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CASE REPORT

SURGICAL MANAGEMENT OF CLADRIBINE-REFRACTORY EXTRANODAL INGUINAL ROSAI-DORFMAN DISEASE: A CASE REPORT

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Abstract

Introduction. Rosai-Dorfman disease is a rare non-Langerhans cell histiocytosis that may closely mimic malignant disease, particularly in extranodal soft tissue. Its progression during active systemic therapy has been only rarely reported.
Case presentation. We report a case of localized extranodal inguinofemoral Rosai-Dorfman disease progressing despite six cycles of cladribine. A 52-year-old man presented with progressive enlargement of a right inguinofemoral mass despite six cycles of cladribine. The lesion subsequently developed tissue necrosis, hemorrhage, and secondary infection. The histopathological diagnosis had been established before initiation of systemic therapy. Because of continued disease progression, complete surgical excision was performed under spinal anesthesia, without preoperative cross-sectional imaging because of local resource limitations. The postoperative course was uneventful, and no evidence of local recurrence or disease progression was observed at 3-month follow-up.
Conclusions. Localized extranodal Rosai-Dorfman disease may continue to progress despite appropriately administered systemic therapy, ultimately requiring surgical management. In our case, salvage surgical

Résumé

Prise en charge chirurgicale d'une maladie de Rosai-Dorfman inguinale extranodale réfractaire à la cladribine: rapport du cas

Introduction. La maladie de Rosai-Dorfman est une histiocytose rare non langerhansienne pouvant simuler étroitement une pathologie maligne, en particulier lorsqu'elle atteint les tissus mous extranodaux. Une progression de la maladie au cours d'un traitement systémique actif n'a été rapportée que de manière exceptionnelle.
Rapport du cas. Nous rapportons un cas de maladie de Rosai-Dorfman extranodale inguinofémorale localisée, ayant progressé malgré six cycles de cladribine. Un homme de 52 ans a été consulté pour une augmentation progressive du volume d'une masse inguinofémorale droite malgré six cycles de cladribine. La lésion s'est secondairement compliquée d'une nécrose tissulaire, d'une hémorragie et d'une infection secondaire. Le diagnostic histopathologique avait été établi avant l'instauration du traitement systémique. En raison de la progression persistante de la maladie, une exérèse chirurgicale complète a été réalisée sous rachianesthésie, sans imagerie préopératoire en coupe, en raison de contraintes locales de ressources. Les suites opératoires

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excision achieved effective short-term local disease control after cladribine failure. Persistent progression during active systemic therapy should prompt consideration of timely surgical reassessment, particularly in resource-limited settings.

Keywords: histiocytosis, emperipolesis, sarcoma, necrosis, resource-limited settings.

List of abbreviations:
CD1a – cluster of differentiation 1a
CD68 – cluster of differentiation 68
Ki-67 – marker of proliferation Ki-67
RDD – Rosai-Dorfman disease

ont été simples et aucune récidive locale ni progression de la maladie n'a été observée après trois mois de suivi. **Conclusions.** Une maladie de Rosai-Dorfman extranodale localisée peut continuer à progresser malgré un traitement systémique correctement administré, conduisant finalement à une prise en charge chirurgicale. Dans le cas présenté, l'exérèse chirurgicale de sauvetage a permis un contrôle local efficace à court terme après échec de la cladribine. Une progression persistante sous traitement systémique actif devrait conduire à envisager précocement une réévaluation chirurgicale, en particulier dans les contextes où les ressources diagnostiques avancées demeurent limitées.

Mots-clés: histiocytose, emperipolèse, sarcome, nécrose, ressources limitées.

Introduction

Rosai-Dorfman disease is an uncommon non-Langerhans cell histiocytosis whose greatest clinical challenge lies not in its rarity, but in its ability to mimic malignant disease in the absence of a standardized therapeutic pathway[1,2]. Its presentation – massive, painless, bilateral cervical lymphadenopathy – obscures a more heterogeneous reality. Extranodal disease is documented in a substantial proportion of cases and may involve skin, bone, soft tissue, and viscera, with no reliable predictor of which patients will experience indolent, self-limited disease and which will progress toward destructive, treatment-resistant forms[1,3]. When Rosai-Dorfman disease arises in soft tissue outside the classic nodal distribution, it doesn't have a distinguishing clinical signature; multiple published cases describe lesions clinically and radiologically indistinguishable from sarcoma, with the diagnosis established only once tissue is placed under a microscope[4-8]. Consequently, definitive diagnosis frequently depends on histopathological examination after tissue sampling.

The treatment of the disease reflects this uncertainty. Although consensus recommendations are available, no universally applicable therapeutic algorithm exists, because disease behavior ranges from spontaneous regression to life-threatening multisystem involvement[1,2]. The therapeutic management is individualized according to disease extent, symptom burden, anatomical site, and organ involvement: observation where indolence is evident, excision where disease is solitary and accessible, systemic therapy where it is not[1,2,9]. Cladribine has emerged as one of the most consistently active systemic agents in refractory and disseminated disease, with response rates approaching two-thirds in the largest retrospective series[3,10,11]. Data about the disease that recurs after a completed course of therapy and the disease that continues to advance, while the patient is actively receiving the treatment, are lacking. The latter scenario, progression under treatment, rather than after it, is the less examined of the two, and it carries different clinical weight: it forces a decision under active therapeutic failure, not after its conclusion.

Evidence guiding the transition from unsuccessful systemic therapy to definitive surgical management remains limited, particularly in patients with localized extranodal Rosai-Dorfman disease.

We report the case of a man with extranodal inguinofemoral Rosai-Dorfman disease. Despite systemic cladribine, the lesion continued to enlarge, and what began as a histiocytic proliferation evolved into a necrotic, hemorrhagic, secondarily infected mass, a surgical problem superimposed on a hematologic one. The surgical decision was made without the benefit of prior cross-sectional imaging, on clinical examination and histopathology alone, a circumstance not of preference but of the resource environment in which the patient was treated.

This case illustrates how localized extranodal Rosai-Dorfman disease may transform from a chronic histiocytic disorder into an acute surgical condition when systemic therapy fails, emphasizing the importance of timely operative management in carefully selected patients.

Case presentation

A 52-year-old man was admitted to the Department of General Surgery, University Hospital Center "Mother Teresa", Tirana, Albania, because of progressive enlargement of a right inguinofemoral mass associated with localized pain, spontaneous bleeding, and purulent discharge.



Figure 1. Preoperative clinical appearance of the right inguinofemoral mass. Photograph demonstrating a large, indurated right inguinofemoral mass (approximately 6 × 4 × 5 cm), with active hemorrhage and areas of superficial necrosis, complicated by secondary infection. The lesion had progressively enlarged despite six completed cycles of cladribine therapy.

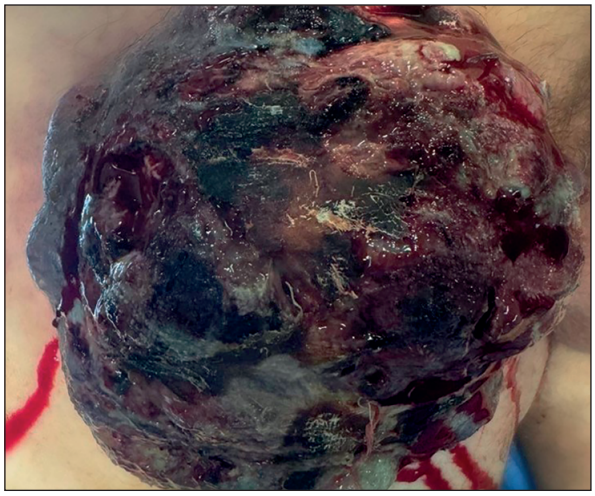


Figure 2. Intraoperative appearance following circumferential incision. Intraoperative photograph obtained after a circumferential incision around the lesion, showing extensive gangrenous degeneration with multiple abscess cavities and purulent material both within and surrounding the mass.

Approximately one year before admission, the patient first noticed a slowly enlarging right inguinal lymph node. An outpatient core biopsy established the diagnosis of Rosai-Dorfman disease, after which systemic therapy with cladribine was initiated. The patient completed six cycles of treatment over the following months. No objective clinical response was observed; instead, the lesion enlarged progressively throughout therapy, with particularly rapid growth during the final two months before admission. By the time of presentation, the lesion measured approximately 6×4×5 cm and had developed extensive cutaneous necrosis, active hemorrhage, and secondary infection with purulent drainage. The patient denied fever, weight loss, night sweats, or similar lesions elsewhere. His past medical and family history was otherwise unremarkable.

On admission, the patient was hemodynamically stable and in good general condition, with a blood pressure of 120/70 mmHg, heart rate of 70 beats/min, and oxygen saturation of 98% on room air. The local examination revealed a large indurated, markedly tender, hyperemic right inguinofemoral mass measuring approximately 6×4×5 cm, with extensive cutaneous necrosis, active hemorrhage, and purulent drainage consistent with secondary abscess formation (Figure 1). Cardiology consultation was requested because of intermittent sinus tachycardia detected during the preoperative evaluation. On electrocardiogram, no ST-T abnormalities were identified, the transthoracic echocardiography was unremarkable, and the patient was considered fit for surgery. The remainder of the physical examination was unremarkable.

The histopathological review of the original biopsy confirmed the diagnosis. The microscopic examination demonstrated complete effacement of the lymph node architecture by a histiocytic proliferation involving markedly dilated lymphatic sinuses. Immunohistochemical analysis showed diffuse CD68 positivity, variable S100 expression, negative CD1a staining, and a Ki-67 proliferation index of approximately 30%. Additional epithelial, lymphoid, and melanocytic markers were negative, excluding alternative neoplastic and lymphoproliferative processes.

Given the absence of clinical response after six cycles of cladribine, together with progressive local enlargement, hemorrhage, tissue necrosis, and secondary infection, continued medical therapy was considered unlikely to achieve durable local disease control. Following multidisciplinary evaluation by the hematology and general surgery teams, the surgical excision was recommended. Cross-sectional imaging was not performed because of local resource limitations, and the indication for surgery relied on progressive clinical deterioration in the setting of a previously established histopathological diagnosis.

The patient underwent surgical excision under spinal anesthesia. A circumferential incision was made around the lesion, which was carefully dissected from the surrounding tissues. The intraoperative findings revealed a large inflammatory mass occupying the anterior right femoral region, with extensive gangrenous degeneration, multiple abscess cavities, and abundant purulent material both within and surrounding the lesion (Figure 2). A gross complete



Figure 3. Gross appearance of the excised surgical specimen. Photograph of the surgical specimen following complete excision within macroscopically healthy margins, after debridement of necrotic and abscessed tissue. The specimen was subsequently submitted for histopathological confirmation.

excision of the lesion was achieved intraoperatively, followed by meticulous debridement of all devitalized tissue, hemostasis, and wound packing (Figure 3). The surgical specimen was submitted for histopathological confirmation.

Postoperatively, the patient received empiric antimicrobial therapy for the secondary soft-tissue infection, thromboprophylaxis, and standard analgesic treatment.

His postoperative course was uneventful, without early surgical or medical complications. He remained clinically and hemodynamically stable throughout hospitalization and was discharged in good general condition, with recommendations for continued hematologic follow-up. At the time of this report, three months after surgery, the patient remains under hematologic surveillance with no clinical evidence of local recurrence or disease progression.

Discussion

Rosai-Dorfman disease is classified as a non-neoplastic histiocytic disorder; however, its clinical presentation may closely resemble malignant disease, particularly when extranodal soft tissues are involved[1,2]. Several reports have described soft-tissue Rosai-Dorfman disease presenting as a suspected sarcoma because of its infiltrative appearance, progressive enlargement, and nonspecific clinical or radiologic findings, with the definitive diagnosis established only after histopathological examination[4-8,14] (Table 1). In our case, the diagnosis was established early by core biopsy, thereby avoiding prolonged diagnostic uncertainty. The principal challenge was not establishing the diagnosis but managing disease progression despite histopathological confirmation and appropriately administered systemic therapy.

Current consensus recommendations advocate an individualized therapeutic approach based on disease extent, anatomical location, symptom burden, and organ involvement[1]. Observation may be appropriate for selected asymptomatic patients, whereas complete surgical excision is generally recommended for localized, accessible disease. Systemic therapy is reserved for symptomatic, multifocal, unresectable, or refractory cases[1,3]. Cladribine has become one of the most frequently used systemic treatments for refractory or disseminated Rosai-Dorfman disease, with encouraging responses reported in retrospective series and individual case reports[3,10,11]. At the same time, published experience shows considerable variability in treatment response, and durable disease control is not achieved in every patient[3,10,11].

In addition, clinically significant hematologic toxicity has been described during cladribine therapy, emphasizing the need for careful patient selection and close monitoring throughout the treatment[16].

Our patient represents a less frequently reported pattern of treatment failure. Despite six completed cycles of cladribine, the lesion demonstrated continuous progression, without any measurable clinical response.

Table 1. Reported cases of extranodal soft-tissue Rosai-Dorfman disease with clinical or radiological mimicry of malignancy

Reference	*Age/Sex*	*Site*	*Initial presentation*	*Initial management*	*Response to systemic therapy*	*Role of surgery*	*Outcome*	*Key relevance*
Komaragiri et al., 2013[4]	Pooled review (n=36); mean age 46.3y (10mo–72y); 17M/19F	Various soft-tissue sites	Soft-tissue masses frequently mimicking sarcoma	16/36 managed surgically; 19/36 managed medically (dapsone, steroids, or observation)	Heterogeneous response among medically managed cases	Primary treatment in selected localized cases; recurrence in 1/16 surgical cases	Variable (spontaneous resolution, partial regression, persistence, or regrowth across cohort)	Largest pooled review of extranodal soft-tissue Rosai-Dorfman disease
Betini et al., 2022[6]	18/F	Lumbosacral soft tissue	Enlarging lower-back mass; orthopedic oncology referral, MDM2 FISH performed to exclude liposarcoma	CT-guided biopsy followed by surgical excision	NR	Primary treatment	Asymptomatic at 17-month follow-up; residual enhancing lesion on MRI at 9 months; postoperative seroma	Illustrates diagnostic challenge of soft-tissue Rosai-Dorfman disease, including histologic ambiguity (emperipolesis not identified on initial biopsy)
Cravero & Ibrahim, 2024[15]	56/M	Right medial thigh (lipoma-associated)	Soft-tissue mass first biopsied in 2005; no excision performed for 7 years	Surgical excision (2012)	No systemic therapy	Initial excision (2012; repeat excision after recurrence (2021)	Watchful waiting after second excision; residual hypermetabolic activity on PET/CT, spontaneously decreasing	Demonstrates recurrent localized soft-tissue disease with prolonged, incomplete resolution
Bouhani et al., 2025[8]	56/M	Right thigh (smaller contralateral left thigh lesion also present)	Deep thigh mass with femoral vascular encasement and venous thrombosis	Surgical biopsy and anticoagulation	No systemic therapy	Diagnostic biopsy only; no therapeutic excision performed	Partial spontaneous regression (50% at 3 months); asymptomatic at 6 months	Demonstrates potential spontaneous regression despite aggressive appearance
Our case	**52/M**	**Right inguinofemoral region**	**Progressive mass despite six cycles of cladribine; necrosis, hemorrhage, and secondary abscess formation**	**Cladribine ×6 followed by surgical excision**	**Primary progression during active therapy**	**Salvage excision after systemic treatment failure**	**No clinical evidence of local recurrence or disease progression at 3-month follow-up**	**To our knowledge, the only reported case of localized inguinofemoral Rosai-Dorfman disease progressing during active cladribine therapy, successfully managed with salvage surgery performed without preoperative cross-sectional imaging**

Table 2. Reported cases of inguinal Rosai-Dorfman disease in the literature.

Reference	*Age/Sex*	*Presentation*	*Treatment*	*Outcome*
Pilania et al., 2019[13]	6/F	Unilateral inguinal lymphadenopathy, diagnosed by fine-needle aspiration cytology	Observation; no specific treatment given	Spontaneous complete resolution at 6 months; well at 2-year follow-up
Rodrigues et al., 2024 (Case 2)[12]	26/M	Painful right inguinal adenomegaly with fever, progressive over 20 days	Biopsy; empiric antimicrobial and corticosteroid therapy before diagnosis was confirmed	Rapid clinical deterioration with sepsis and multi-organ failure; death 15 days after biopsy; Rosai-Dorfman disease diagnosis established postmortem
Our case	**52/M**	**Progressive inguinofemoral Rosai-Dorfman disease refractory to six cycles of cladribine, complicated by hemorrhage, necrosis, and abscess formation**	**Salvage surgical excision**	**No recurrence at 3-month follow-up**

M: male; F: female.
Note: *Rodrigues et al. (2024) reported two patients; Case 2, with inguinal involvement, is shown here. Case 1 of that series (a 57-year-old woman with cutaneous breast involvement, not inguinal) achieved complete remission and is not represented in this table.*

The lesion neither stabilized nor regressed; instead, it enlarged progressively and ultimately developed extensive necrosis, hemorrhage, and secondary infection. This clinical course differs from the more commonly reported scenario of disease recurrence following an initial response to systemic therapy. Instead, it illustrates primary progression during active treatment, a situation that substantially narrows therapeutic options and may require earlier consideration of surgical intervention before local complications become irreversible.

Surgery has traditionally been reported as definitive treatment for localized extranodal Rosai-Dorfman disease, before systemic therapy becomes necessary[1,3]. Published experience with inguinal Rosai-Dorfman disease remains limited to two reported cases, neither of which underwent surgical excision: one resolved spontaneously under observation alone in a pediatric patient, while the other progressed rapidly to sepsis and death before a diagnosis could be confirmed and treatment initiated[12,13] (Table 2). In contrast, surgery in our case was performed only after prolonged failure of systemic therapy. By the time of referral, the lesion had evolved beyond an isolated histiocytic proliferation into a destructive soft-tissue process characterized by extensive necrosis, hemorrhage, and abscess formation. In this setting, surgical excision served two complementary purposes: removal of persistent histiocytic disease and control of its secondary infectious and hemorrhagic complications.

This sequence appears to be uncommon in the current literature and highlights an additional role for surgery as salvage treatment in carefully selected patients with localized extranodal disease that continues to progress despite systemic therapy.

An additional aspect of this case is the absence of preoperative cross-sectional imaging. Imaging was not omitted because it was considered unnecessary, but because of local resource limitations. Although cross-sectional imaging would ideally contribute to operative planning by defining lesion extent and its relationship to adjacent vascular and soft-tissue structures, surgical decision-making in this patient relied on progressive clinical deterioration together with a previously established histopathological diagnosis. Similar diagnostic and therapeutic challenges have been reported in resource-constrained healthcare settings managing rare histiocytic disorders[17]. The favorable postoperative course observed in our patient suggests that, in carefully selected cases with unequivocal histopathological confirmation and clear clinical progression, timely surgical intervention should not necessarily be delayed solely because advanced imaging is unavailable.

This report has several limitations. As a single-patient observation, it cannot establish the comparative effectiveness of surgery following cladribine failure or define the optimal timing of operative intervention in refractory Rosai-Dorfman disease. Furthermore, follow-up currently extends to three months, which is insufficient to exclude late recurrence. Continued clinical surveillance remains essential given the variable natural history of extranodal Rosai-Dorfman disease[1,9].

Conclusions

This case illustrates that localized extranodal Rosai-Dorfman disease may continue to progress despite appropriately administered systemic therapy, evolving from a chronic histiocytic disorder into an acute surgical condition characterized by tissue necrosis, hemorrhage, and secondary infection. Surgical excision achieved effective short-term local disease control after cladribine failure, functioning as salvage

treatment rather than first-line therapy. Clinical assessment, together with histopathological confirmation, was sufficient to guide operative management; the absence of preoperative cross-sectional imaging, a consequence of local resource limitations, was not associated with an unfavorable short-term postoperative outcome. Although no conclusions can be generalized from a single patient, persistent disease progression during active systemic therapy should prompt consideration of timely surgical reassessment before irreversible local complications develop, particularly in settings where advanced imaging is not readily available.

Author Contributions:

N.O. participated in the surgical procedure as an assistant, contributed to the acquisition and organization of the clinical and literature data, and drafted the manuscript. K.L. was responsible for the perioperative clinical management, including the pre- and postoperative period, and critically reviewed and revised the manuscript. Both authors have read and agreed to the published version of the manuscript.

Compliance with Ethics Requirements:

"The authors declare no conflict of interest regarding this article"

"The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from the patient included in the study"

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