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Idiopathic Granulomatous Mastitis and its Mimics on Magnetic Resonance Imaging: A Pictorial Review of Cases from India

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ABSTRACT

Objectives: Idiopathic granulomatous mastitis (IGM) is a rare inflammatory disease of the breast, which is benign but potentially morbid. Mammographic and sonographic findings have been well characterized, but magnetic resonance imaging (MRI) findings have been less thoroughly documented. The objective of this study was to demonstrate characteristic findings for IGM and its mimics via a retrospective review.

Material and Methods: Breast MRI examinations performed at Sir Ganga Ram Hospital in New Delhi, India between 2014 and 2019 were retrospectively reviewed to identify cases in which a pattern suggestive of granulomatous mastitis was seen. Cases of known malignancy were excluded. Any available breast pathology results were then obtained, and cases with presumptive or definitive diagnoses were compiled for analysis.

Results: Overall, cases identified with characteristic imaging findings and confirmed diagnosis included seven cases of IGM, four cases of invasive ductal carcinoma, two cases of tuberculous mastitis, one case of non-tuberculous infectious mastitis, one case of foreign body mastitis, and one case of eosinophilc mastitis. One case of IGM with masses rather than of non-mass enhancement was also identified.

Conclusion: In our review, cases with clustered ring enhancement were found to have inflammatory, idiopathic, infectious and malignant etiologies. While, these etiologies can only be reliably differentiated on pathology, familiarity with the pattern and an awareness of the differential may lead to decreased morbidity due to delays in diagnosis.

Keywords: Idiopathic granulomatous mastitis, breast magnetic resonance imaging, idiopathic granulomatous mastitis

INTRODUCTION

Idiopathic granulomatous mastitis (IGM) is a rare, benign, and aseptic granulomatous inflammatory breast disease of uncertain etiology. It was first described as a distinct entity by Kessler and Wolloch in 1972.[1] The true prevalence of this disease is not well established. IGM typically affects parous women of childbearing age with a history of breastfeeding.[2,3] There are only a few reported cases of IGM in a male.[4,5] Clinically, IGM typically presents as a unilateral erythematous and palpable breast lump, with or without pain. In advanced cases, sinus tracts and/or sterile abscesses may develop.[6-8] Proposed etiologies include autoimmune, hormonal (hyperprolactinemia), occult corynebacter infection, hypersensitivity, and trauma to the ductal epithelium.[2,9-13] Treatment protocols vary by institution and severity of disease; these may

include observation, topical or oral steroids, methotrexate, or surgical excision.[2,14-18]

Mammography and ultrasound are commonly used to evaluate IGM, with well-described findings including focal asymmetries, masses, and skin thickening. These are beyond the scope of this paper, but are well covered in a 2018 radiographic review by Mais *et al*.[2]. Magnetic resonance imaging (MRI) is much less frequently obtained. The literature on MRI findings of IGM is consequently more limited, with smaller case series ranging from 5 to 39 patients.[19-25]

Studies characterizing IGM on MRI have presented a variable set of findings. The largest case series from Yilmaz *et al*. report heterogeneously enhancing masses to be the dominant finding.[25] Other authors report areas of non-mass enhancement (NME) in up to 100% of cases.[23,24] In many cases, there are both masses and NME. MRI findings in IGM are nonspecific, overlapping significantly with findings suggestive of malignancy and other granulomatous disorders of the breast.

The authors' experience at a tertiary care hospital in New Delhi suggests that there is a set of typical findings on MRI which results in a differential of IGM, tuberculous mastitis, or malignancy – most particularly the finding of extensive NME with areas of clustered ring-like pattern [Figure 1]. Clustered ring enhancement is defined by the 2013 edition of BIRADS as a subtype of NME, characterized by "thin rings of enhancement clustered together around the ducts. Enhancement in the periductal stroma, best seen on high-resolution images, implies a suspicious finding."[26] Prior studies have found clustered ring enhancement to have a high positive predictive value for malignancy; 77% in a study of 124 patients by Uematsu *et al*.,[27] and 96% in a study of 61 patients by Tozaki *et al*.[28]

Given the discordance between the literature and our anecdotal experience with IGM and clustered ring enhancement, this study was undertaken to more systematically characterize IGM and its mimics on MRI at Sir Ganga Ram Hospital.

MATERIAL AND METHODS

With the approval of the Institutional Review Board, reports for contrast enhanced breast MRI examinations performed at Sir Ganga Ram Hospital in New Delhi, India, between 2014 and 2019 were retrospectively reviewed to identify cases in which NME in a clustered ring like pattern was seen, or granulomatous mastitis was suspected. Cases with known malignancy classified as BIRADS 6 were excluded from the study. Any available breast pathology results were then obtained. Fifteen cases were identified with a definitive diagnosis based on histopathology. Two additional cases were found to have granulomatous inflammation on histopathology without definitive testing for tuberculosis. One of these was classified as tuberculous mastitis based on clinical response to anti-tubercular treatment. The other was classified as idiopathic granulomatous mastitis based on the clinical resolution in the absence of therapy. Cases in which neither pathology nor clinical follow-up could provide definitive diagnosis were excluded from the study; as these cases were more numerous than confirmed cases, conclusions regarding the relative prevalence of etiologies at our institution cannot be considered reliable.

All magnetic resonance examinations were performed at Sir Ganga Ram Hospital on a 3T scanner with a dedicated phased-array breast coil. Axial non-fat saturated T1W images were obtained through both the breasts, followed by sagittal fat-suppressed and ep2D-STIR diffusion images with 4b values. Dynamic transverse 3D fat-suppressed spoiled gradient-echo volume acquisition was then obtained through both the breasts before and 5 times sequentially following the intravenous administration of 0.1 mmol/kg Gd-DTPA with a pressure injector for a total of 6 min after injection. This was followed by a delayed high resolution, contrast enhanced axial sequences. The dynamic sequences were viewed with subtraction and maximum intensity projection technique. Images were reconstructed in multiple planes, and kinetic analysis was performed. In addition, coronal TIRM images through the axilla using a body matrix coil were obtained.

RESULTS

Overall, cases identified with clustered ring enhancement and confirmed diagnosis included seven cases of IGM, four

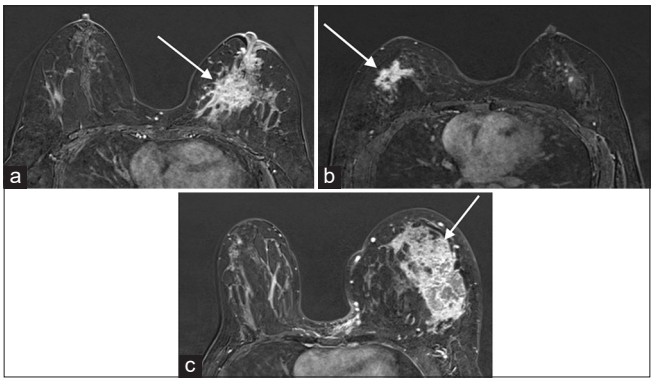

Figure 1: T1 post-contrast subtraction magnetic resonance images with clustered ring enhancement of differing etiologies (arrows). (a) 35-year-old female with palpable left breast lump post-fine-needle aspiration at an outside hospital, found to have idiopathic granulomatous mastitis. (b) 39-year-old female with palpable right breast lump and bloody discharge, as well as prior history of uterine tuberculosis, found to have infiltrating ductal carcinoma. (c) 31-year-old female with enlargement of the left breast 1 year after ceasing lactation, found to have tuberculous infection of the breast.

cases of invasive ductal carcinoma, two cases of tuberculous mastitis, one case of non-tuberculous infectious mastitis, one case of foreign body mastitis, and one case of eosinophilic mastitis. One case of IGM characterized by mass-like enhancement rather than NME was also identified.

DISCUSSION

General MR characteristics of IGM

Seven cases of confirmed IGM were identified [Table 1]. All patients were females presenting with a palpable lump. Six of the seven were of childbearing age, with ages ranging from 25 to 35. One patient was 64 at the time of diagnosis. Data regarding postpartum state were not available.

All but one case of IGM demonstrated NME with a clustered ring like pattern in either a segmental or regional distribution [Figure 2]. In the one case without NME, there were multiple round to oval lesions with irregular margins diffusely scattered through the breast [Figure 3]. All cases demonstrated architectural distortion, perilesional to diffuse edema, and rapid wash-in of enhancement [Figure 4]. Delayed enhancement was persistent in two cases, plateau in four cases, and washout in one case. Diffusion restriction was present to some degree in all but one case; this was not found to be a useful discriminating factor. Five of the seven cases demonstrated duct ectasia and skin thickening. Axillary lymphadenopathy was present in four of seven cases, though with preserved fatty hila in all cases.

Table 1: Characteristics of IGM cases.

Figure	Age	Breast density	Background parenchymal enhancement	Distribution of abnormal enhancement	Clustered ring pattern	Kinetics (wash-in)	Kinetics (delayed)	Diffusion	Abscess	Architectural distortion	Skin thickening	Lymphadenopathy
2a	25	Extreme	Minimal	Regional NME (unilateral)	Yes	Rapid	Plateau	Restricted	Yes	Yes	Yes	Yes, with fatty hilum
2b	34	Extreme	Minimal	Segmental NME (unilateral)	Yes	Rapid	Persistent	Non restricted	No	Yes	Yes	No
2c	35	Heterogeneous	Minimal	Regional NME (unilateral)	Yes	Rapid	Persistent	Restricted, patchy	Yes	Yes	Yes	Yes, with fatty hilum
2d	31	Fatty	Minimal	Segmental NME (unilateral)	Yes	Rapid	Washout	Restricted	No	Yes	Yes	Yes, with fatty hilum
2e	64	Scattered	Minimal	Regional NME (unilateral)	Yes	Rapid	Plateau	Non restricted	No	Yes	No	No
2f	35	Extreme	Mild	Regional NME (bilateral)	Yes	Rapid	Plateau	Restricted	Yes	Yes	No	Yes, with fatty hilum
4	27	Scattered	Minimal	Scattered masses	n/a	Rapid	Plateau	Restricted	Yes	Yes	Yes	No

MR characteristics of malignancy

Four of the cases with NME in a segmental or regional clustered ring pattern were found to be invasive ductal carcinoma [Table 2 and Figure 5]. Clinical presentation was variable: Two patients presented with a lump, one with bloody discharge, and one with eczema of the nipple. The patients were slightly older than most of the IGM patients, with ages ranging from 37 to 65. All of these cases had rapid wash-in of contrast, with either plateau or progressive kinetics. Three cases had lymphadenopathy, with loss of fatty hila in two of these cases. Duct ectasia was present in two cases. An associated irregular mass with plateau delayed kinetics was present in one case (the case without lymphadenopathy). Diffusion restriction was noted in two of the four cases.

MR characteristic of tuberculous mastitis

Two cases with NME in regional clustered ring patterns were found to be consistent with unilateral tuberculous mastitis [Table 3 and Figure 6]. The first patient was a 47-year-old female, who had had a prior history of invasive ductal carcinoma, and was status post-breast conserving surgery, followed by chemotherapy and radiation; her MRI

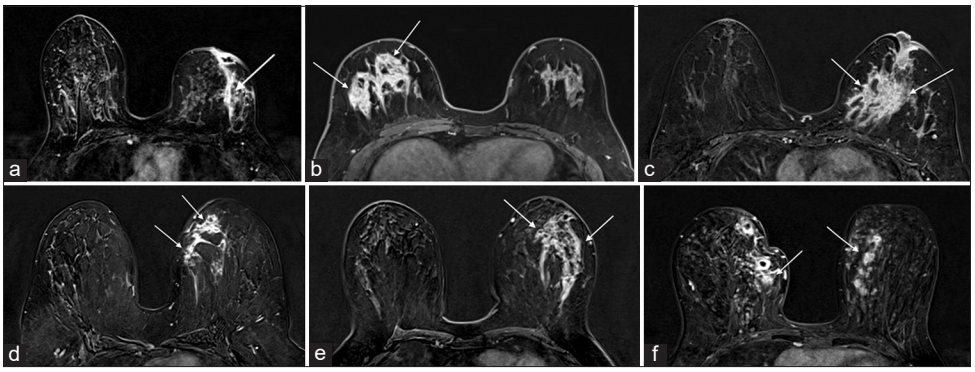

Figure 2: T1 post-contrast subtraction magnetic resonance images for six patients, all of whom presented with palpable breast lumps and were found to have idiopathic granulomatous mastitis. These images demonstrate clustered ring enhancement (arrows), which was the most common finding among IGM cases at our institution. (a) 25-year-old female, (b) 34-year-old female, (c) 35-year-old female, (d) 31-year-old female, (e) 64-year-old female, (f) 35-year-old female.

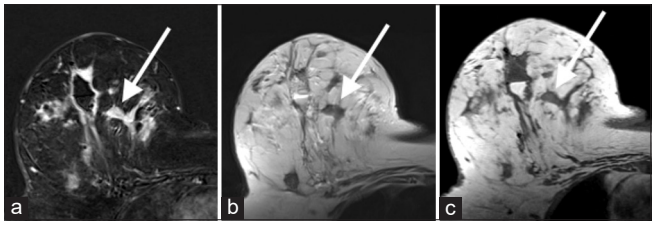

Figure 3: 27-year-old female with a right breast lump found to have idiopathic granulomatous mastitis with masses (arrows) rather than clustered ring enhancement. (a) T1 post-contrast subtraction magnetic resonance image demonstrates multiple round to oval lesions with irregular margins scattered in the breast parenchyma. (b) These lesions show hyperintense to isointense signal on T2- and (c) T1-weighted magnetic resonance images.

Figure 4: 25-year-old female with a palpable lump in the left breast, found to have idiopathic granulomatous mastitis (same patient as in Figure 2a). T1-weighted magnetic resonance image of the bilateral breasts demonstrates the typical findings of architectural distortion with skin thickening (arrow) and lymphadenopathy (circle).

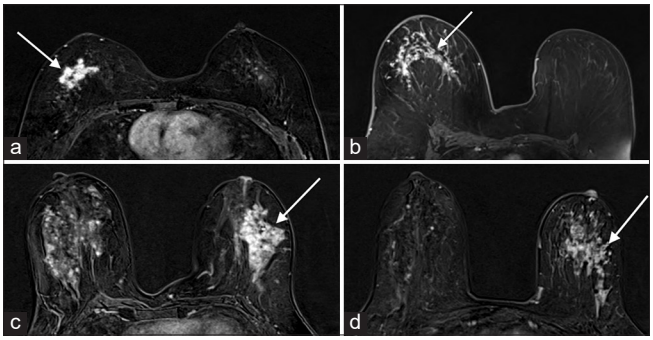

Figure 5: T1 post-contrast subtraction magnetic resonance images for four patients, all of whom were found to have invasive ductal carcinoma. These images demonstrate clustered ring enhancement (arrows). (a) 39-year-old female who presented with bloody discharge. (b) 65-year-old female who presented with a palpable lump in the right breast. (c) 47-year-old female who presented with a painful lump in the left breast. (d) 37-year-old female who presented with eczema of the left nipple.

findings were initially read as consistent with recurrence of malignancy. The other patient was a 31-year-old female with increasing hardness and size of the left breast 1 year after ceasing lactation; this was initially read as most likely IGM. Both cases were characterized by diffusion restriction, as well as rapid wash-in of contrast and plateau delayed kinetics. In both cases, the affected breasts were edematous and skin was thickened. One case had normal-appearing lymph nodes; the other demonstrated massive adenopathy with loss of fatty hila.

Other etiologies

Three additional cases of NME in a clustered ring-like pattern were identified with other etiologies on pathology; eosinophilic mastitis, foreign body mastitis, and non-tuberculous infectious mastitis [Table 3].

Table 2: Cases of invasive ductal carcinoma.

Figure	Age	Breast density	Background parenchymal enhancement	Distribution of abnormal enhancement	Clustered ring pattern	Kinetics (wash-in)	Kinetics (delayed)	Diffusion	Abscess	Architectural distortion	Skin thickening	Lymphadenopathy
5a	39	Extreme	Minimal	Segmental	Yes	Rapid	Progressive with areas of plateau	Non-restricting	No	No	No	No
5c	47	Extreme	Minimal	Regional	Yes	Rapid	Plateau	Non-restricting	No	No	No	Yes, with fatty hilum
5d	37	Heterogeneous	Minimal	Segmental	Yes	Rapid	Plateau	Yes	No	No	No	Yes, with loss of fatty hilum
5b	65	scattered	Minimal	regional	yes	Rapid	Progressive with areas of plateau	Yes	No	No	Yes	Yes, with loss of fatty hilum

Table 3: Other etiologies.

Figure	Age	Case type	Density	BPE	Distribution	Clustered ring pattern	Kinetics (wash-in)	Kinetics (delayed)	Diffusion	Skin thickening	Lymphadenopathy
6	47	TB	Scattered	Minimal	Regional	Yes	Rapid	Progressive with areas of plateau	Yes	Yes	No
6	31	TB (empiric)	Extreme	Minimal	Regional	Yes	Rapid	Plateau	Yes	Yes	Yes, massive
7	39	Mastitis, eosinophilic	Extreme	Moderate	Multi Regional	Yes	Rapid	Plateau	Yes, patchy	Yes	Yes, with fatty hilum
8	61	Mastitis, foreign body	Heterogeneous	Minimal	Segmental	Yes	Rapid	Plateau	No restriction	Yes	Yes, loss of fatty hilum
9	35	Mastitis, infection	Scattered	Minimal	Segmental	Yes	Rapid	Persistent	Yes, centrally	Yes	No

Eosinophilic mastitis was found in a 39-year-old woman who presented with complaints of burning and heaviness of the left breast for 1 month. Imaging demonstrated a massively enlarged and edematous left breast [Figure 7]. The multi-regional NME was predominantly heterogeneous and clumped in pattern, with small areas of clustered ring pattern. Areas of enhancement had rapid wash-in of contrast with plateau delayed kinetics. Lymphadenopathy with preserved fatty hila was noted. It is unknown whether this patient had a systemic eosinophilic disorder.

The case of foreign body mastitis was a 61-year-old female with multiple prior breast surgeries for adenoid cystic disease, who presented with a palpable lump. Imaging demonstrated subareolar segmental NME in clustered ring-like pattern with plateau kinetics [Figure 8]. Lymphadenopathy with loss of fatty hila was noted. There was no diffusion restriction in this case.

The patient with non-tuberculous infectious mastitis was a 35-year-old female who had been treated with antibiotics for infectious mastitis 8 months prior and presented

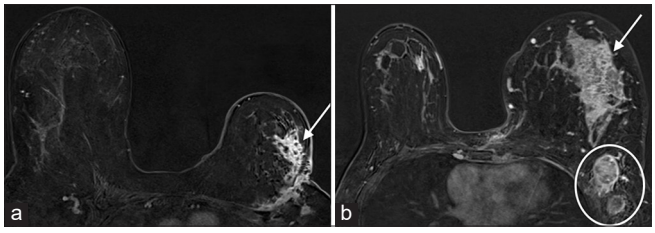

Figure 6: T1 post-contrast subtraction magnetic resonance images demonstrate clustered ring enhancement (arrows) for two patients found to have tuberculous mastitis. (a) 47-year-old female with continued pain and erythema of the left breast almost 1 year after partial mastectomy, chemotherapy and radiation. (b) 31-year-old female with enlargement of the left breast 1 year after ceasing lactation. This patient's MRI also demonstrated bulky axillary adenopathy (oval).

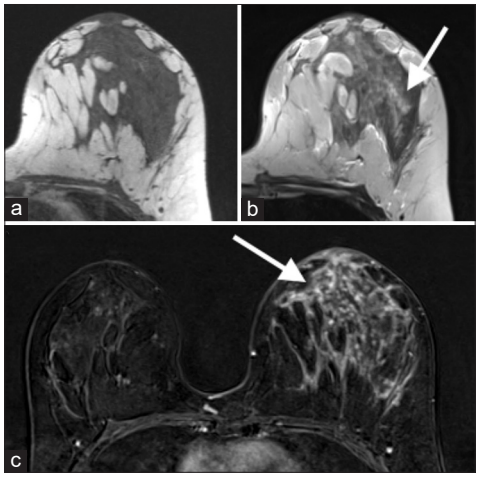

Figure 7: 39-year-old female with 1 month of burning sensation and heaviness of the left breast, found to have eosinophilic mastitis. (a) T1-weighted magnetic resonance image of the left breast demonstrates no mass lesion. (b) T2-weighted magnetic resonance image demonstrates diffuse edema (arrow). (c) T1 post-contrast subtraction magnetic resonance image demonstrates an asymmetric enlargement of the left breast with diffuse inflammation and areas of clustered ring enhancement (arrow).

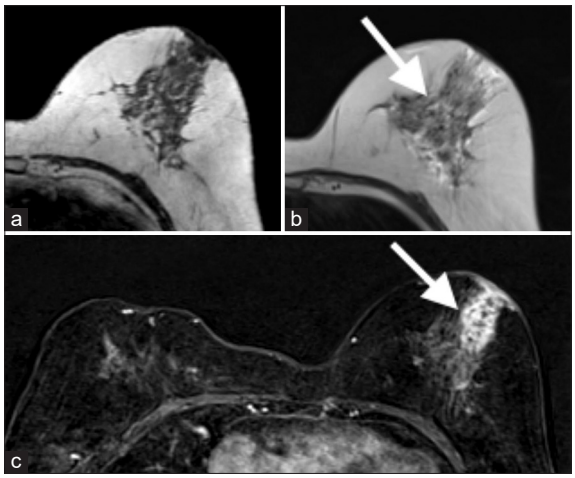

Figure 8: 61-year-old female with history of prior left lumpectomy presenting with a palpable left breast lump for 1 week, found to have foreign body mastitis. (a) T1-weighted magnetic resonance image of the left breast demonstrates no mass lesion. (b) T2-weighted magnetic resonance image demonstrates diffuse edema (arrow). (c) T1 post-contrast subtraction magnetic resonance image demonstrates sub-areolar clustered ring enhancement (arrow).

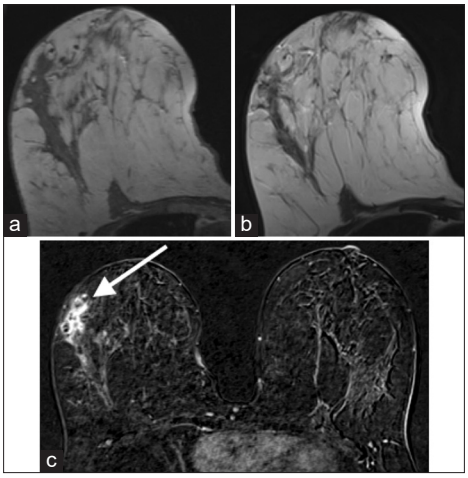

Figure 9: 35-year-old female with palpable lump in the right breast, found to have non-tuberculous infectious mastitis. (a) T1-weighted magnetic resonance image of the right breast demonstrates no mass lesion. (b) T2-weighted magnetic resonance image demonstrates no significant edema. (c) T1 post-contrast subtraction magnetic resonance image demonstrates an area with clustered ring enhancement (arrow).

with a recurrent palpable lump. Imaging demonstrated a small area of NME with clustered ring pattern, as well as small abscesses [Figure 9]. Diffusion restriction was noted.

CONCLUSION

The clinical presentation of idiopathic granulomatous mastitis is often dramatic and needs urgent evaluation. Knowing the differential diagnosis is very important to allay anxiety while still using appropriate steps to arrive at the correct diagnosis as quickly as possible. In some countries, tuberculosis is not commonly seen and, therefore, not in the differential. However, with the increasing movement of people around the globe, this paper serves as an important reminder of this very important and treatable condition.

In our review, cases with extensive NME, particularly the clustered ring subtype, were found to have inflammatory, idiopathic, infectious, and malignant etiologies. Due to the high proportion of cases for which pathologic confirmation was not available, no conclusions regarding the relative frequencies of these etiologies should be drawn. However, considering idiopathic or infectious granulomatous mastitis in the differential, especially in the case of younger women, may lead to improved accuracy and speed of diagnosis. It is important to emphasize, as in other case series documented in the literature, that our series does not identify any sufficiently specific findings to render biopsy unnecessary.

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Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

Dr. Vikram Dogra is the editor-in-chief of this journal. This manuscript was **double-blind** peer reviewed by independent reviewers who are not connected with the journal in any personal capacity.

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