







Vascular synovial sarcoma masquerading as deep vein thrombosis: a diagnostic pitfall-a case report

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ABSTRACT

Background: Intravascular synovial sarcoma is a rare disease with only 14 cases documented globally to date. To the best of our knowledge, we present the 15th case, highlighting the diagnostic challenge, the rapidly progressive course of this malignancy, and the need for greater clinical awareness.

Case Presentation: A female patient in her early 20s presented with a painful swelling in the right inguinal region and right lower limb oedema, initially considered to be DVT. Imaging revealed a mass involving the right external iliac and common femoral veins. She underwent surgical excision of the mass, and histopathological evaluation confirmed intravascular biphasic synovial sarcoma, supported by molecular diagnostic testing. The patient received postoperative chemotherapy. However, there was local recurrence of the disease within 5 months of completing chemotherapy and within a year of surgical resection.

Conclusions: This case emphasizes that not all cases presenting as DVT may be benign, especially in young patients without apparent risk factors. Underlying malignancies, including sarcomas, should be considered in the differential diagnosis. Advanced imaging techniques are critical for early detection and surgical planning. Early multidisciplinary involvement is essential for optimizing outcomes. Given the rarity and aggressive nature of this disease, further research is needed to guide standardized treatment strategies and improve survival.

Keywords: 15th case, intravascular synovial sarcoma, deep vein thrombosis, thromboembolic events, diagnostic challenge

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Background

Synovial sarcoma is a rare subtype of soft tissue sarcoma that generally affects young adults. While it has traditionally been associated with the musculoskeletal system, there have been an increasing number of cases with presentation in unusual locations. Amongst these, the rarest is intravascular synovial sarcoma. These tumours often present with non-specific symptoms with features resembling thromboembolic events, making diagnosis challenging. Accurate diagnosis requires a combination of advanced imaging, histopathology, immunohistochemistry, and molecular testing. Due to its rarity, there is limited understanding of the disease's behaviour, optimal management, and long-term outcomes. We present a case of a young female patient with intravascular synovial sarcoma involving the right external iliac and femoral veins. We aim to add to the limited published data to raise awareness of this unusual presentation and highlight the importance

of early suspicion, timely diagnosis, and multidisciplinary care.

Case Presentation

A female of South Asian descent in her early 20s presented with a 2-month history of a swelling in the right inguinal region. It was insidious in onset, gradually increasing in size, associated with progressive worsening of pain and concurrent swelling of the right lower limb. There was no history of trauma to the leg, insect bite, fever, loss of function or sensation of the affected limb, joint swellings, abdominal pain or distension, and any abnormal vaginal discharge or bleeding.

On examination, a large, firm, tender mass measuring approximately 10 × 8 cm was palpable extending from the right iliac fossa toward the umbilicus. The right lower limb showed pitting oedema from the thigh to the ankle, along with warmth, tenderness, and erythema along the deep venous territory. Prominent superficial varicosities

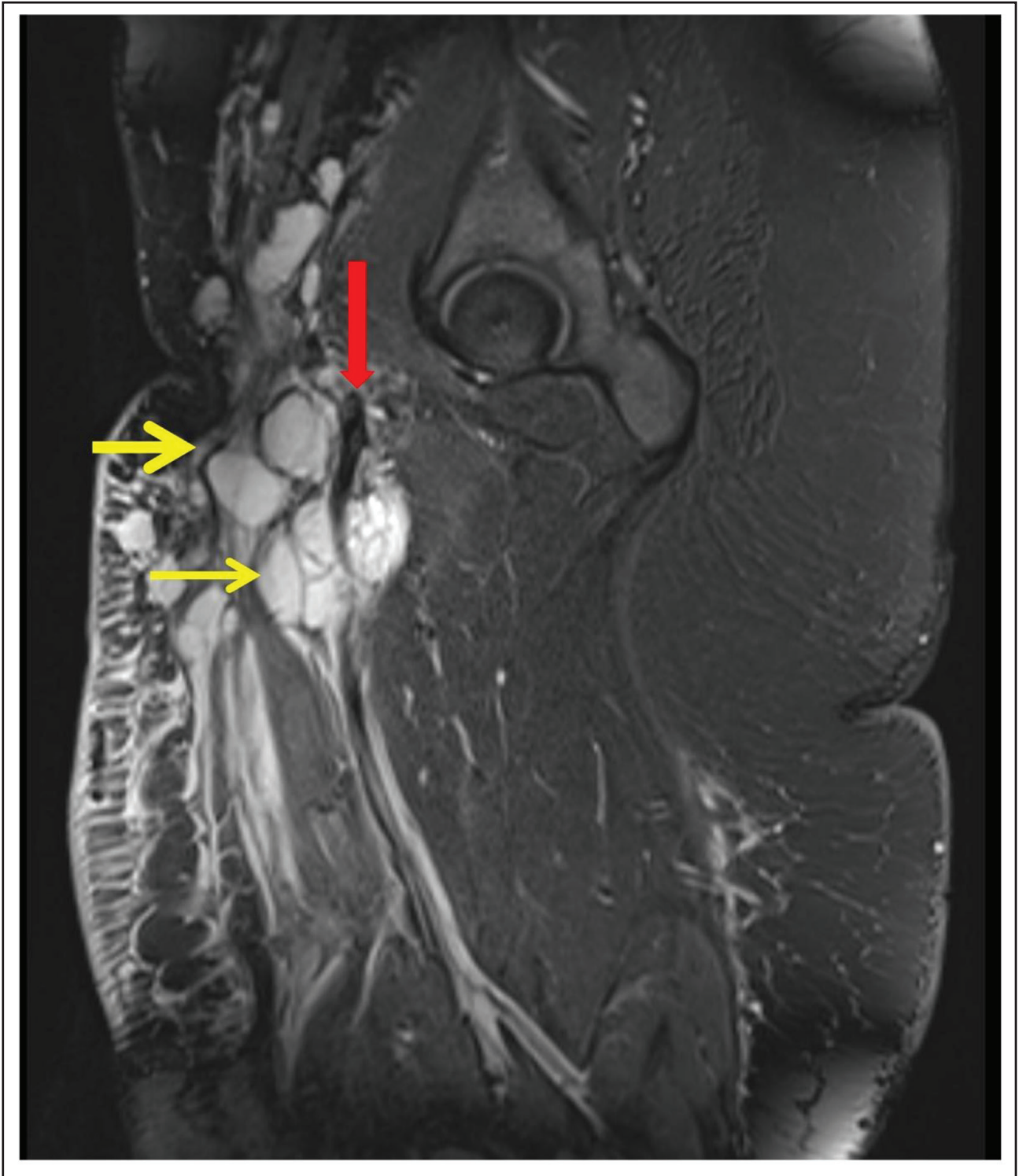


Figure 1. Sagittal STIR image of right upper thigh showing multiple variable sized T2W hyperintense enhancing lesions seen in subcutaneous and intramuscular planes (yellow arrow) encasing the vessel (red arrow).

73 were noted over the posterior and lateral aspects of the
74 right thigh, and all distal pulses were palpable. The neu-
75 rological, systemic, abdominal, and pelvic examinations
76 were unremarkable.

77 In view of the patient's presentation, a bilateral lower
78 limb ultrasonography (USG) with venous Doppler was
79 done, which revealed a large, heterogeneously hypoechoic

80 lesion in the right inguinal region $\sim 11.5 \times 5.5$ cm, contain-
81 ing internal specks of calcification and exerting compres-
82 sive effects on the right common femoral vein. No definite
83 colour flow or venous spectral waveform was identified,
84 suggesting a deep vein thrombosis (DVT), and features of
85 cellulitis were also observed.

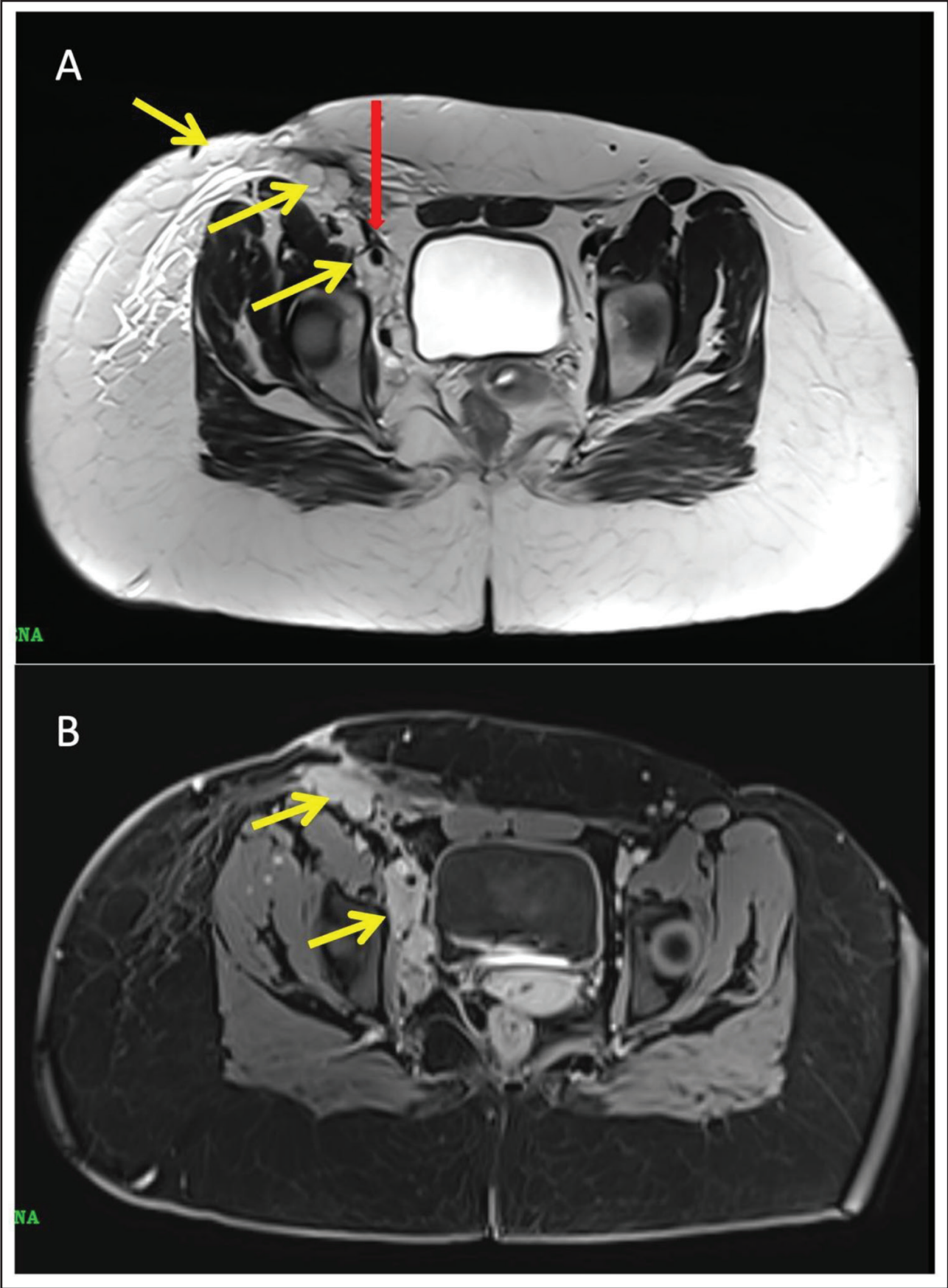


Figure 2. Axial T2W image (A) and axial post-contrast T1W image (B) of right upper thigh showing subcutaneous and intramuscular plane enhancing lesions (yellow arrows) encasing vessels (red arrow).

89 A CT venography of the abdomen and bilateral thighs
 90 revealed a soft tissue density mass extending inferiorly
 91 into the right thigh and superiorly into the lower pelvis.
 92 It exhibited heterogeneous enhancement with internal
 93 vascularity and calcific foci, which were seen tracking
 94 along the expected anatomical course of the right external
 95 iliac and common femoral veins. Multiple right inguinal
 96 lymph nodes were seen. These radiological features raised
 97 a strong suspicion of an intravascular tumour mimicking
 98 the clinical and sonographic appearance of a DVT. A met-
 99 astatic workup was initiated, and a whole-body PET-CT
 100 scan revealed that the disease was localized (Figure 3).

101 To establish a definitive diagnosis through histopatho-
 102 logical evaluation of the mass, the patient underwent En
 103 bloc (surgical removal of the tumour along with surround-
 104 ing healthy tissue in one single piece) surgical excision of
 105 the right iliac mass with excision of the right external iliac
 106 vein, right common femoral vein, along with para-aortic,
 107 retroperitoneal, and right inguinal lymph nodes dissec-
 108 tion. This was followed by vascular reconstruction of both
 109 veins using the saphenous vein autograft.

110 Intraoperatively, a large mass approximately 15×10
 111 cm in size was identified arising from the right external
 112 iliac vein and common femoral vein. There was significant
 113 compression of the right external iliac and common fem-
 114 oral veins, contributing to chronic venous insufficiency.
 115 Additionally, there was enlarged right inguinal lymphad-
 116 enopathy, raising concern for locoregional spread. There
 117 was no evidence of DVT in the bilateral lower limb venous
 118 systems. This confirmed that the initial diagnosis of DVT
 119 was inaccurate and caused by the tumour compression and
 120 luminal obstruction.

121 Grossly, the specimen was a segment of the right iliac
 122 vein with attached adipose tissue, measuring $13 \times 5 \times 4$
 123 cm. The external surface appeared congested. On the cut
 124 section, a well-circumscribed, encapsulated, grey-white
 125 soft to firm nodule measuring $6 \times 3.2 \times 3$ cm was identi-
 126 fied. Microscopic evaluation demonstrated a highly cel-
 127 lular, biphasic tumour composed of gland-like epithelial
 128 structures interspersed with spindle cell components.
 129 Numerous vascular channels were noted, and the tumour
 130 was seen expanding within a large vein. Tumour deposits

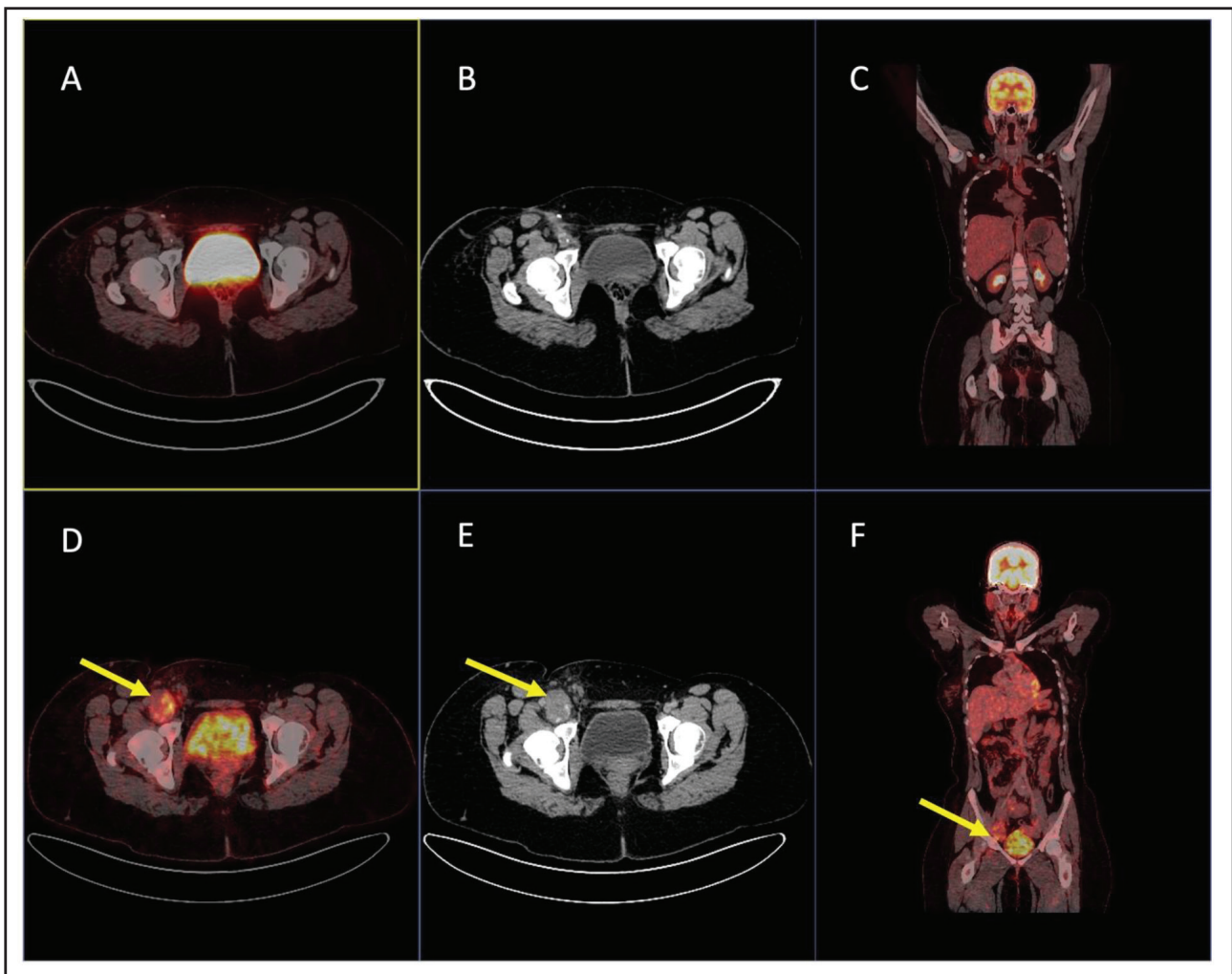


Figure 3. (A–C) No metabolically active lesion seen in right external iliac and inguinal region (post treatment). (D–F) Metabolically active defined soft tissue lesion (yellow arrow) in right inguinal and external iliac region (before treatment).

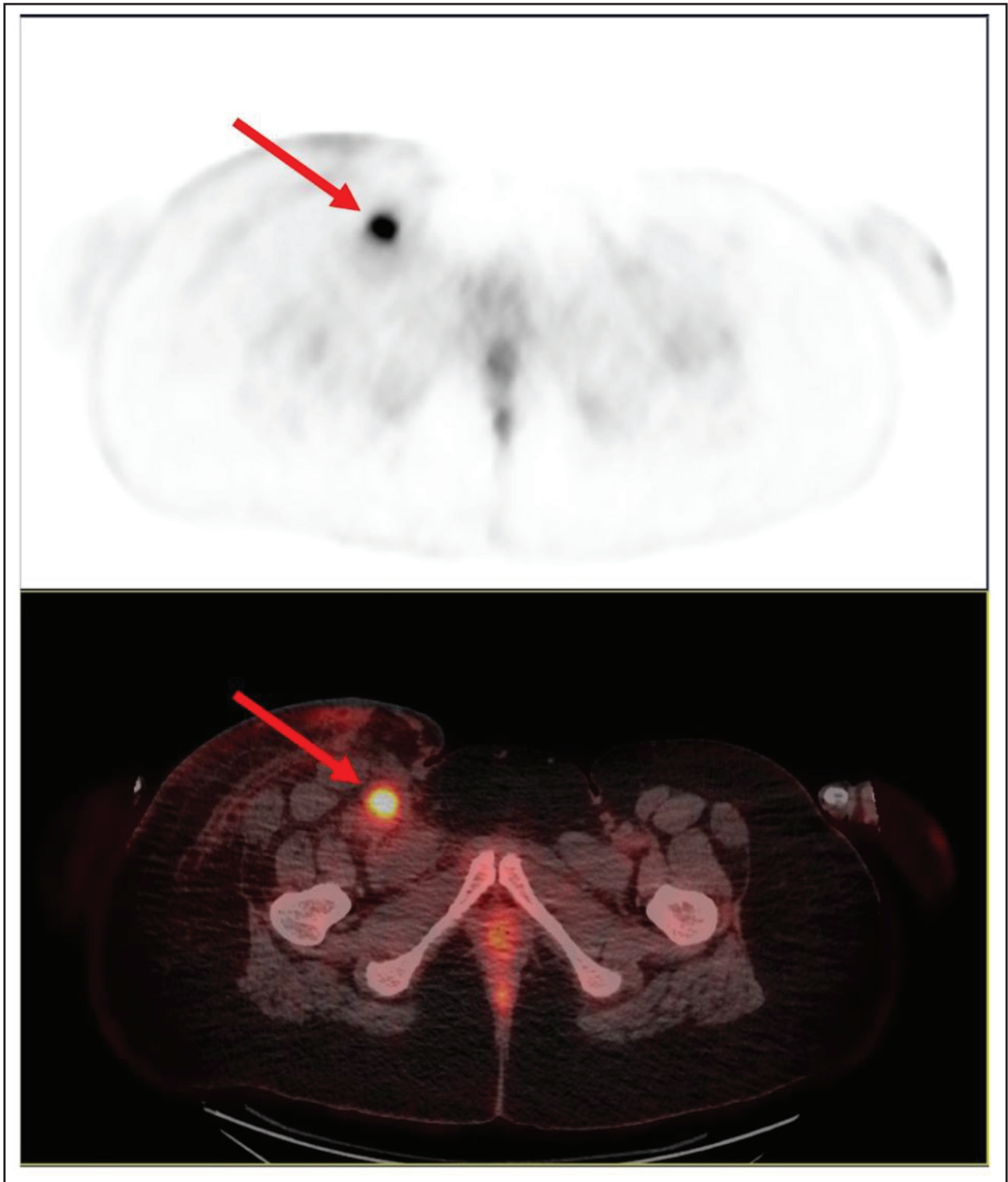


Figure 4. Multiple mildly metabolically active soft tissue density nodular lesions (red arrow) seen in right inguino-femoral region muscle and subcutaneous plane and associated with subcutaneous fat strandings/edema in right limb (recurrence) with multiple lymph nodes.

137 were also present in the surrounding soft tissue. All 19
138 dissected lymph nodes were free of tumour involvement,
139 and all resected surgical margins were negative for tumour
140 (R0 resection).

141 Immunohistochemistry (IHC) revealed strong and dif-
142 fuse SS18 expression in both epithelial and spindle cell
143 components, with CK7 positivity in the epithelial areas.

The tumour was negative for SMA, TTF-1, GATA3, 144
PAX8, MYOD1, S100, and CK20. There was significant 145
downregulation of INI1 expression. These findings collec- 146
tively made the diagnosis of intravascular synovial sar- 147
coma (IVSS), and it was confirmed by the detection of 148
the SYT-SSX1 gene fusion via FISH (Fluorescence in-situ 149
hybridization) analysis on the specimen. Postoperative 150

151 imaging was unremarkable. There were no postoperative
152 complications.

153 Following surgical management, the patient received
154 five cycles of chemotherapy (CT) with an ifosfamide
155 and adriamycin regimen. A multidisciplinary discussion
156 with the radiation oncology team was undertaken to dis-
157 cuss the role of local radiotherapy (RT), which was sub-
158 sequently deferred due to the high risk of chronic right
159 lower limb lymphedema associated with the anatomical
160 site of disease. At 1 and 3 months following the comple-
161 tion of treatment, imaging revealed no evidence of resid-
162 ual or recurrent disease. The patient was kept on regular
163 follow-up.

164 However, 5 months after completing CT and within 1
165 year after surgical resection, the patient presented with
166 recurrent swelling of the right lower limb and pain at the
167 postoperative site. MRI and Doppler imaging revealed
168 enhancing multifocal lesions of varying sizes in the subcu-
169 taneous and intermuscular planes of the upper right thigh,
170 along with multiple iliac and inguinal region lymph nodes
171 (Figures 1,2). These findings were suggestive of locoreg-
172 ional recurrence. To confirm the diagnosis, a biopsy was
173 performed from the right inguinal subcutaneous lesion,
174 which came back positive for recurrence (Figure 4). A
175 follow-up whole-body PET-CT scan further confirmed the
176 findings without evidence of distant metastasis (Figure
177 4). The patient was advised to initiate second-line CT
178 with gemcitabine and docetaxel, and Next-Generation
179 Sequencing (NGS) testing of the new lesions to guide fur-
180 ther management. Unfortunately, the patient was lost to
181 follow-up thereafter, and no further clinical information
182 is available regarding subsequent management or disease
183 progression.

184 **Timeline**

TIME POINT (DAY)	CLINICAL COURSE AND INTERVENTIONS
Day 0 (Presentation)	The patient presented with swelling and pain in the right inguinal region
Day 2-7	Diagnostic evaluation performed (laboratory investigations and radiological imaging.)
Day 15	Underwent surgery
Day 70	Post-operative assessment and investigations completed.
Day 82	Full clinical recovery documented.
Day 85	Adjuvant chemotherapy initiated.
Day 175	Completion of chemotherapy (final cycle administered).
Day 348	recurrence of disease seen.

185 **Discussion and Conclusions**

186 Synovial sarcoma (SS) is a rare and aggressive subtype
187 of soft tissue sarcoma (STS), comprising only 5%-10%
188 of all STSs [1,2]. It is a malignant tumour of mesen-
189 chymal origin exhibiting variable degrees of epithelial

190 differentiation [2]. Despite its name, SS is in fact a misno-
191 mer as it does not arise from synovial tissue [3-5] and is
192 driven by a specific SS18-SSX fusion oncogene resulting
193 from the t(X;18)(p11.2;q11.2) translocation [1-16].

194 The intravascular presentation of SS (IVSS) is
195 an exceptionally rare entity. To the best of our knowledge,
196 only 14 cases of IVSS [3-6,8-15] have been reported in the
197 global literature, making this the 15th report worldwide.

198 IVSS is highly aggressive and characterised by tumour
199 growth within vascular structures. Its prognosis is influ-
200 enced by several factors, including tumour size, depth,
201 anatomical location, invasion into surrounding tissues, and
202 most importantly, achieving a complete surgical resection
203 [1,5,10,13]. The intravascular location of the tumour con-
204 tributes to a significantly higher risk of distant metastasis
205 [15]. Our patient’s clinical course underscores this aggres-
206 sive nature, where local recurrence was detected only 5
207 months after completion of CT.

208 In our case, the clinical presentation and initial imag-
209 ing were suggestive of a DVT. However, it was actually
210 the mass exerting significant extrinsic compressive effects
211 and luminal obstruction of the vein. This resulted in an
212 absence of definite colour flow or a venous spectral wave-
213 form, which was initially misinterpreted as a DVT. It can
214 also present as a pulmonary embolism (PE) [4,13], supe-
215 rior vena cava (SVC) syndrome/obstruction (SVCO) [3],
216 pleural effusion [14], and other thromboembolic events
217 depending upon the location of the mass.

218 This is well illustrated in the case reported by Tong et
219 al. [3], where the IVSS involved the SVC, presenting clin-
220 ically as a cervical mass with features of SVC syndrome.
221 Similar obstacles have been documented by Schreiner
222 et al. [4] and Schoneveld et al. [13], who reported cases
223 of IVSS initially mimicking common thromboembolic
224 events. This creates a critical diagnostic pitfall where we
225 can mistake a malignant intravascular process for a pri-
226 mary DVT.

227 To navigate this, a multimodal approach includ-
228 ing clinical assessment, imaging, histopathology,
229 IHC, and molecular studies [3-5,10,14,15] is required.
230 Differentiating tumour thrombus from bland thrombus
231 is key, and while Doppler USG is first-line for DVT,
232 advanced imaging is crucial when atypical or malignant
233 features such as internal vascularity and calcific foci are
234 present, as seen in our case [12]. CT venography iden-
235 tified the enhancing mass, and FDG PET CT (Figure 3)
236 confirmed the strong suspicion for a malignant intravascu-
237 lar process. The above-mentioned radiological red flags,
238 along with atypical thrombotic presentations, particularly
239 in young patients with a failure to respond to anticoagu-
240 lation, should prompt thorough assessment and consider-
241 ation of intravascular neoplasms to help prevent delay in
242 diagnosis [3,4,10,12].

243 In our case, histopathological examination and IHC
244 played a crucial role in the diagnostic workup, where the

245 strong expression of SS18 helped in making the diagnosis
246 of SS [17]. SS18 expression is a positive immunoexpres-
247 sion of the SS18::SSX fusion-specific antibody, which
248 is highly specific for SS [18]. IHC also helped rule out
249 neural origin tumours [7], mesothelioma, sex cord-strom-
250 al tumours, and carcinomas of the female genital tract
251 [17]. Our case demonstrated significant downregulation
252 of INI1 (SMARCB1) expression. In SS, several studies
253 have reported reduced or mosaic loss of SMARCB1/
254 INI1 protein expression in a large number of cases. This
255 reduction is not due to gene deletion but is attributed to
256 post-transcriptional regulatory mechanisms affecting
257 protein expression within tumour cells. Therefore, the
258 observed downregulation in our sample supports our diag-
259 nosis [19]. This IHC profile is consistent with previously
260 published reports. Given the significant morphologic
261 heterogeneity exhibited by SS [2], the use of molecular
262 techniques remains critical for confirming the diagnosis
263 [1-5,10,13-15].

264 The diagnosis in this case was definitively confirmed
265 by the detection of the SYT-SSX1 gene fusion by FISH,
266 a characteristic molecular alteration unique to this tumour
267 type [1,2,4,5,14]. It is seen approximately in 95% of all
268 cases [4], making it an exceptionally reliable diagnostic
269 marker and also believed to be the cause [1]. This chromo-
270 somal reciprocal translocation [5] forms from the fusion
271 of the SS18 gene on chromosome 18 with an SSX gene
272 (SSX1 or SSX2) on the X chromosome [1,2,10,14].

273 The management of IVSS remains undefined due to
274 the lack of standardized treatment guidelines and presents
275 a significant predicament. Surgical resection remains
276 the cornerstone of treatment [5,13], RT playing a crucial
277 adjunctive role in improving prognosis [13] and reduc-
278 ing the risk of local recurrence. However, the role of CT
279 remains controversial [5,13].

280 Several reports highlight the need for adapted strate-
281 gies in IVSS due to its intravascular location and technical
282 surgical challenges. Schreiner et al. [4] utilized a combi-
283 nation of neoadjuvant CT (doxorubicin and ifosfamide)
284 and RT before surgical resection [4]. Maekura et al. [14]
285 reported a case of unresectable pulmonary artery IVSS,
286 in which combined CRTT was utilized as a disease-con-
287 trolling strategy. Jonathan et al. [10] also reported a case
288 wherein neoadjuvant RT was employed before radical en-
289 bloc excision of the tumour, followed by combined arte-
290 rial and venous reconstruction, resulting in 2 years of dis-
291 ease-free survival. These approaches suggest that in cases
292 where the tumour is large or located in anatomically crit-
293 ical regions, upfront surgery may not be feasible. Hence,
294 preoperative RT or combined chemoradiotherapy (CRTT)
295 may be employed in such cases.

296 In our case, the patient underwent surgery and was
297 pathologically staged as pT2N0Mx with clear margins.
298 Margin status is recognized as one of the most signifi-
299 cant prognostic indicators for local recurrence in STS

[16]. Achieving an R0 resection is therefore of paramount
importance [5,16], as conservative surgical approaches
have been associated with recurrence rates as high as 70%
[5]. Additionally, tumour size has also been shown to cor-
relate strongly with both local recurrence and systemic
outcomes [10]. Lesions measuring greater than 5 cm in
diameter are associated with a significantly increased risk
of recurrence [13].

308 Postoperatively, our patient received five cycles of
309 adjuvant CT with ifosfamide and doxorubicin. Although
310 the role of adjuvant CT in synovial sarcoma remains
311 debated [1,5,13], it was considered appropriate in this case
312 due to the tumour's size (>5 cm), high-grade histology,
313 localized disease, negative lymph nodes, and the patient's
314 young age. RT was not administered given the anatomical
315 location and the elevated risk of chronic lymphedema,
316 particularly following extensive lymph node dissection
317 and vascular involvement.

318 Management strategies are typically extrapolated from
319 conventional synovial sarcoma, and reported cases show
320 variability in therapeutic approaches [4-6,8,10,13-15],
321 reflecting the need for an individualized nature of deci-
322 sion making based on tumour location, size, and extent of
323 vascular involvement. A notable clinical feature is its ten-
324 dency for late recurrence, frequently occurring beyond 5
325 years after initial diagnosis and treatment [2,6,16], under-
326 scoring the necessity for prolonged follow-up.

327 What sets our case apart is the unusually early locoregional
328 recurrence within 5 months of receiving adjuvant
329 CT (Figures 1-3) and within a year of surgical resection.
330 This suggests that IVSS may have a more aggressive
331 biology, possibly influenced by factors associated with
332 the tumour microenvironment and mechanisms of vascular
333 spread, and this is a major learning point showing the
334 necessity for stringent monitoring.

335 A notable limitation of this case is the relatively short
336 surveillance period, as the patient was lost to follow-up
337 shortly after recurrence was documented. Consequently,
338 any further interventions could not be carried out, and the
339 ultimate clinical outcome could not be further evaluated.

340 Conclusion

341 In conclusion, this case represents a rare intravascular
342 presentation of synovial sarcoma in a young woman,
343 masquerading as DVT, a critical diagnostic pitfall. It
344 highlights the critical importance of maintaining a high
345 index of suspicion in atypical presentations with unpro-
346 voked thrombotic events and employing advanced imag-
347 ing modalities for differentiation. Furthermore, the early
348 locoregional recurrence despite optimal management
349 emphasizes the aggressive nature of this disease. Given
350 the limited literature, there is an unmet need for enhanced
351 research into tumour biology, recurrence mechanisms,
352 advanced molecular testing, and larger cohort-based stud-
353 ies to better define disease behaviour, refine prognostic

354 markers, and guide tailored management approaches in
355 the future.

356 What is new?

357 Intravascular synovial sarcoma (14 cases documented
358 worldwide) is a rare condition whose management remains
359 undefined, and surgical resection remains the standard
360 treatment. Radiation has an adjunctive role in improving
361 prognosis, and the role of chemotherapy remains controver-
362 sial. Management strategies are typically extrapolated from
363 conventional synovial sarcoma. It has a tendency for late
364 recurrence and is aggressive in nature.

365 This case (15th case) demonstrates the early locoregional
366 recurrence after an R0 surgical resection, despite negative
367 lymph nodes, clear margins, and receiving adjuvant CT. This
368 early relapse suggests that IVSS may have a more aggres-
369 sive biology, possibly influenced by factors associated with
370 the tumour microenvironment and mechanisms of vascular
371 spread.

372 List of Abbreviations

373	CT	Chemotherapy
374	DVT	Deep vein thrombosis
375	IHC	Immunohistochemistry
376	IVSS	Intravascular synovial sarcoma
377	MRI	Magnetic resonance imaging
378	PET-CT	Positron Emission Tomography Computed
379		Tomography
380	PE	Pulmonary embolism
381	RT	Radiotherapy
382	STS	Soft tissue sarcoma
383	SVC	Superior vena cava
384	SVCO	Superior vena cava obstruction
385	SS	Synovial sarcoma
386	USG	Ultrasonography

387 Conflict of interest

388 The authors declare that they have no conflict of interest
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394 Ethics approval and consent to participate

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396 Availability of data and materials

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400 manuscript.

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508 **Summary of the case**

PATIENT (GENDER, AGE)	22 YEARS, FEMALE
Final diagnosis	Intravascular synovial sarcoma arising from the right external iliac vein and common femoral vein.
Symptoms	Swelling and pain in the right inguinal region
Medications	Ifosfamide and adriamycin regimen
Clinical procedure	Surgery followed by chemotherapy
Specialty	Oncology