



EPITHELIOID HEMANGIOENDOTHELIOMA - A RARE VASCULAR NEOPLASM PRESENTING AS SUPERFICIAL SOFT TISSUE MASS AT AN UNUSUAL LOCATION – CASE REPORT

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ABSTRACT

Superficial soft-tissue masses are among the most common indications for imaging of the extremities. A broad array of benign and malignant processes may be manifested in palpable cutaneous or subcutaneous masses or nodules. Because the imaging characteristics of many benign soft-tissue lesions overlap with those of malignant ones, knowledge of the patient's clinical history (including any laboratory test results) and direct visual examination of the lesion often are important for differentiation. Histopathological analysis may be necessary to achieve a definitive diagnosis.

A 82 years old male was referred for investigation to our department of radiology with the complaints of superficial soft tissue mass in right scapular and shoulder region for past 8years. The patient underwent ultrasonogram , CT scan and MRI to assess the nature of the swelling and was diagnosed as myxoid variant of liposarcoma radiologically. The excision biopsy was reported as Epithelioid hemangioendothelioma, a rare superficial soft tissue vascular neoplasm. No previous reports of Epithelioid hemangioendothelioma occurring in right scapular and shoulder region superficially as soft tissue mass have been recorded in the literature so far.

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INTRODUCTION

Cutaneous and subcutaneous masses of the extremities comprise a broad and potentially bewildering array of benign and malignant processes. It can be difficult to find a description of lesions of this type in the musculoskeletal radiology literature, because these lesions are rarely identified or classified according to their superficial location and because some of them are seen only by dermatologists, without radiologic evaluation.

Superficial soft-tissue masses are among the most common indications for imaging of the extremities. Because the imaging characteristics of many benign soft-tissue lesions overlap with those of malignant ones,

knowledge of the patient's clinical history (including any laboratory test results) and direct visual examination of the lesion often are important for differentiation. Histopathological analysis may be necessary to achieve a definitive diagnosis.

The purpose of this case report is to enlighten radiologists about this rare vascular tumour - Epithelioid hemangioendothelioma occurring in skin and subcutaneous tissue, to study its radiological features and to add it into the list of differential diagnosis at apt places.

Case Report

A 80years male presented to our radiology department with a large superficial soft tissue tumour in right scapular

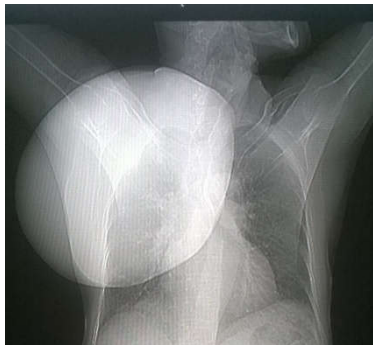
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and shoulder region. It was present for past 8 years and had attained the present size by gradual increase in size over these years. Patient correlates it with a history of trauma. No history of fever or loss of weight noted. Past history of surgery for a similar lesion at an adjacent site was done 20 years back for which records were not available.

Clinical examination shows a well defined superficial soft tissue mass of 20x17 cm size with cystic consistency located in right scapular and shoulder region. It appears sessile and shows restricted mobility. No active skin ulceration, but an old scar and skin excoriation is seen over the lesion. Dilated superficial veins and stretched skin noted over the mass. Transillumination and fluid thrill were positive. No obvious palpable nodes noted in neck and axillary region bilaterally. Blood investigations were normal. HIV test was nonreactive.

Radiological investigations: X ray chest AP and Lateral views showed a large superficially located radio opaque lesion in right scapular and shoulder region. It appeared homogenous without visible calcifications. Subcutaneous fat plane appeared involved by the tumour. No adjacent rib, scapular erosions or bone remodelling seen.



X ray chest AP view shows a welldefined extrathoracic opaque lesion in the region of right scapula and shoulder.

Ultrasonogram abdomen was normal. No evidence of any secondary deposits in abdomen.



Ultrasound of the mass lesion shows solid and necrotic areas.

Ultrasonogram of the mass lesion shows well defined, round predominantly heterogenous looking soft tissue

mass with focal hyperechoic and hypoechoic areas in it. It showed involvement of the skin and subcutaneous plane. Thick internal septation with vascularity seen. Focal hyperechoic area showed post acoustic shadowing. Disorganised vascular pattern noted in the solid areas by Doppler study. No perilesional edema seen. Superficial skin was thickened.

Computed Tomography of the mass showed well defined superficial soft tissue mass lesion (size 20x18x15cm) in right scapular and shoulder region with predominantly central necrotic component, thick wall, thick septations, focal areas of fat attenuation, focal areas of calcification and showing heterogenous peripheral enhancement after contrast.



Prone CT study of the mass lesion shows thick walled predominantly necrotic lesion with peripheral foci of fat attenuation.

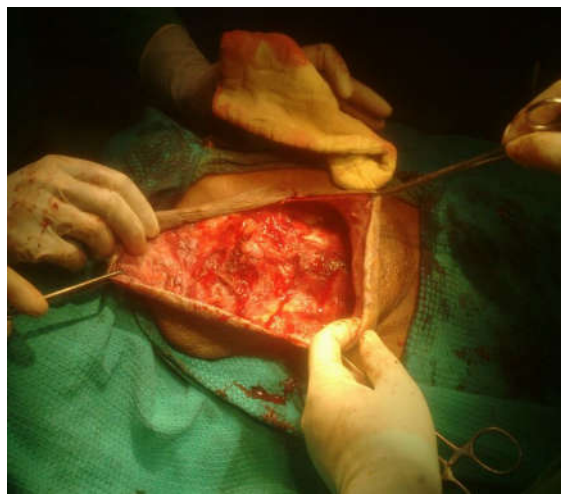


Sagittal reconstruction of CT scan shows the extent of the mass with foci of fat and calcification within it.

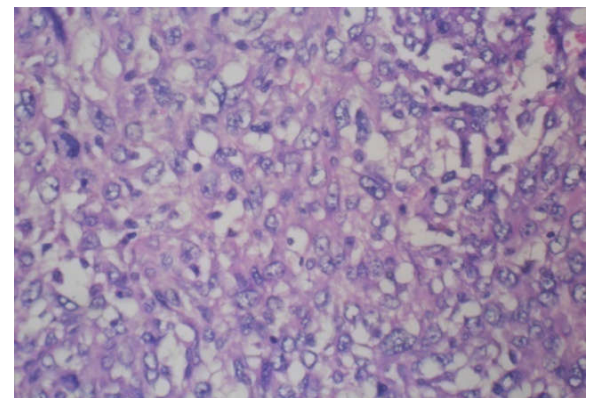
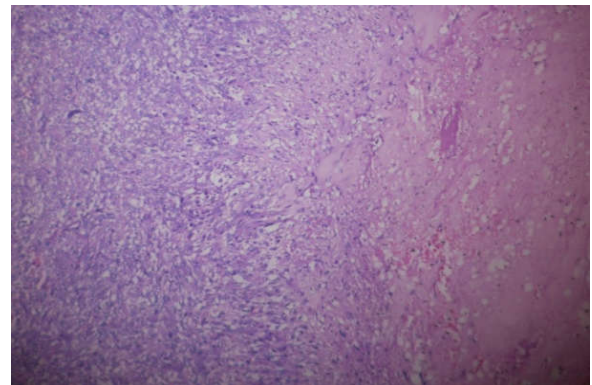
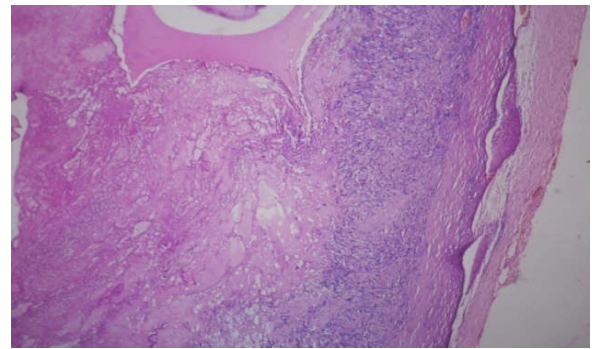
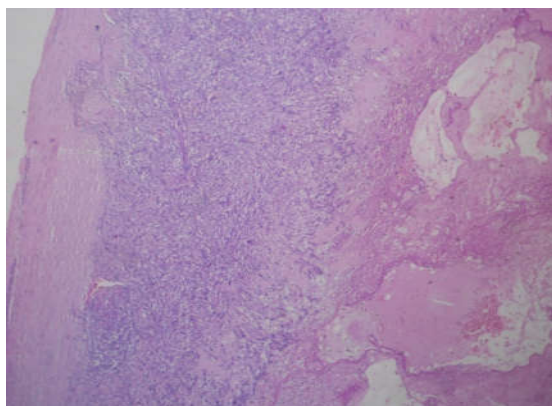
Magnetic resonance imaging (image not provided) shows the predominantly T2 hyperintense and T1 hypointense superficially located mass in right scapular and shoulder region with focal T1 and T2 hyperintense areas suggestive of fat and focal area of blooming in gradient images suggestive of calcification. Infiltration into superficial skin and underlying fascial and muscular plane were noted without involvement of underlying bones.

Imaging features, its huge size, pseudocystic CT/MRI appearance, disorganized vascular pattern in Doppler, focal presence of fat and calcification and infiltration into skin, fascia and underlying trapezius muscle suggested that it could be a myxoid variant of liposarcoma. The patient underwent complete excision of the mass and the tumour was sent for histopathological analysis. Gross

pathological examination showed a multilobulated partly solid and necrotic lesion with sloughy material inside. Central hemorrhagic fluid was seen. Microscopic examination showed a cellular tumour with hemorrhagic necrosis. Tumour cells are elongated, spindle shaped, arranged in sweeping bundle exhibiting anaplasia and pleomorphism. Tumour cells seen around blood vessels in peritheliomatous pattern. Lymphocyte infiltration and hyalinization seen. Tumour with extensive area of hemorrhagic necrosis and dilated vascular channels seen with congested vessels. Tumour cells are round to elongated plump cells that tend to form vascular spaces. Tumour cells are arranged as sheets suggestive of epithelioid hemangioendothelioma. No previous reports of Epithelioid hemangioendothelioma occurring in right scapular and shoulder region superficially as soft tissue mass have been recorded in the literature so far.



Preoperative and peroperative clinical photograph of the mass lesion.



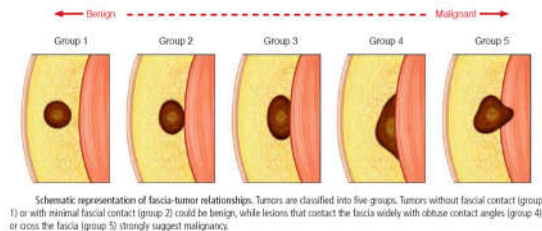
Histopathological slides of the mass lesion showing tumor cells which are elongated, spindle shaped, arranged in sweeping bundle exhibiting anaplasia and pleomorphism.

DISCUSSION

The ultrasonography (US) findings that might suggest benignancy of a soft tissue mass are a small size, (<5cm) superficial location, homogeneous echo pattern, and hypovascularity. However, these findings are not sufficiently reliable to definitively characterize the nature of a lesion.^(1,2) US findings can be misleading, since similar findings also occur in synovial sarcoma, liposarcoma, melanoma, lymphoma, myeloid sarcoma and small metastasis. For soft tissue tumors, large size, deep location, heterogeneous signal intensity and echo, and internal hemorrhage or necrosis suggest the possibility of malignancy rather than a benign tumor.⁽⁴⁻⁷⁾

For superficial masses, there are some factors indicative of malignancy. Unlike deep-seated lesions, size is not an important factor because a significant proportion of superficial malignant tumors measure less than 5 cm in maximal diameter. Fascial edema, skin thickening, skin

contact, hemorrhage, and necrosis are highly significant factors indicative of malignancy. Lobulation and peritumoral edema are also significant features.⁽⁹⁾ Obtuse angles between the superficial investing fascia and the subcutaneous mass crossing the fascia strongly suggest malignancy.⁽³⁾ Galant *et al.*⁽³⁾ described these fascia-tumor relationships with schematic representation. Malignant tumors of the subcutaneous compartment have a higher tendency to develop a close relationship with the fascia than benign lesions.⁽⁸⁾



Malignant superficial soft-tissue masses are primary or metastatic neoplasms and the incidence of sarcoma increases with age. The most common malignant sarcoma in first two decades is rhabdomyosarcoma and in fifth to seventh decades is malignant fibrous histiocytoma.⁽¹²⁾ On US, malignant soft-tissue tumors commonly appear hypochoic and hyper-vascular and can be well-defined. Cystic components, areas of necrosis, and dystrophic calcifications may also be seen. Tumor vascularity correlates with the degree of neoangiogenesis. Many authors have suggested that color and Power Doppler US (PDUS) may be useful in differentiation of benign and malignant tumors and in staging of malignant tumors.⁽¹³⁻¹⁵⁾ Linear and regular course of the vessels are more suggestive of benignity, whereas scattered and irregular course of the vessels and sudden change in diameter of the vessel might be associated with irregular tumor angiogenesis and suggestive of malignancy.⁽¹⁶⁾ The use of resistive index (RI) was not found to be successful in differentiation of malignancy and benignity.⁽¹⁷⁾ Also, diastolic and venous velocities and pulsatility index (PI) were not found to be useful in distinguishing between malignant and benign lesions. Mean systolic peak flow velocity was found to be higher in malignant tumors.^(13,18,19) Mean peak velocity was found to be 27 cm/s in benign lesions, whereas mean peak velocity in malignant lesions was 55 cm/s. Flow velocities greater than 50 cm/s have been reported to be useful in distinguishing benign from malignant lesions.⁽¹⁶⁾ Sonography can also be used for following the therapeutic response and recurrence with a relatively high accuracy.⁽¹¹⁾ The only role of USG in malignant tumors is to define the extent and relationship of the mass with the surrounding structures. It is usually not possible to assess the histology.⁽¹⁰⁾

Liposarcoma

Liposarcoma is the second most common type of soft-tissue sarcoma, accounting for 10%–35% of these lesions. The World Health Organization has categorized soft-tissue liposarcomas into five distinct histologic subtypes: well-differentiated, dedifferentiated, myxoid, pleomorphic, and mixed type. Well-differentiated liposarcomas frequently demonstrate a diagnostic appearance on computed

tomographic (CT) or magnetic resonance (MR) images, with a largely lipomatous mass (>75% of the lesion) and nonlipomatous components in thick septa or focal nodules. The CT or MR imaging finding of a nodular dominant focus (>1 cm in size) of nonlipomatous tissue in a well-differentiated liposarcoma suggests dedifferentiated liposarcoma, and biopsy should be directed at the nonadipose component. The high water content of myxoid liposarcoma seen at pathologic analysis and constituting the majority of the lesion is reflected at sonography, CT, and MR imaging. However, the detection of a small amount of adipose tissue in the septa or as small nodular foci superimposed on the background of myxoid tissue allows prospective diagnosis in 78%–95% of myxoid liposarcomas. Pleomorphic liposarcomas are high-grade sarcomatous lesions and typically appear as heterogeneous soft-tissue masses, although small amounts of fat are seen on MR images in 62%–75% of cases, findings that suggest the diagnosis. Mixed-type liposarcomas have features representing a combination of the other subtypes.

Radiographs of myxoid liposarcoma may appear normal or more frequently reveal a nonspecific soft-tissue mass. Calcification occurs much less frequently than with well-differentiated liposarcoma⁽²⁰⁾. Similarly, a radiolucent fat is also seen much less often compared with well-differentiated liposarcoma, owing to the much smaller volume of adipose tissue (often <10%) in these lesions^(21,22). US reveals a complex, well-defined, hypochoic but solid, noncystic mass with posterior acoustic enhancement. Although adipose tissue typically cannot be definitively identified in most cases at sonographic evaluation to suggest the diagnosis, US findings can be very helpful in several specific clinical scenarios. For example, in cases in which the CT or MR imaging findings suggest a cyst, sonography can demonstrate that the mass is not truly a cyst (anechoic mass that may contain thin septa) and thus further investigation with biopsy is necessary. In addition, a popliteal location of myxoid liposarcomas is common, and such lesions may simulate a Baker cyst. However, as described by Ward and colleagues⁽²³⁾, all popliteal cysts have a fluid-filled neck that extends to the joint between the gastrocnemius and semimembranous tendons. This finding is not seen with a popliteal myxoid liposarcoma, since these lesions are not as superficial as a Baker cyst, and again the mass does not meet sonographic criteria for a true cyst. At CT and MR imaging, myxoid liposarcoma are typically large, well-defined, and multilobulated intermuscular lesions. The high water content of the lesion is reflected as predominant low attenuation on CT images, low signal intensity on T1-weighted MR images, and marked high signal intensity on T2-weighted MR images. However, the pathognomonic feature is the adipose tissue seen in the mass. MR imaging is superior to CT in this important depiction of fat, owing to its improved contrast resolution. Fat also typically constitutes only a small volume of the overall mass size (<10% of the lesion) and is often seen in septa (lacy or linear pattern) or as subtle small nodules in the lesion. This pathognomonic appearance of fatty septa or small adipose nodules in a myxoid mass has been reported in 42%–78% of cases⁽²²⁾. 90%–95% of myxoid liposarcomas demonstrate fat at MR imaging⁽²¹⁾.

Identification of this subtle fat is aided by the careful comparison of T1- and T2-weighted images in the same plane (usually axial is optimal). Use of fat-suppression or fat-saturation techniques can also be very helpful to further increase confidence in the detection of adipose content in these regions. According to the literature, myxoid liposarcoma may simulate a cyst because of its homogeneous low attenuation on CT images or homogeneous low to intermediate signal intensity on T1-weighted MR images and very high signal intensity on T2-weighted MR images in 21%– 22% of cases ⁽²²⁾. The prevalence of myxoid liposarcoma simulating a cyst (“cyst mimicker”) at MR imaging is much lower (5%–10%), but this remains an important radiologic diagnostic dilemma ⁽²¹⁾. The strongest indications that one may be dealing with a “cyst mimicker” such as a myxoid liposarcoma include the following observations: (a) when the lesion is not in the expected location of a synovial cyst or ganglion, (b) when the lesion has no thick wall or surrounding edema, or (c) when there is no appropriate clinical history to suggest abscess or liquefied hematoma. These features mandate further radiologic evaluation with either US or contrast material enhancement. Those lesions identified as solid masses (with high water content) require biopsy. Myxoid liposarcomas enhance with contrast material at MR imaging, a characteristic that easily distinguishes these lesions from a cystic mass. Tateishi and colleagues⁽²⁴⁾ reported on the patterns of myxoid liposarcoma enhancement at MR imaging, which included peripheral nodular (61% of cases), central nodular (44%), and diffuse (17%). Their findings are in marked contrast with those for a true cystic mass, which enhances with thin and nonnodular, peripheral and septal patterns only.

Epithelioid hemangioendothelioma

Epithelioid hemangioendothelioma is a rare, slowly progressive, distinct pathological vascular tumor that can occur at any age anywhere in the body. It is most common in the skeleton, a location not primary to vascular neoplasms.^(25,26)

Because of the rarity of this lesion, its nonspecific imaging appearance, and its varied locations and ages of presentation, the pathologist is usually the first to diagnose this tumor, and it is not typically part of the radiology differential diagnosis.^(26,27)

Clinical features

Epithelioid hemangioendothelioma was originally described by Weiss and Enzinger in 1982 as a distinctive low-grade angiosarcoma. Usually, the neoplasm presents as a painful and poorly circumscribed mass involving subcutaneous soft tissues of the extremities,⁽²⁸⁾ The neoplasm may appear at any age, although is rare in children,⁽²⁹⁾ and affects both sexes with similar frequency. In half the cases, the neoplasm was in connection with a preexisting vessel, almost always a large vein.⁽²⁸⁾ In some of these cases, the occluded vessel caused edema and thrombophlebitis of the involved area. Before a diagnosis of cutaneous epithelioid hemangioendothelioma is established, the possibility of cutaneous metastasis from a visceral epithelioid hemangioendothelioma should be ruled out.^(30,31)

Histopathologic features

Cutaneous epithelioid hemangioendothelioma presents as a well-circumscribed dermal nodule, which is sometimes covered by hyperplastic epidermis. Epithelioid hemangioendothelioma is composed of cords, strands, and solid aggregates of round, oval, and polygonal cells, with abundant pale eosinophilic cytoplasm, vesicular nuclei, and inconspicuous nucleoli, embedded in a fibromyxoid or sclerotic stroma. Many neoplastic cells exhibit prominent cytoplasmic vacuolization as expression of primitive vascular differentiation. Sometimes, nuclear pleomorphism and mitotic figures are present. In rare instances, vascular channels and wellformed large vessels are seen in the central areas of the lesion. Occasionally, bone metaplasia has been described in the stroma of epithelioid hemangioendothelioma.⁽³²⁾ Lesions that arise in a preexisting vessel extend centrifugally to adjacent soft tissues, and the architecture of the original vessel is spared. In rare instances, the lumen of the vessel appears occluded by necrotic material and dense collagen bundles. Histopathologic differential diagnosis between epithelioid hemangioendothelioma and metastatic signet-ring cell adenocarcinoma may be challenging because neoplastic cells of signet-ring cell adenocarcinoma may show cytoplasmic vacuoles containing mucin. In these cases, the presence of erythrocytes within the cytoplasmic vacuoles is a helpful clue for diagnosis of epithelioid hemangioendothelioma.⁽³³⁾ Immunohistochemistry is also helpful in this differential diagnosis because neoplastic cells of epithelioid hemangioendothelioma express immunoreactivity for endothelial markers, such as von Willebrand factor, CD31, and CD34.^(28,33) They also express positivity for podoplanin, Lyve-1, and Prox-1, supporting a lymphatic line of differentiation.⁽³⁴⁾ However, caution should be taken with the immunostains for cytokeratins 7 and 18,^(33,35) as well as for SMA,⁽³³⁾ as neoplastic cells of epithelioid hemangioendothelioma contain abundant intermediate filaments and may express positivity for these markers, leading to a wrong diagnosis.

Table 1 International Society for the Study of Vascular Anomalies Classification System

Vascular (or vasoproliferative) Neoplasms	Vascular Malformations
Infantile hemangioma	Slow-flow vascular malformations
Congenital hemangiomas	Capillary malformation
RICH	Venous malformation
NICH	Lymphatic malformation
Kaposiform hemangioendothelioma and tufted angiomas (with or without Kasabach-Merritt syndrome)	Fast-flow vascular malformations
Spindle cell hemangioendothelioma	Arterial malformation
Epithelioid hemangioendotheliomas	Arteriovenous malformation
Other rare hemangioendotheliomas (ie, composite, retiform, and others)	Arteriovenous fistula
Angiosarcoma	Combined vascular malformations (various combination of the above)
Dermatologic acquired vascular tumors (ie, pyogenic granuloma)	

RICH, rapidly involuting congenital hemangioma; NICH, noninvoluting congenital hemangioma.

Electron microscopy studies have demonstrated that neoplastic cells of epithelioid hemangioendothelioma show ultrastructural characteristics of endothelial cells, with well-developed basement membrane, pinocytotic vesicles, and occasional Weibel-Palade bodies. These cells differ from normal endothelial cells by the abundant number of intermediate filaments within their cytoplasm.⁽³⁶⁾ Cytogenetic studies in epithelioid hemangioendothelioma failed to demonstrate microsatellite instability,⁽³⁷⁾ although 2 cases showed a t(1;3)(p36.3;q25) translocation.

Treatment

Surgical excision with clear margins is the best treatment for this neoplasm. Regional lymph nodes should be also evaluated, as they are the most frequent sites for metastases. Metastases seem to be more common when the primary neoplasm exhibits cytologic atypia. Less than half the patients with lymph node metastases will die of the neoplasm because surgical excision of the primary neoplasm and the involved lymph nodes is usually curative. Some authors have suggested that epithelioid hemangioendothelioma should be considered as an authentic angiosarcoma, with better prognosis than classic angiosarcoma, but with higher potential for metastatic disease than other hemangioendotheliomas.⁽³³⁾

CONCLUSION

In summary, superficial soft-tissue masses are manifestations of a wide variety of benign and malignant processes. Knowledge of the patient's clinical history and direct visual examination of the lesion may help narrow the differential diagnosis. Imaging findings can be used to direct biopsy of representative regions from superficial soft tissue masses in these usually large neoplasms and lead to improved pathologic evaluation and a specific histologic diagnosis. Understanding and recognizing the spectrum of radiologic appearances and the pathologic basis allows improved patient assessment and is vital for optimal clinical management.

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