

Case Report

Malignant Chondroid Syringoma: A Report of Two Cases with a Sarcomatous Mesenchymal Component

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Keywords

Malignant mixed tumour · Chondroid syringoma · Carcinosarcoma · Adnexal neoplasms · Skin

Abstract

Malignant chondroid syringoma (MCS; malignant mixed tumour) is a rare neoplasm typically arising on the extremities and trunk. We report 2 unique cases of MCS, one occurring on the scalp of a 78-year-old man and the other on the trunk of a 72-year-old woman. Both tumours harboured malignant epithelial and malignant mesenchymal components. The latter was represented by liposarcoma in the first case. The malignant components of the second tumour comprised spindle cell squamous cell carcinoma (SCC) and osteosarcoma. Origin from a pre-existing benign chondroid syringoma was clearly evident in both neoplasms. The presence of heterologous malignant mesenchymal components, however, is hitherto unreported in the context of MCS, while a spindle cell SCC component is exceptionally rare. The 2 cases presented herein highlight an expanded morphological spectrum of MCS, with resultant blurring of the boundaries between MCS and cutaneous carcinosarcoma.

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Introduction

Chondroid syringoma, also known as benign mixed tumour of skin, usually manifests as an asymptomatic dermal or subcutaneous nodule in the region of the head and neck [1, 2]. The malignant counterpart thereof, termed malignant chondroid syringoma (MCS; malignant mixed tumour) is a rare neoplasm that typically occurs on the extremities or trunk, and

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exhibits somewhat of a female predilection [3]. The tumour lacks distinctive clinical features and the diagnosis is made on its pathological features [3, 4]. MCS is a potentially aggressive neoplasm with a propensity to recur following inadequate surgical excision [5, 6]. Invasion of surrounding tissues and spread to distant sites have been reported [4, 5, 7–9]. Herein we report our experience with 2 cases of MCS harbouring a sarcomatous mesenchymal component, and showing origin in association with a benign mixed tumour of skin.

Case Report

Case 1

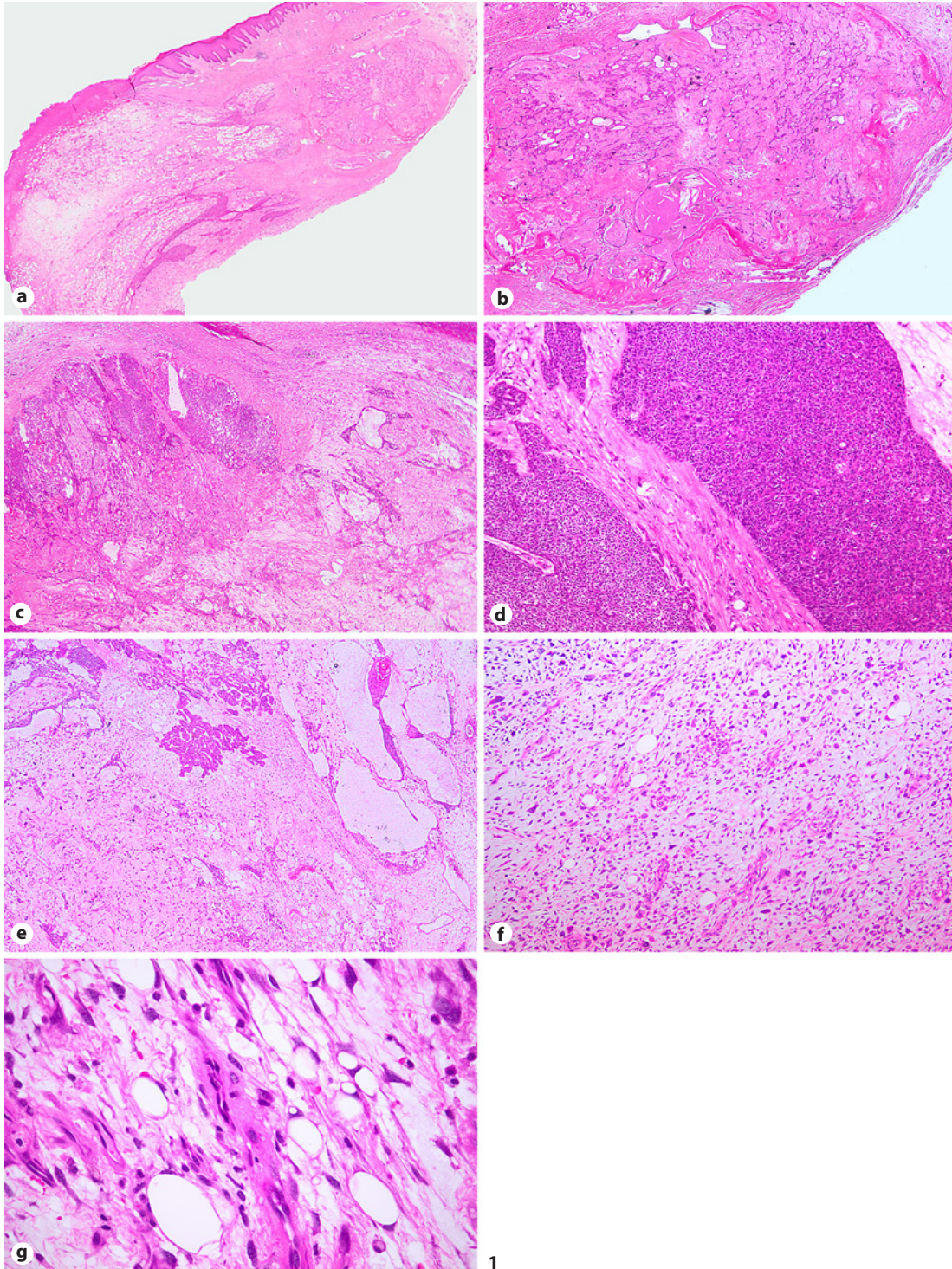
A 78-year-old black male presented with a long-standing history of a fungating scalp mass involving the parieto-occipital region. No pre-operative imaging studies were performed. The tumour was excised with a wide surgical margin. An orientated skin ellipse measuring 2.8 × 2.2 cm with a subcutaneous depth of 1.0 cm was received. Present centrally was an ulcerated mass measuring 4.0 × 3.6 × 1.2 cm. Histopathological examination (Fig. 1) revealed a non-encapsulated malignant neoplasm composed of malignant epithelial cells embedded within a malignant stroma. The overlying epidermis was ulcerated. There was no demonstrable continuity between the neoplasm and the epidermis. The malignant epithelial cells formed irregular nests, ducts, glands and anastomosing cords. Some of these nests showed squamous differentiation. The epithelial cells were epithelioid with abundant eosinophilic cytoplasm and central nuclei. The nuclei were markedly pleomorphic and hyperchromatic, with irregular nuclear contours. Mitotic activity was brisk within the epithelial component. The malignant stroma was heterogeneous, comprising predominantly myxoid material within which neoplastic cells were embedded. These cells showed marked pleomorphism as well as eosinophilic cytoplasm, irregular hyperchromatic nuclei, and occasional multinucleation. Numerous mitoses were identified. In some areas the stroma had a chondromyxoid appearance. Foci of unequivocal liposarcomatous differentiation were discernible, the latter comprising vacuolated lipoblasts with scalloped, hyperchromatic nuclei. Neither lymphovascular space invasion nor perineural infiltration was observed. The tumour was strongly positive for S100 protein in the liposarcomatous foci and displayed weaker positive staining in the myoepithelial component. The malignant mesenchymal component was negative for CAM5.2 and carcinoembryonic antigen (CEA) which were both positive in the benign chondroid syringoma. Present within the dermis adjacent to the aforementioned malignant neoplastic proliferation and distinctly separate from the latter was a benign mixed tumour of skin. The patient was clinically well at the time of his last follow-up visit 6 months post-surgery, with no evidence of local recurrence or metastatic disease.

Fig. 1. Malignant chondroid syringoma (MCS), case 1. **a** Low-power image of the ulcerated, intradermal neoplasm, which comprises a circumscribed benign chondroid syringoma (BCS) component (right) undergoing transition to an MCS (left). **b** Bland anastomosing epithelial cords and tubular structures embedded in a collagenous stroma typify the pre-existing BCS. The transition from BCS to MCS (**c**) is evident on the left of this field, while a closer view of the carcinomatous areas (**d**) declares solid sheets of atypical epithelial cells with hyperchromatic nuclei, abundant eosinophilic cytoplasm and brisk mitotic activity. There is a relatively abrupt transition between the carcinomatous component and adjacent sarcomatous foci (**e**), with the latter comprising pleomorphic, hyperchromatic spindled and larger plump cells set within a richly vascular background of myxoid stroma (**f**). **g** Numerous vacuolated lipoblasts with scalloped, hyperchromatic nuclei characterise the associated liposarcomatous component.

(For figure see next page.)

Case 2

A 72-year-old African female presented with a hard, mobile mass on the lateral aspect of the thigh for “many years.” The lesion had, however, shown progressive enlargement over a 2-year period prior to excision. The resected specimen consisted of an ellipse of skin



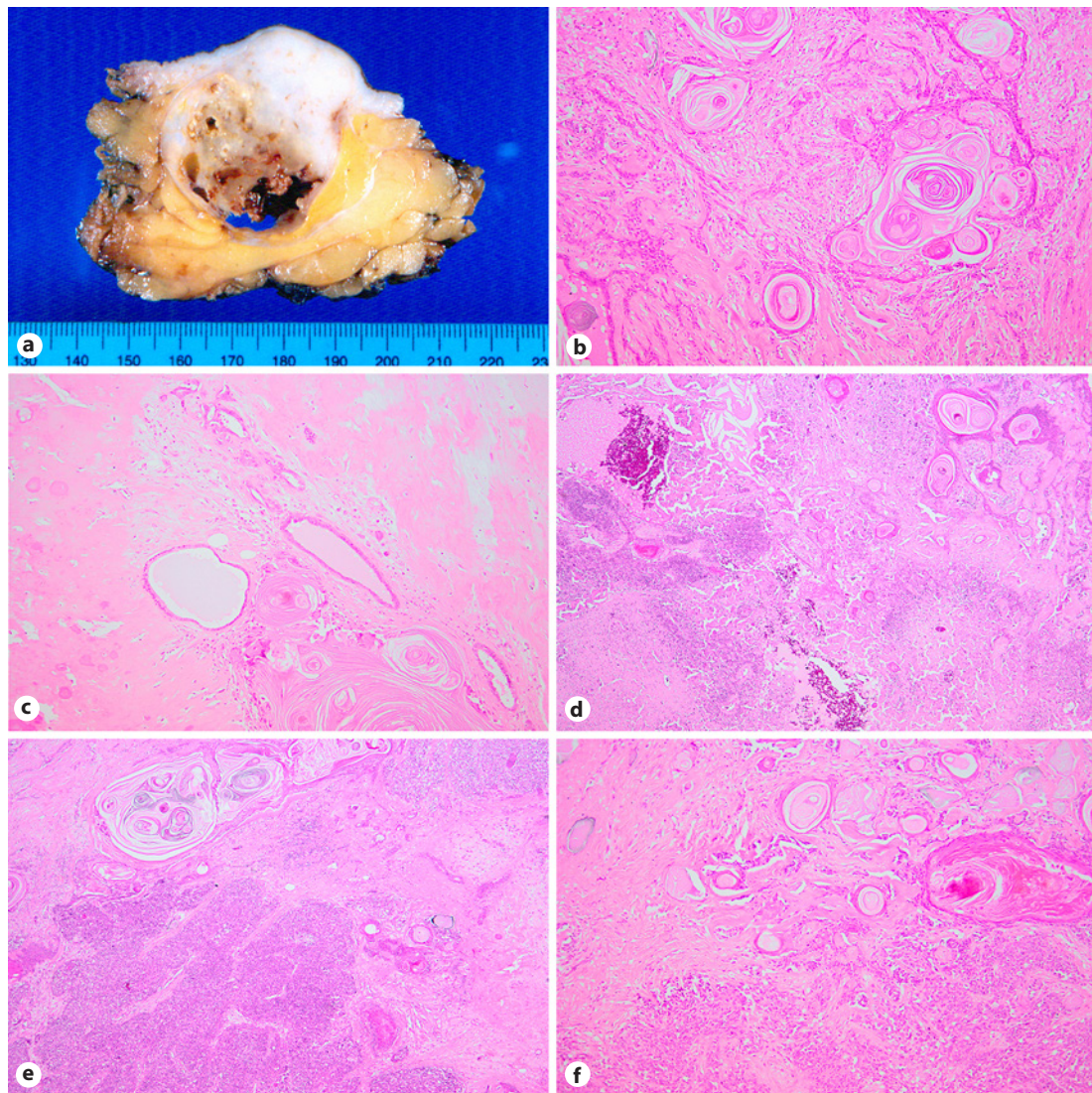
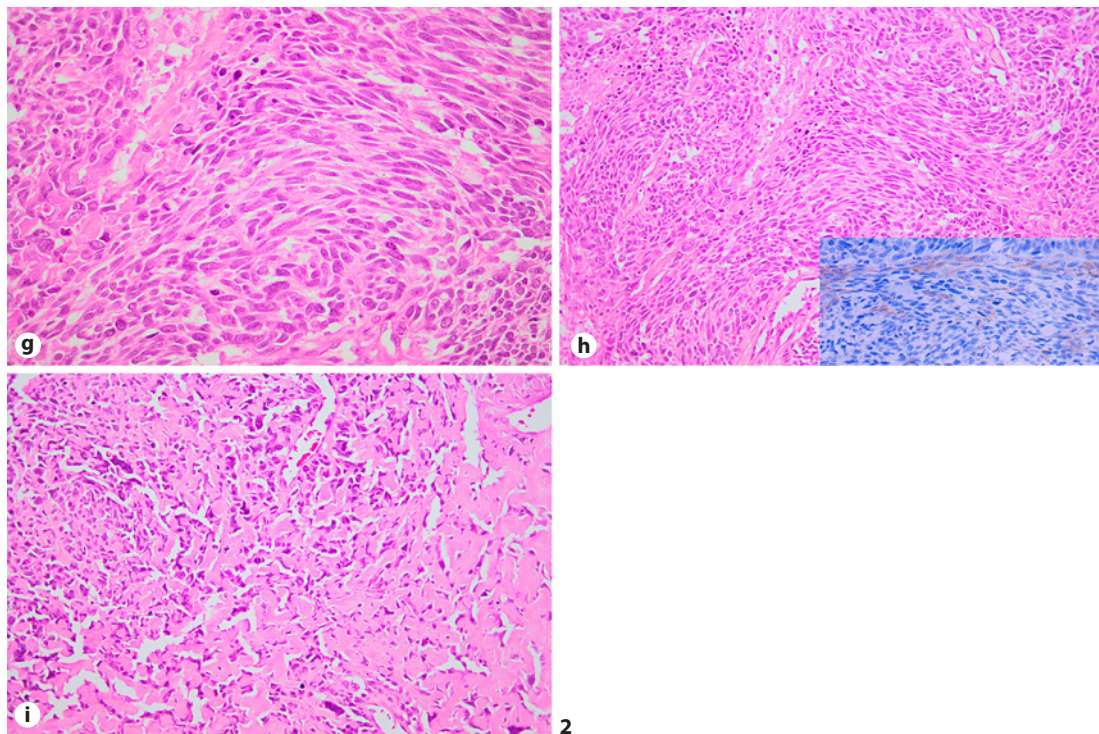


Fig. 2. Malignant chondroid syringoma (MCS), case 2. **a** Macroscopic image of the resected neoplasm, with the cut surface thereof revealing partial cystic degeneration and necrosis. The more solid white protuberant area corresponds to a benign chondroid syringoma (BCS) component, which is characterised microscopically by bland epithelial cords enveloping keratinous cysts (**b**), banal tubular structures, and an associated chondromyxoid stroma (**c**). **d** Low-power examination reveals a residual BCS in the upper part of the field, which is somewhat overshadowed by an adjacent malignant neoplasm showing areas of necrosis and dystrophic calcification. There is clear transition from a precursor BCS to spindle cell squamous cell carcinoma (SCC) (**e, f**), with the latter comprising haphazardly arranged fascicles of pleomorphic, mitotically active spindled cells (**f, g**) exhibiting focal pancytokeratin (MNF116) immunoreactivity (**h, inset**). The sarcomatous SCC in turn gives way to an osteosarcomatous component (**i**), with seams of eosinophilic osteoid material flanked by pleomorphic hyperchromatic cells, including multinucleate forms.

(Figure continued on next page.)

with underlying subcutaneous tissue. Centred on the deep dermis and involving the subcutis was a large, almost dumbbell-shaped tumour with a maximal diameter of 8 cm. There was demonstrable continuity with a raised, somewhat protuberant 2-cm-diameter nodular component in the upper dermis. On sectioning, the mass presented a glistening



grey-white cut surface with occasional cystic and haemorrhagic foci (Fig. 2). Microscopic examination revealed a malignant biphasic deep dermal tumour lacking continuity with the overlying epidermis. There were extensive areas of necrosis. Thorough sampling declared a background benign mixed tumour of skin, with lobules of chondromyxoid stroma and solid islands of cytologically bland cartilage separated by an epithelial component consisting of banal ductal structures, anastomosing epithelial strands and keratin-filled cysts of varying diameter lined by bland squamous epithelium. Numerous foci of dystrophic calcification were observed throughout. Benign bone was encountered in other sections. A malignant, predominantly spindle cell component was seen to originate directly from the benign epithelial component. This malignant epithelial component comprised solid islands and fascicles of markedly pleomorphic spindled and epithelioid cells with hyperchromatic nuclei and a high mitotic index. The fascicles of malignant spindled cells showed direct continuity with the benign squamous epithelial elements, which showed progressive atypia and transition to a spindle cell carcinoma. Elsewhere, anastomosing strands of malignant cells enveloped seams of homogenous, unmineralised eosinophilic osteoid. Epithelial membrane antigen (EMA) and CEA immunohistochemical stains highlighted the presence of benign ductal structures in the benign chondroid syringoma component. A population of S100 protein and smooth muscle actin immunoreactive myoepithelial cells was also demonstrated in the latter. The malignant component showed focal immunostaining with antibodies to EMA and cytokeratin (MNF116, AE1/AE3 and 34 β E12), including the spindled cells and rounder pleomorphic cells associated with the osteoid material. These cells, however, did not stain with antibodies to muscle-specific actin and smooth muscle actin negative. Invasion of vascular structures, lymphatic spaces or nerves was not evident. The patient was lost to follow-up after being discharged from hospital.

Discussion

MCS is a very rare malignant cutaneous adnexal neoplasm and is said to account for only 0.01% of all primary skin tumours [1]. The majority of cases recorded in the English medical literature have been in the form of single case reports [4, 7, 10–14]. Synonymous terms include malignant mixed tumour of skin [14], cutaneous malignant mixed tumour [15], metastasising chondroid syringoma [16] and aggressive chondroid syringoma [17]. Cases of “atypical mixed tumour of skin” may perhaps represent additional examples of MCS [16]. The tumour typically occurs as a rapidly enlarging nodule on the extremities either proximally or distally and on either the upper or lower limb [3, 7, 8, 11, 18]. Other reported sites include the sacral region [5, 11] and the head and neck area, including the scalp, face and external acoustic meatus [3–5, 10, 11, 13]. The tumour appears to be more prevalent among females. Usual presentation is in the fourth decade of life [8, 13]. The age range, however, is wide with the youngest recorded patient aged 14 years and the oldest 86 years at the time of diagnosis [3, 13]. Tumour size is variable, with some documented neoplasms attaining a diameter of up to 8 cm, similar to case 2 in the present report [9].

Although the presence of an associated benign chondroid syringoma facilitates an irrefutable diagnosis of MCS, a benign component is only rarely observed [3, 13, 19]. The majority of cases, therefore, appear to arise *de novo*, with anaplastic changes likely occurring early in the evolution of the neoplasm [3]. It is, however, conceivable that a precursor benign component might be overrun by the malignant proliferation in some cases. On rare occasions a primary benign mixed tumour may undergo transformation to an MCS after an interval of many years, with subsequent metastasis [10, 12, 13].

Apocrine benign mixed tumours of the skin may exhibit a wide variety of potential metastatic changes in respect of their epithelial, myoepithelial and/or stromal components [19, 20]. Both cases of MCS presented herein arose in association with a classic benign mixed tumour of skin, consisting of interconnected, double-layered ducts embedded in a chondromyxoid or fibromyxoid matrix. Banal keratin-filled, follicular-derived cystic structures were particularly prominent in case 2. MCS is classically described as a biphasic tumour with a malignant epithelial component admixed with a benign chondroid mesenchymal component [2]. The malignant epithelial component is characterised by increased cellularity, lack of cellular cohesion, frequent absence of glandular or ductal differentiation, infiltrative growth, necrosis, nuclear pleomorphism and increased mitotic activity [2, 3, 10, 13, 15]. Dermal satellite nodules [6] and osseous metaplasia have also been reported [3]. MCS show a similar immunohistochemical staining pattern to its benign counterparts, with positive staining for cytokeratins, CEA (in the ductal component) and S100 protein in the chondroid areas [1, 12, 14]. The histological differential diagnosis includes other malignant skin adnexal neoplasms, such as malignant cylindroma [21], eccrine porocarcinoma [22], malignant eccrine spiradenoma [23], malignant proliferating trichilemmal cyst [24] and pilomatrix carcinoma [25].

To date, malignancy in MCS has been described exclusively in relation to the epithelial component. The malignant epithelial component in case 1 comprised an undifferentiated carcinoma. The occurrence of a malignant spindle cell carcinomatous component, as described in case 2 in the present report, is an exceptionally rare event [19]. Case 2 also harboured an osteosarcomatous mesenchymal component. The aforementioned combination of features is hitherto unreported in MCS, as is the heterologous liposarcomatous component observed in case 1. The presence of malignant epithelial and mesenchymal components in our 2 cases, therefore, raises the possibility of a primary cutaneous carcinosarcoma in the differential diagnosis. A confident diagnosis of MCS, however, was made possible based on the identification of an unequivocal background of benign chondroid syringoma in both neoplasms. One could nevertheless argue that our cases might indeed represent additional examples of cuta-

neous carcinosarcoma, as the aforementioned term has been applied to other biphasic malignant tumours arising in concert with pre-existing benign adnexal neoplasms; these include rare examples of eccrine porocarcinoma, malignant cylindroma, malignant spiradenoma and pilomatrical carcinosarcoma [2, 21, 23, 25].

MCS has an unpredictable clinical course and a variable outcome, ranging from death 9 weeks after surgery to survival 12 years following initial diagnosis [5, 7]. The tumour is said to have a 60% rate of metastasis and mortality in the order of 25% [2]. Achieving wide, clear surgical margins is the mainstay of treatment, with possible postoperative radiation therapy [5, 6]. Careful long-term clinical follow-up for metastatic disease is imperative [26]. The most frequent sites of metastases are lymph nodes and lung [4, 5, 7, 17, 18]. Metastasis to bone and the brain have also been reported [1, 19, 24, 25].

In summary, MCS is a rare, potentially aggressive neoplasm. The dearth of larger case series accounts for the limited information regarding incidence, absence of uniform criteria for malignancy, uncertainly regarding its exact metastatic potential and the lack of standardised management protocols. The documented histomorphologic spectrum is broadened by the addition of these 2 unique examples of MCS.

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Statement of Ethics

The authors have no ethical conflicts to disclose. The study was approved by the human research ethics committee (medical) of the University of the Witwatersrand as both patients have been lost to follow-up. No information regarding the patients' identities has been used in the paper or in the images. No real names or identifiers have been used.

Disclosure Statement

The authors have no conflicts of interest to declare.

Author Contributions

All three authors contributed equally to this case report.

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