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## ORIGINAL ARTICLE

# Mucinous Carcinoma of the Breast: Imaging Features and Pathological Correlation

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## ABSTRACT

***Objective:*** *To review the imaging features of mucinous carcinoma of the breast, a rare subtype of ductal carcinoma of the breast.*

***Methods:*** *Clinical data; mammographic, ultrasonographic, and magnetic resonance imaging features; and histological findings from patients diagnosed with mucinous carcinoma of the breast at the Queen Elizabeth Hospital, Hong Kong, from January 2005 to July 2016 were reviewed.*

***Results:*** *A total of 11 cases of mucinous carcinoma of the breast were identified. Of the eight available mammography studies, all detected masses, with seven showing high density and one equal density; five masses had a circumscribed margin and none showed malignant calcification. All 11 mucinous carcinomas were detected on ultrasound scans, mostly as oval or round masses. For all five patients with complete magnetic resonance imaging records, mucinous carcinomas were detected as oval masses. All five lesions had hypointense signals on T1-weighted images and hyperintense signals on T2-weighted sequences, owing to the presence of extracellular mucin. According to histological analysis, seven cases were pure-type mucinous carcinoma and four were mixed-type mucinous carcinoma.*

***Conclusion:*** *Mucinous carcinoma of the breast is readily detected by mammography and ultrasonography. These lesions commonly appear as circumscribed masses on both mammography and ultrasonography. On magnetic resonance imaging, they typically show hyperintense signals on T2-weighted sequence. Correlation with histopathologic findings assists in arriving at the diagnosis and guiding further management.*

***Key Words:*** *Adenocarcinoma, mucinous; Breast; Magnetic resonance imaging*

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# 中文摘要

## 黏液型乳腺癌：影像學表現與病理相關性分析

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**目的：**回顧黏液型乳腺癌這種罕見亞型乳腺管癌的影像學特點。

**方法：**回顧2005年1月至2016年7月期間在香港伊利沙伯醫院確診黏液型乳腺癌的患者其臨床資料，以及乳腺X光、超聲檢查、磁共振成像和組織學檢查結果。

**結果：**研究共包括11例黏液型乳腺癌。在8個現有乳房X光片中，全部均檢測出腫塊；7例屬高密度、1例屬等密度。5例為邊緣清晰的腫塊，均未見惡性鈣化。這11例黏液型乳腺癌均透過超聲檢查測出，大多為橢圓形或圓形腫塊。在5名有完整磁共振成像記錄的患者中，黏液型乳腺癌均呈橢圓形。由於存在細胞外黏蛋白，以上5個病灶均在T1加權像上呈低信號，T2加權像上則呈高信號。根據組織學檢查分析，7例為純型黏液型乳腺癌，其他4例則為混合型黏液型乳腺癌。

**結論：**乳腺X光和超聲檢查均能檢出黏液型乳腺癌，而且通常顯示為邊緣清晰的腫塊。磁共振成像通常在T2加權序列呈現高信號。與組織病理組織學結果的相關性有助確診並指導進一步治療。

## INTRODUCTION

Most breast cancers are ductal in origin. Invasive ductal carcinoma not otherwise specified (invasive carcinoma of no special type) and ductal carcinoma in situ are the two most common types, accounting for 85% of breast tumours.[1] 'Not otherwise specified' refers to the lack of differentiation of the tumour.[2] The other subtypes of ductal carcinoma are relatively uncommon and are named according to the differentiating features on histological examination.

Mucinous carcinoma of the breast is rare type of breast ductal carcinoma. It is diagnosed when the dominant histological feature is a tumour-like arrangement of neoplastic cells that produce mucin. Mucinous carcinoma can be further divided into two subtypes: pure and mixed. Pure-type mucinous carcinoma is a homogeneous tumour in which there is excessive secretion of mucin surrounding the neoplastic cells; the latter constitute less than 10% of the tumour as its non-mucinous component.[3] In mixed-type mucinous carcinoma, a greater proportion of the tumour is made up of neoplastic cells as its non-mucinous component, and there is less extracellular mucin.

This article highlights the imaging features of mucinous carcinoma of the breast, with a focus on mammographic, sonographic, and magnetic resonance imaging (MRI) features. Histological findings are also reviewed.

## METHODS

This study, conducted at the Queen Elizabeth Hospital, Hong Kong, was approved by the Hong Kong Hospital Authority's Kowloon Central Cluster / Kowloon East Cluster Research Ethics Committee. Patients' informed consent was not required for this retrospective audit study. A computer search of the hospital's radiology and pathology records from January 2005 to July 2016 was performed. A total of 11 cases of mucinous carcinoma of the breast were identified. All 11 patients had undergone core biopsy using a 14-G core biopsy needle (Bard, Tempe [AZ], USA) under sonographic guidance. The diagnosis of mucinous carcinoma was confirmed by histological examination. All 11 patients were included for retrospective analysis (age range, 29-87 years; mean age, 58.1 years). Ten of the patients presented with breast masses; the remaining patient had an incidental breast mass detected on positron-emission tomography–computed tomography. Following diagnosis, three patients underwent simple mastectomy with axillary lymph node sampling and dissection, four had breast-conserving surgery, one received palliative radiotherapy, and three declined to undergo further treatment.

### Mammographic Findings

Mammography images were available for review in eight patients. Two patients had undergone mammography in another centre and the images were not available for

review. For another patient, mammography had not been performed owing to the large fungating breast mass. Mammography in the other eight cases had been performed in two standard imaging planes (mediolateral oblique and craniocaudal). The presence of a mass, density of the mass (low density, equal density, or high density), shape of the mass (round, oval, lobular, or irregular), margin of the mass (circumscribed, microlobulated, obscured, indistinct, or spiculated), and the presence of calcification (benign or malignant) were analysed.

### Sonographic Findings

All 11 patients had undergone ultrasonography of the breast. The dimensions of all lesions, presence of a mass, margin of the mass (circumscribed, microlobulated, obscured, indistinct, or spiculated), parallel or non-parallel configuration, echogenicity of the mass (hypoechoic, isoechoic, heterogeneous, mixed cystic, or solid), presence of vascularity within the mass, and posterior feature of the mass (shadowing or enhancement) were analysed.

### Magnetic Resonance Imaging Findings

Findings from MRI were available for six patients. However, because one of these patients had been unable to remain still during MRI, image acquisition was incomplete and those images were thus excluded from this study. All five completed MRI studies had been performed with a 1.5-T unit (Magnetom Avanto; Siemens, Erlangen, Germany) using a breast coil. The following sequences had been used: gradient echo localiser, T2-weighted turbo-spin echo with fat-saturation axial sequence, T1-weighted turbo-spin echo axial sequence, 3-dimensional fat-suppressed T1-weighted gradient echo sequence (both post-gadolinium dynamic sequences and delayed sequences), diffusion-weighted spectral adiabatic inversion recovery sequence, and apparent diffusion coefficient map. Post-processing reconstruction including rotational maximum intensity projection images and post-gadolinium wash-in colour maps had also been performed.

The MRI images were analysed for the following features: size of mass, shape of mass (round, oval, lobulated, or irregular), margin of mass (circumscribed, irregular, or spiculated), signal intensity on T1-weighted and T2-weighted images (hypointense, isointense, or hyperintense), enhancement characteristics (homogeneous or heterogeneous), and the type of kinetic curve at the region of interest within the tumour (type 1, 2 or 3 kinetics).

### Histological Findings

The histological and cytological slides of the tumours from these patients were re-analysed retrospectively by the pathologists participating in this study. The materials had been fixed in formalin, routinely processed and sectioned, and stained with haematoxylin and eosin. The percentage of volume of extracellular mucin was calculated, and the carcinomas were classified as either pure mucinous (≥90% mucin) or mixed mucinous (<90% mucin) types. Nuclear grade was also reviewed: tumours with grade 1 nuclei showed low-grade features; tumours with grade 3 nuclei showed a higher degree of pleomorphism.

## RESULTS

The mammographic, sonographic, and MRI findings from four selected patients are shown in Figures 1 to 4. Histological findings are also included for two of these patients.

### Mammographic Findings

Of the eight available mammography studies, all detected masses, with seven (87.5%) showing high density and one (12.5%) equal density. Five (62.5%) of these lesions were oval and three (37.5%) were round. Five (62.5%) masses had a circumscribed margin, one (12.5%) had a microlobulated margin, and two (25%) had an indistinct margin. Benign calcification was found in two (25%) lesions, while the six (75%) other lesions showed no calcification. None of these six lesions were associated with malignant calcification.

### Sonographic Findings

All 11 mucinous carcinomas were detected on ultrasound scans as masses. Eight (73%) masses were oval, one was round, one was lobulated, and one was irregular. Six (55%) tumours had a circumscribed margin, four (36%) had a microlobulated margin, and one (9%) had an indistinct margin. Ten (91%) of these masses were parallel in configuration and the other one was non-parallel. Eight (73%) masses were hypoechoic, two (18%) were heterogeneous, and one (9%) showed mixed solid and cystic components. Vascularity was present in five (45) lesions. Six (55%) masses had no posterior feature, whereas five (45%) showed posterior enhancement.

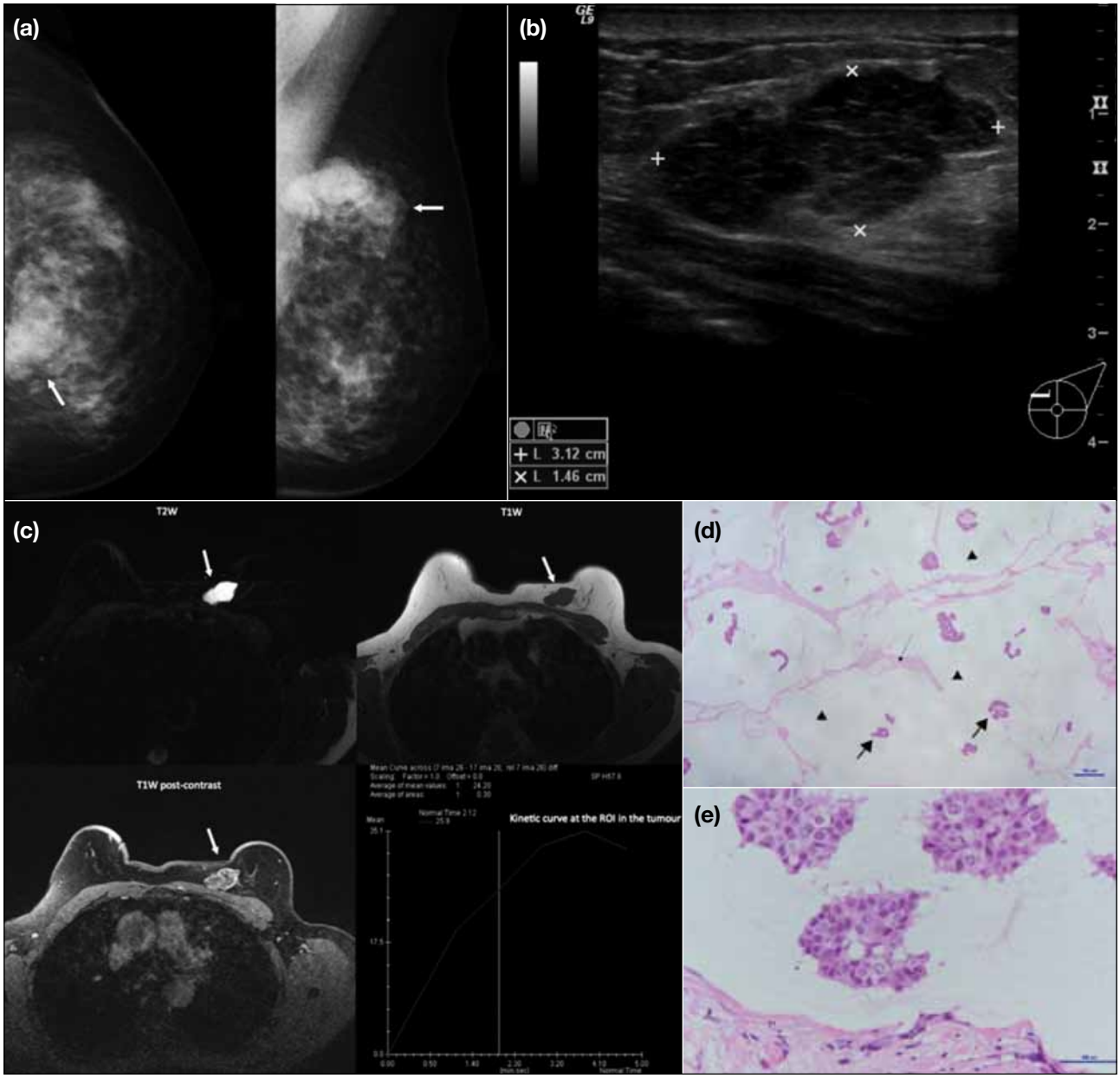


**Figure 1.** A 52-year-old woman presenting with a self-detected breast mass of 1-month duration who underwent breast conservation surgery following diagnosis. (a) Mammograms of craniocaudal (left) and mediolateral-oblique (right) views showed an oval, high-density mass with microlobulated margins in the upper medial aspect of the left breast (arrow); benign microcalcifications were also visible. (b) Ultrasonogram showed an oval, parallel and hypoechoic mass with microlobulated margins; internal vascularity was absent but posterior enhancement was present. (c) Magnetic resonance image showed the lesion as a T2-weighted hyperintense signal, a typical feature of mucinous carcinoma due to the abundance of extracellular mucin. The mass showed low signal intensity on T1-weighted sequence and heterogeneous enhancement with avid rim enhancement on post-contrast sequence. The kinetic curve at the region of interest within the tumour showed progressive enhancement, indicative of type 1 kinetics. Ultrasound-guided core biopsy of the lesion confirmed mucinous carcinoma. (d) Photomicrograph showing the mucinous carcinoma with characteristic pools of mucin (arrowheads) separated by delicate fibrous septa (thin arrow); floating in the mucin are small clusters of carcinoma cells (large arrow) [H&E, 40x]. (e) Photomicrograph showing the carcinoma cells with low nuclear grade and mild nuclear atypia (H&E, 400x).

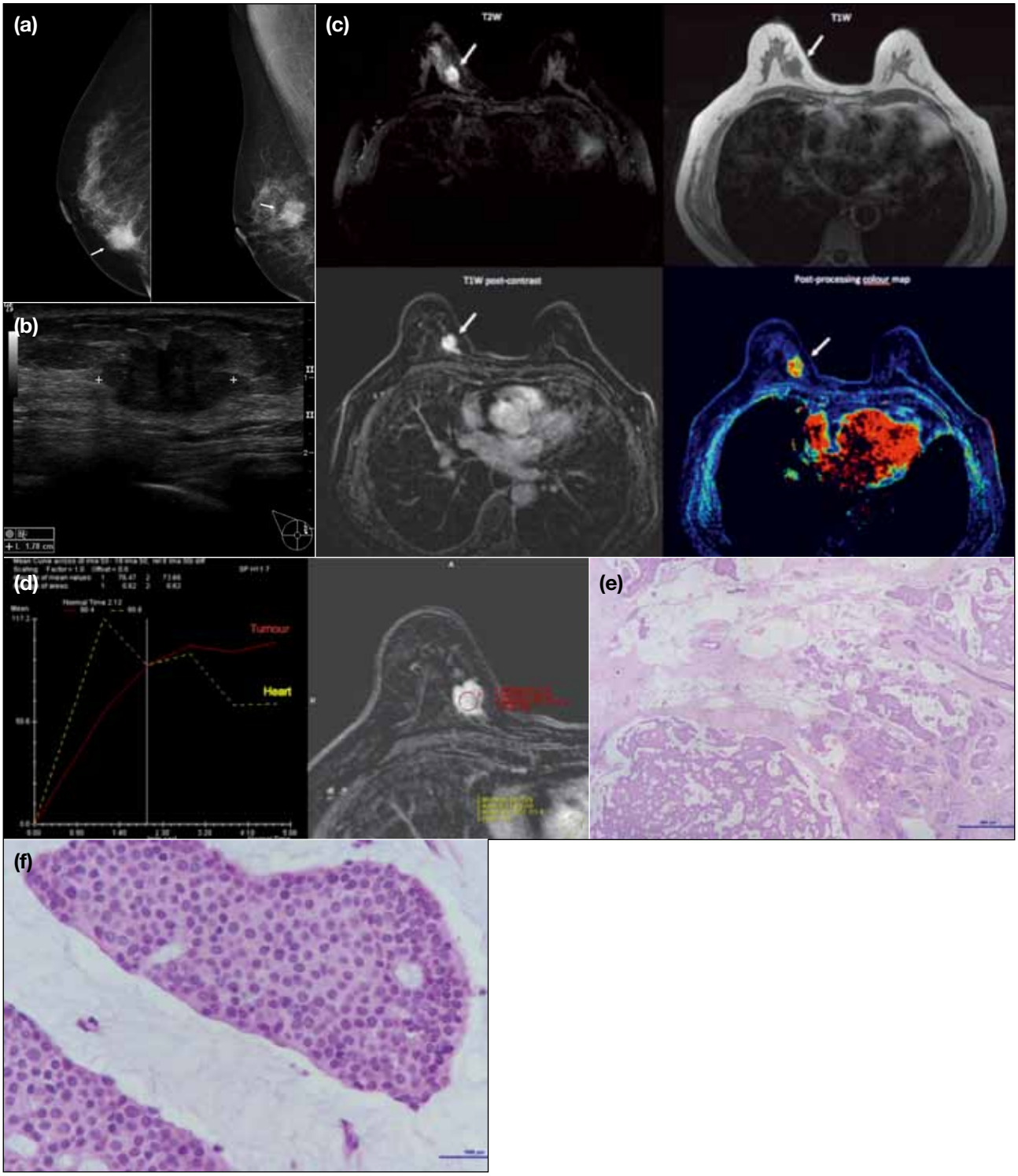


**Figure 2.** A 72-year-old woman presenting with a self-detected breast mass. The patient underwent lumpectomy of the right breast after ultrasound-guided core biopsy of the breast mass. Final pathology confirmed mucinous carcinoma. (a) Mammograms with craniocaudal (left) and mediolateral-oblique (right) views showed a round, high-density mass with indistinct margins in the right breast upper inner quadrant (arrow); microcalcification was absent. (b) Ultrasonogram showed a parallel and hypoechoic mass with microlobulated margins, without posterior features. (c) Magnetic resonance imaging showed high signal intensity on T2-weighted image, low signal intensity on T1-weighted image, and enhancement on post-contrast sequence. Red regions were seen on the post-processing colour map, indicating areas of suspicious rapid enhancement. (d) The kinetic curve at the region of interest within the tumour showed initial uptake followed by a plateau, indicative of type 2 kinetics, possibly due to increased blood flow in high-cellularity tumour cell clusters. (e) Photomicrograph showed a hypercellular variant with large clusters of carcinoma cells in mucin pools (H&E, 40x). (f) Photomicrograph of carcinoma cells of hypercellular variant, showed mild nuclear atypia (H&E, 400x).

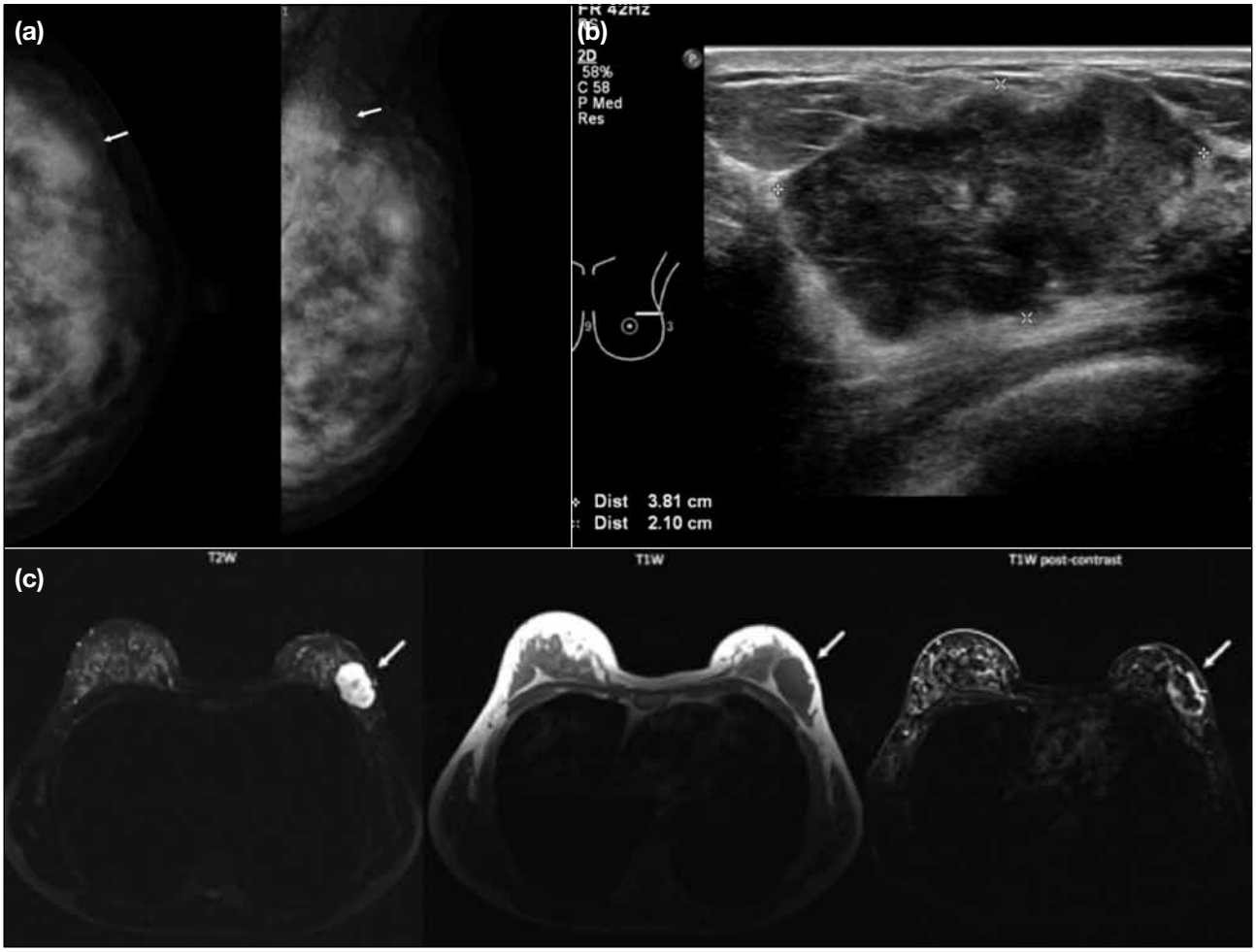


**Figure 3.** A 39-year-old woman presenting with a history of self-detected breast mass for 3 months. Following diagnosis, neoadjuvant chemotherapy was given, followed by skin and areolar sparing mastectomy with transverse rectus abdominis muscle skin flap reconstruction surgery. (a) An oval equal-density mass (arrow) was seen in the left breast upper outer quadrant on mammogram with craniocaudal (left) and mediolateral-oblique (right) views. (b) Ultrasonogram showed a parallel and hypoechoic mass. (c) On magnetic resonance imaging, the lesion showed high signal intensity on T2-weighted image, low signal intensity on T1-weighted image, and rim enhancement on post-contrast sequence. The lesion extended close to the pectoralis major without involvement.

### Magnetic Resonance Imaging Findings

For all five patients with complete MRI records, mucinous carcinomas were detected as oval masses. The margin was circumscribed in three (60%) lesions and irregular in two (40%). All five lesions had hypointense signals on T1-weighted images. On T2-weighted sequences, all five lesions showed hyperintense signals. On dynamic contrast-enhancing sequences, four (80%) lesions demonstrated heterogeneous enhancement and one (20%) showed homogeneous enhancement. In two (40%) lesions, the kinetic curve at the region of interest within the tumour showed progressive enhancement, indicative of type 1 kinetics. In the other three (60%) lesions, the kinetic curve at the region of interest within the tumour showed initial uptake followed by a plateau phase, indicative of type 2 kinetics.

### Histological Findings

On histological analysis, seven (64%) patients had pure-type mucinous carcinoma and four (36%) had mixed-type mucinous carcinoma. After nuclear grading, six (54.5%) tumours were classified as grade 1, three (27%) as grade 2 (27%), and two (18%) as grade 3.

## DISCUSSION

Mucinous carcinoma accounts for only about 2% of breast cancers[1] and is more commonly found in elderly women.[4] It is named according to the histological

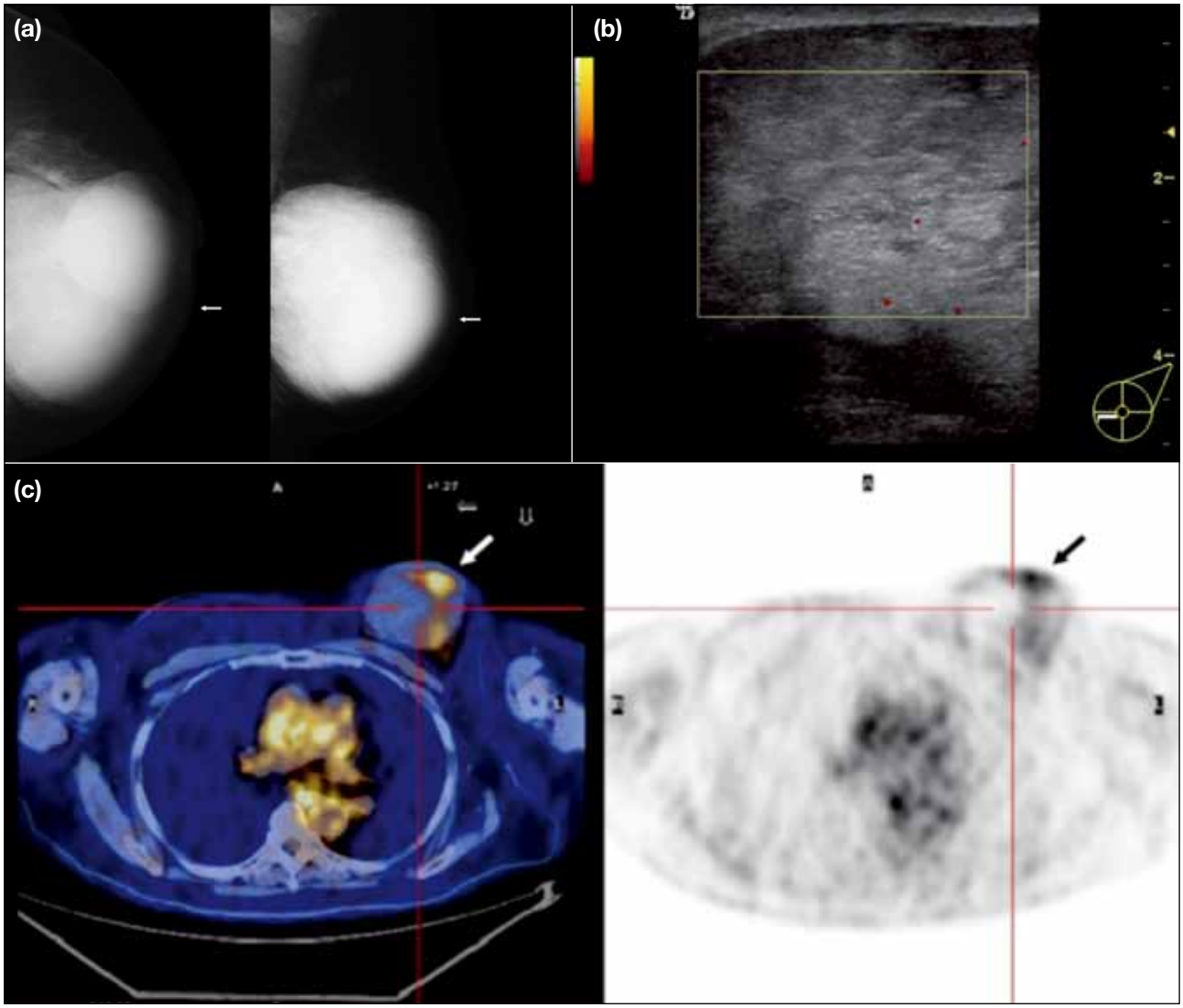


**Figure 4.** A 60-year-old woman with late presentation of a huge left breast mass. Ultrasound-guided core biopsy confirmed mucinous carcinoma. The patient received palliative radiation therapy and chemotherapy (a) Mammograms with craniocaudal (left) and mediolateral-oblique (right) views showed a large (>10-cm) round, high-density mass with circumscribed margins in the left breast, with an enlarged axillary lymph node. (b) Ultrasonogram showed a large hypoechoic solid mass with circumscribed margins and mild internal vascularity. (c) Positron-emission tomography–computed tomography scan showed hypermetabolic areas within this tumour, with lung secondaries (not shown).

findings of neoplastic cells in relation to extracellular mucin. Pure-type mucinous carcinoma is reported to carry a better prognosis than mixed-type mucinous carcinoma[5] and to have a lower incidence of axillary lymph node metastasis.[6] Overall, the 10-year disease-free survival rate is higher for patients with pure-type mucinous carcinoma than for patients with invasive ductal carcinoma.[7]

Because of the presence of extracellular mucin, a semisolid substance, patients with mucinous carcinoma usually present with soft breast masses.[2] In our series, most patients (91%) had self-detected breast masses. Only one (9%) patient had incidental discovery of the breast tumour, after positron-emission tomography–computed tomography performed for a suspected lung lesion. For patients with symptomatic breast masses, mammography and ultrasonography are the standard investigations.

On mammography, mucinous carcinoma is typically described as a 'circumscribed' breast tumour.[2] In our

series, all mucinous carcinomas were detectable as masses on mammography. The margins were more commonly circumscribed than non-circumscribed. None of the tumours in our series demonstrated malignant calcifications.

Ultrasonography demonstrated high sensitivity, with all lesions visualised as masses. In our series, the lesion was more commonly seen as round or oval masses with circumscribed or microlobulated margins. Echogenicity was hypoechoic or heterogeneous in most cases. One tumour, a large fungating mass on presentation, demonstrated mixed solid and cystic components on ultrasonography. Mixed solid and cystic appearance is a sonographic feature of mucinous carcinoma of the breast.[8] Five lesions showed posterior enhancement, which is also a common feature of mucinous carcinoma.[8]

On MRI, the morphology of mucinous carcinoma was similar to that found in the mammographic and ultrasonographic images, and commonly seen as an oval mass. It is one of the few cancers that demonstrates a hyperintense signal on T2-weighted images, owing to the presence of abundant extracellular mucin.[9] This appearance is contrary to most typical invasive ductal carcinomas of the breast, which show short T2-relaxation times and hypointense T2 signals because of their high cellularity.[10] The signal intensity on T2-weighted sequence correlates with the degree of extracellular mucin.[11] However, the presence of T2 hyperintense signal is not specific to mucinous carcinoma, as numerous other breast lesions can also demonstrate high T2 signals. These conditions include tumour necrosis, cystic or fatty components, mucinous stroma, loose myxoid stroma, stromal oedema, and haemorrhage.[10]

On dynamic contrast-enhanced images, most lesions showed heterogeneous enhancement. Two lesions showed a gradual enhancing pattern with a type 1 kinetics curve. This is a known enhancement characteristic of pure-type mucinous carcinoma, possibly due to slow diffusion of contrast material through the stroma, which contains a large amount of mucin.[9,12] Three lesions in our series demonstrated early rapid enhancement, followed by a plateau phase, which indicates type 2 kinetics. On histological examination, these three tumours showed cellularity of grade 2 or 3. The rapid initial enhancement in these tumours might be due to the increased blood flow in these high-cellularity tumour cell clusters.[13]

There are several published studies that have compared the differences in imaging features of pure- and mixed-types of mucinous carcinoma. Lam et al[8] reported that pure-type mucinous carcinoma more commonly shows circumscribed margins on mammography, whereas mixed-type mucinous carcinoma shows indistinct margins. Memis et al[14] found that most of the pure-type mucinous carcinomas were isoechoic in echogenicity, whereas mixed-type mucinous carcinomas were hypoechoic. After analysing MRI features, Kawashima et al[9] reported that pure-type mucinous carcinoma classically demonstrates very high signal intensity on T2-weighted images and has a gradually enhancing (persistent) pattern. When an area within a suspected mucinous carcinoma shows isointensity on T2-weighted images and strong early enhancement, a mixed-type mucinous carcinoma containing non-mucinous component would need to be considered, according to their findings. Hence, MRI-guided biopsy aimed at this portion of the tumour may help to confirm the diagnosis pre-operatively.[9] Owing to the relatively small sample size of our study, subgroup analysis of the imaging features of different subtypes of mucinous carcinoma was not performed.

## CONCLUSION

Mucinous carcinoma of the breast is readily detected by mammography and ultrasonography. These lesions commonly present as circumscribed masses on images obtained by both modalities. On MRI, lesions typically show hyperintense signals on T2-weighted sequence as a result of the presence of extracellular mucin. This feature, however, is not specific to mucinous carcinoma of the breast. Correlation with histopathological findings therefore assists in arriving at the diagnosis and in guiding further management.

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