<br>• A mass attached to the mid and basal septum<br>• CMR: a 3.8 × 4.2 cm mass arising from the IVS and base of the left ventricle protruding into the left ventricular cavity<br>• CAG: Ectatic changes of the RCA | • Open heart surgery |
| Minsart et al.[10] | Newborn 39 weeks | Multiple purple cutaneous hemangiomas on the baby's skin, lower limbs, and perineum | • Pregnancy ultrasound: Anechoic cyst of 1.0 cm diameter in the superior third of the IVS<br>• TTE: translucent cyst of 1.0 × 1.5 cm, small muscular ventricular septal defect, and septo-apical hypokinesis | • At 6 months, the mass was 3 mm in diameter |
| Sotoda et al.[11] | 74-year-old male | NL | • CXR: NL<br>• ECG: NSR<br>• TEE: a 2.5–3.0 cm mass extending from the IVS to the apex of the right ventricle<br>• CT: Hypo-enhanced mass<br>• CAG: feeding artery of the tumor arising from the RCA<br>• PET: NL | • Open heart surgery |
| Lee et al.[12] | 54-year-old female | • Palpitation<br>• Anterior chest tightness<br>• Bilateral crackling sound<br>• Neck vein engorgement | • CXR: cardiomegaly<br>• ECG: atrial fibrillation with rapid ventricular response<br>• TTE: LV enlargement and hypertrophy, Trivial mitral regurgitation<br>• CAG: Two tumors in the RCA:<br>1. right atrial side of the IAS: 1.8 × 1.0 cm mass<br>2. IVS: 4.4 × 1.0 cm mass | • Sublingual nitroglycerin<br>• Digitalis |

**TABLE 1** (Continued)

| Study | Patient profile | Symptoms and signs | Imaging and cardiac findings | Treatment strategy and follow-up |
|---|---|---|---|---|
| Grenadier et al.[13] | 41-year-old female | • Chest pain<br>• Recurrent palpitation | • ECG: Inverted T and small Q waves in the lateral leads<br>• TTE: Large, multiloculated echo-free spaces around the great vessels and at the apical and anterolateral borders of the left ventricle. Echo-free spaces detected anteriorly to the right ventricular cavity<br>• CAG: uplifting of the left anterior descending coronary artery and lateral displacement of the right coronary artery by the mass<br>• Surgical View: Large spongy mass Extends into IVS and both ventricles | • Open heart surgery |
| Newell et al.[14] | 40-year-old male | Precordial chest pain | • ECG: inverted T waves across the precordial leads<br>• TTE: a small mass with increased echogenicity in the IVS<br>• CMR: a small focal mass in the IVS with a slight increase in the signal intensity<br>• CAG: two areas of increased vascularity within the IVS<br>• Surgical View: a 1.5 cm arteriovenous hemangioma from the mid-muscular IVS, and a 0.5 cm capillary hemangioma from the outflow portion of the IVS | • Sublingual nitroglycerin-Intravenous heparin<br>• Open heart surgery |
| Soherman et al.[15] | 3.5-year-old male | At birth left-sided systolic Murmur | • CXR: Cardiomegaly<br>• ECG: RV hypertrophy<br>• TTE: thickening of the IVS protruding into the RV<br>• Right ventriculogram: Sub-valvular obstruction of the RV<br>• Left ventriculogram: Vascular blush filling from the LADA at the level of obstruction<br>• CMR: a mass in the IVS | • Open heart surgery |
| Leijala et al.[16] | 7-year-old | N.A. | • ECG: Systolic-diastolic Congenital murmur, complete A-V<br>• Block<br>• Autopsy: Large hemangioma of the ventricular septum and chambers | • Died |

Abbreviations: BP: blood pressure; CAG: coronary angiography; CMR: cardiac Magnetic Resonance imaging; CXR: chest X-ray; ECG: electrocardiogram; IVS: interventricular septum; LADA: left anterior descending coronary artery; LV: Left Ventricle; LVOT: left ventricular outflow tract; MRI: Magnetic Resonance Imaging; N.A.: not available; NL: normal; NSR: normal sinus rhythm; PET: positron emission tomography; RCA: right coronary artery; RV: Right Ventricle; RVOT: right ventricular outflow tract; TEE: transesophageal echocardiography; TTE: transthoracic echocardiography.

## 5 | DISCUSSION

CH presents a profound challenge both clinically and diagnostically, exemplified by its multifaceted manifestations and intricate diagnostic pathways. Epidemiologically, a retrospective cohort review study revealed approximately 14.6% of patients, may remain asymptomatic initially. However, as the tumor progresses, experienced by 20.6% of cases, dangerous events such as syncope, angina, and stroke may be seen as hemodynamic alterations.[4]

Etiologically, the pathogenesis of CH unfolds against a backdrop of intricate genetic predispositions intertwined with environmental factors. Notably, statistical analysis by Li et al. unveiled an association between tumor location and patient demographics, with septal hemangiomas being significantly more prevalent ($p < 0.001$; odds ratio, 5.205) and emerging as an independent predictor of CH-related mortality.[4]

These tumors also exhibit distinct localization patterns (intra-, peri-, and paracardial) and can originate from various cardiac layers (endocardium, myocardium, and

**TABLE 2** Differential diagnosis of cardiac hemangioma with their imaging features.

| Differential diagnosis | General imaging features | Location | Preferred imaging characteristics |
|---|---|---|---|
| Myxoma[18,19] | Typically appears as a heterogeneous mass with a gelatinous consistency, often attached to the interatrial septum in the left atrium. May cause obstruction and exhibit calcifications | Primarily in the left atrium | Echo: shows a mobile, pedunculated mass, often with heterogeneous echogenicity |
| Lipoma[20] | Homogeneous, hyperechoic mass due to fat content. Well-circumscribed and non-infiltrative | Any cardiac chamber or pericardial space | MRI: high signal intensity on T1-weighted images and suppression on fat-saturated sequences. |
| Fibroma[21] | Dense, homogenous, hyperechoic mass on echocardiography. Usually located within the myocardium | Typically found in the ventricles | MRI: low signal intensity on both T1- and T2-weighted images due to fibrous content. |
| Rhabdomyoma[19] | Homogeneous, hyperechoic mass. Often multiple and associated with tuberous sclerosis | Commonly in the ventricles | MRI: isointense or slightly hyperintense on T1, and hyperintense on T2-weighted images |
| Sarcoma[22] | Heterogeneous mass with areas of necrosis and hemorrhage. Invasive and infiltrative growth pattern | Often in the right atrium, but can occur in any chamber | MRI: variable signal intensity on T1 and T2, with enhancement after gadolinium administration |
| Metastatic tumors[31] | Often multiple, irregular masses. The appearance depends on the primary tumor type | Any part of the heart, often in the pericardium | CT/MRI: features consistent with the primary malignancy; may show pericardial effusion |
| Thrombus[23] | Typically appears as a hypoechoic or isoechoic mass, often in areas of blood stasis or in dilated chambers. Non-enhancing on CT and MRI | Commonly found in the left atrium or left ventricle | Echo: shows a mobile or fixed mass with variable echogenicity; may have a layered appearance |

Abbreviations: CT, Computed Tomography; Echo, Echocardiography; MRI, Magnetic Resonance Imaging.

epicardium), with morphological classifications including cavernous, capillary, and arteriovenous types.[1]

Differential diagnosis mandates a discerning evaluation to differentiate CH from other cardiac neoplasms, thrombi, and vegetations. While imaging modalities facilitate preliminary differentiation, histopathological confirmation remains paramount in establishing a definitive diagnosis.[4]

Differential diagnosis is crucial to distinguish CH from other cardiac masses. Imaging aids in differentiation, but histopathological confirmation is essential. Hemangiomas, which can be asymptomatic or present with dyspnea, appear highly echogenic on TTE with contrast and show a heterogeneous signal on CMR.[17] Key features on CMR include high T1w and very high T2w signals, centripetal contrast enhancement, and heterogeneous LGE.[17] The summary of numbers of its differential diagnosis (Myxoma, Lipoma, Fibroma, Rhabdomyoma, Sarcoma, Metastatic Tumors, and Thrombus) along with their diagnostic features is present in Table 2.

Treatment paradigms for CH are nuanced, with surgical excision emerging as the cornerstone for symptomatic cases, mitigating risks of embolism, rupture, and sudden demise. However, the advent of conservative modalities like radiotherapy, corticosteroids, vascular endothelial growth factor antagonists, and beta-blockers presents a tantalizing avenue warranting further exploration, albeit in select cohorts.[24-26] Emerging research suggests that certain chemotherapy agents possess antiangiogenic properties that may impact hemangioma growth.[27,28] However, the advent of conservative modalities like radiotherapy, corticosteroids, and beta-blockers presents a tantalizing avenue warranting further exploration, albeit in select cohorts. However, the decision for treatment should be individualized based on factors like tumor location, size, and patient's overall health.[4]

In this article, we reported a young male diagnosed unexpectedly with cardiac IVS hemangioma following eight sessions of chemotherapy for colon cancer, who underwent adjuvant treatment including Capecitabine (a pro-drug of 5-FU). Notably, 5-FU has been associated with vasospastic angina, likely mediated by nitric oxide synthase (NOS) dysregulation and subsequent NO depletion.[29] Therefore, based on the imaging findings in our case, the cause of the patient's chest pain is more related to the side effects of chemotherapy.

Additionally, while there is currently no direct evidence linking CHs with chemotherapy, rare instances of chemotherapy affecting the size of liver hemangiomas have been reported, albeit poorly documented in the context of CHs. Notably, Aguilera et al. reported a case of radiation-induced cavernous hemangiomas in a pediatric patient undergoing treatment with Bevacizumab.[30] This suggests a potential correlation between chemotherapy agents and vascular abnormalities, albeit requiring further investigation.

## 6 | CONCLUSIONS

We presented a 21-year-old male who was receiving adjuvant chemotherapy with Capecitabine (a pro-drug of 5-FU) for colon cancer. He experienced atypical chest pain as a side effect of the medication. Cardiac evaluations revealed an unexpected finding of an IVS hemangioma, which was monitored closely and just followed-up due to the absence of clinical symptoms.

### AUTHOR CONTRIBUTIONS

**Yasamin Afsari Zonooz:** Methodology; writing – original draft. **Azin Alizadehasl:** Project administration. **Delaram Narimani Davani:** Writing – original draft; writing – review and editing. **Seyedeh Fatemeh Hosseini Jebelli:** Validation; visualization. **Azam Yalameh Aliabadi:** Investigation; resources. **Soroush Najdaghi:** Writing – review and editing. **Shahla Meshgi:** Investigation. **Soudabeh Shafieeardestani:** Methodology.

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### CONFLICT OF INTEREST STATEMENT

The authors have no funding, financial relationships, or competing interests to disclose.

### DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

### CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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