Radiological Findings of Idiopathic Granulomatous Mastitis: Review

İdiopatik Granülomatöz Mastitin Radyolojik Bulguları

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ABSTRACT Idiopathic granulomatous mastitis (IGM) is a rarely seen benign chronic inflammatory breast disease. Etiology is still unknown, many factors mainly including hormonal factors are proposed. Clinical findings include inflammation of the breast, induration, palpation of a mass galactorrhea and retraction of the nipple. Unilateral, usually right sided involvement is encountered. IGM may mimic fibroadenoma, fibrocystic changes, abscess and especially malignancy both clinically and radiologically. Although definite diagnosis is made by cytologic or histopathologic evaluation, radiological evaluation plays an important role in diagnosis and differentiating it from malignancy. Mammography (MG) and ultrasonography (US) are used basically for the diagnosis, but due to wide spectrum and low sensitivity, the findings are challenging. The most common finding of MG is ill-defined asymmetrical density that does not cause mass effect. On US, the radiological finding spectrum is quite wide. On conventional magnetic resonance imaging (MRI) lesion may demonstrate irregular or spiculated contours which may lead to misdiagnosis. However dynamic contrast-enhanced MRI plays an important role in differentiating the lesion from malignancy if a benign type (increasing contrast enhancement) Type 1 signal intensity time curve is obtained. On the other hand, sometimes Type 2 (plateau type) or even malignant type (early washout) Type 3 curve can be obtained. In these cases differentiation from malignancy by radiological means is quite difficult. New MRI techniques including diffusion MRI and MR spectroscopy (MRS), to our knowledge, are not reported yet. In this report MG, US, dynamic contrast-enhanced MRI,diffusion MRI and MR spectroscopy findings of IGM will be presented and the differential diagnosis will be discussed.

Key Words: Mastitis; mammary; mammography; magnetic resonance imaging

ÖZET İdiopatik granülomatöz mastit (IGM) memenin nadir görülen, benign, kronik inflamatuar bir hastalığıdır. Etiyoloji hala net olmayıp başta hormonal faktörler de dahil olmak üzere pek çok faktör suçlanmaktadır. Klinikte memede inflamasyon, ciltte endürasyon, ele gelen kitle, galaktore, meme başında retraksiyon görülebilir. Tutulum genellikle tek taraflı ağırlık olarak sağdadır. IGM, klinik ve radyolojik olarak fibroadenom, fibrokistik değişiklik, abse ve özellikle maligniteyi taklit edebilir. Kesin tanı sitolojik veya histopatolojik inceleme ile konulsa da radyolojik incelemeler tanıda ve maligniteden ayrımında önemli rol oynar. Radyolojik incelemede genellikle mamografi (MG) ve ultrasonografi (US) kullanılmakta ancak bulguların çok çeşitli olması ve özgül olmaması nedeniyle tanı zorluğu yaşanmaktadır. MG'de en sık rastlanan bulgu keskin sınırları olmayan veya kitle etkisi oluşturmayan asimetrik dansite artışıdır, US'de ise radyolojik bulgu spektrumu oldukça geniştir. Konvansiyonel manyetik rezonans görüntüleme (MRG)'de lezyon konturları düzensiz veya spiküle olabildiğinden tanı yanılgıları olabilmektedir. Ancak dinamik kontrastlı incelemede benign tipte (artan kontrast tutulumu tarzında) Tip 1 sinyal intensite-zaman eğrisi maligniteden ayrımında önemli rol oynar. Yine de bazen ara form (plato tarzında) Tip 2 veya malign tipte (erken yıkanma gösteren) Tip 3 kontrast eğrisi görülmektedir. Bu durumlarda radyolojik olarak maligniteden ayrımı çok zordur. Yeni MRG tekniklerinden difüzyon MR ve MR spektroskopi (MRS) bulguları bilgimiz dahilinde literatürde henüz bildirilmemiştir. Bu yazıda IGM'nin MG, gri skala US, Doppler US, dinamik kontrastlı MRG, difüzyon MRG ve MRS bulguları sunulacak ve ayırıcı tanı tartışılacaktır.

Anahtar Kelimeler: Mastit; meme,mamografi; manyetik rezonans

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GENERAL ASPECTS OF IDIOPATHIC GRANULOMATOUS MASTITIS

Idiopathic granulomatous mastitis (IGM) is a rarely seen, usually unilateral, benign, chronic, noncaseous, necrotizing granulomatous lobulitis with or without abscess formation that can clinically and radiologically mimic breast carcinoma.[1-5] It was first described by Kessler and Wolloch[1] in 1972. The first definition was breast masses characterized by florid granulomatous mastitis that were not associated with granulomatous infections, trauma or foreign body reactions. Etiology is still unclear; multifactorial etiology including hormonal factors seems to be more likely etiology. Microorganisms and oral-contraceptives are the main postulated causes,[1,2,4] additionally and underlying autoimmune process, an immune response to extravasated fatty and proteinous secretions from lobules were also suggested.[1,2,6] Associations with alpha1-antitrypsin deficiency and hyperprolactinemia have also been reported.[2,3]

Clinically, patients come up with a breast mass that mimics carcinoma which may lead to nipple retraction and sinus formation.[1-3,7] Galactorrhea, inflammation, indurations, and ulcerations of the skin can also be seen.[1-4] IGM is usually unilateral,[2,3] predominantly right sided,[6] rarely bilateral[8] and can affect any quadrant.[2,3] Regional lymphadenopathy may be present in up to 15%.[4,9] Association with pregnancy and lactation has been reported.[3,6] The patients are usually at child-bearing age, ranging from 17-42 years. Most were diagnosed within 6 years of their last pregnancy.[9-11] Oral-contraceptive usage as an etiological factor is conflicting and reported between 0%[8] to 33%[2].

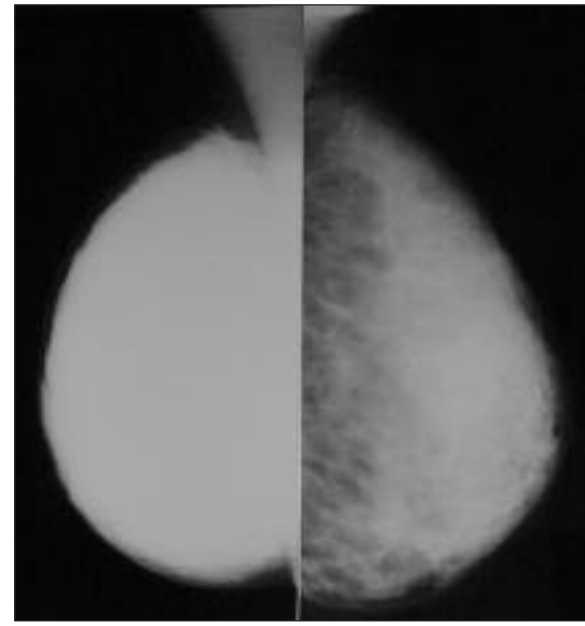

FIGURE 1: Mammography MLO projection images demonstrate a dense mass lesion with indistinct borders occupying the right breast.

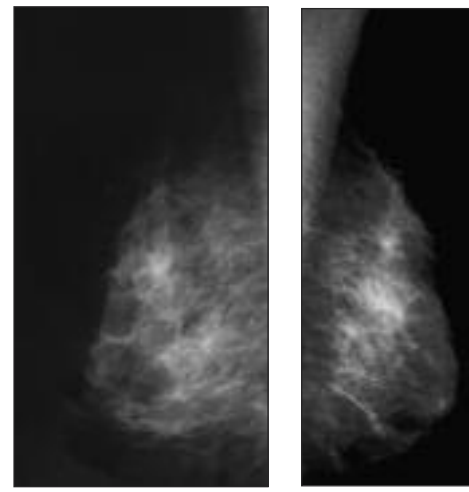

FIGURE 2: Mammography MLO projection images of demonstrate bilateral ill-defined densities without mass formation or microcalcifications.

RADIOLOGICAL FINDINGS

MAMMOGRAPHY (MG)

Radiological diagnosis by the use of MG is limited due to low sensitivity of MG in this age group.[9] Although nonspecific, the most common finding is asymmetrically increased density without a distinct margin or mass effect (Figure 1). Additionally, small, multiple, ill-defined masses without microcalcification (Figure 2), solitary or multiple focal asymmetric dansities without mass formation, diffuse increased densities or oval obscured masses, ill-defined masses with spiculated contours (Figure 3), nodular opacities with indistinct margins, bilateral multiple ill-defined nodules, skin thickening and parenchymal distortion may also be seen. Rarely, MG may be normal.[4,5,9,10]

ULTRASOUND (US) AND DOPPLER IMAGING

On US, irregular tubular hypoechoic lesions, tubular connections, irregular or oval or discrete hete-

FIGURE 3: Left MLO mammogram reveals an ill-defined spiculated mass lesion in the upper quadrant. Note that there are a few scattered microcalcifications.

rogeneous hypoechoic masses with or without hypoechoic tubular extentions, tubuler-multinodular hypoechoic areas, well-defined hypoechoic areas with tubular extentions, lobulated masses with minimal parenchmal distortion, inhomogeneous hypoechoic lesion or area with or without posterior shadow, heterogeneous hypo- and hyperechoic areas with parenchymal distortion, parenchymal heterogeneity or distortion without definite mass lesion, oval mass, increased echogenity surrounding lesions, solitary or multiple abscess cavities with or without sinus tracts, central hypoechoic peripheral hyperechoic lesions, subcutaneous fat obliteration, skin thickening and diffuse parenchymal edema were defined (Figure 4, 5 and 6a).[4,5,9-12] On Doppler examination, increased arterial and venous vascularity can be seen (Figure 6b).[10,12] MG and US are used mainly to rule out malignancy rather than to confirm the diagnosis.[4]

MAGNETIC RESONANCE IMAGING (MRI)

MRI is a second step diagnostic modality in breast lesions. Evaluation of the MRI characteristics of the breast lesions firstly includes margins. Although there are few exceptions, the margins of malignant breast lesions are usually spiculated and irregular, whereas those of benign breast lesions are usually smooth or lobulated.[13] IGM is one exception; contours of IGM lesion may be smooth, lobulated or

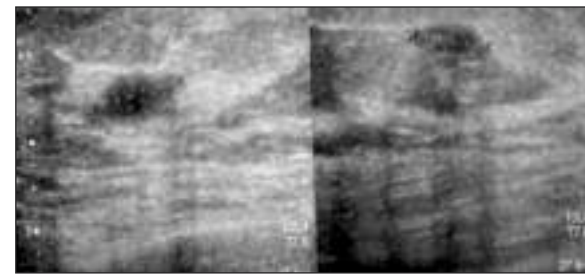

FIGURE 4: US examination demonstrates irregular heterogeneously hypoechoic mass lesion.

FIGURE 5: Abscess cavity and increased echogenity surrounding the lesion on US image.

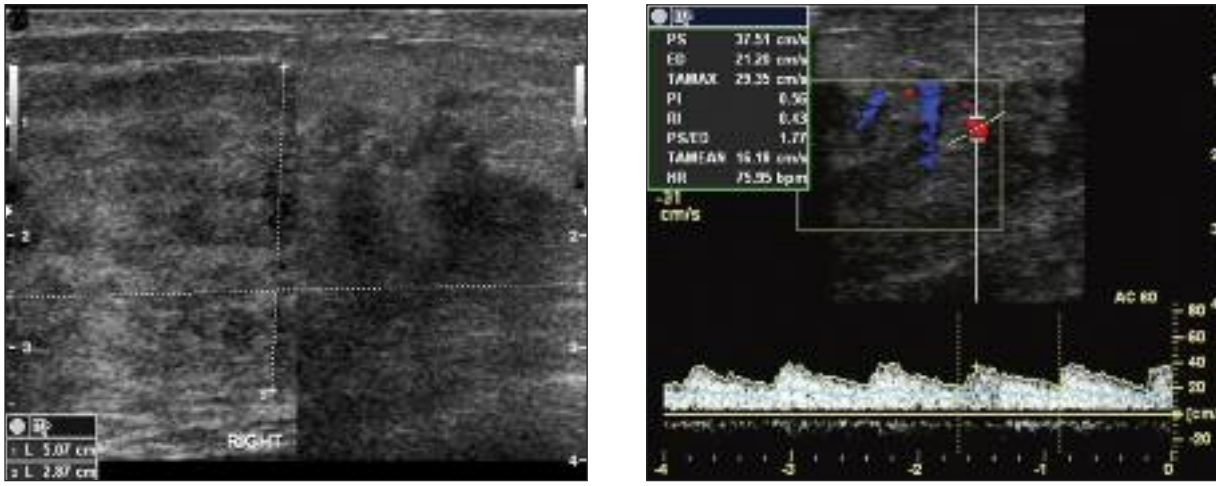

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FIGURE 6a: US examination of the same patient in Figure 1, IGM of the right breast is seen as large heterogeneous hypoechogenicity containing internal hypoechoic tubular lesions giving no posterior enhancement or shadowing with indistinct borders. **6b:** On Doppler US examination spectral analysis of arterial sampling reveals low resistance arterial flow with peak systolic velocity 37.51cm/s, end diastolic velocity 21.2cm/s,RI:0.43,PI:0.56.

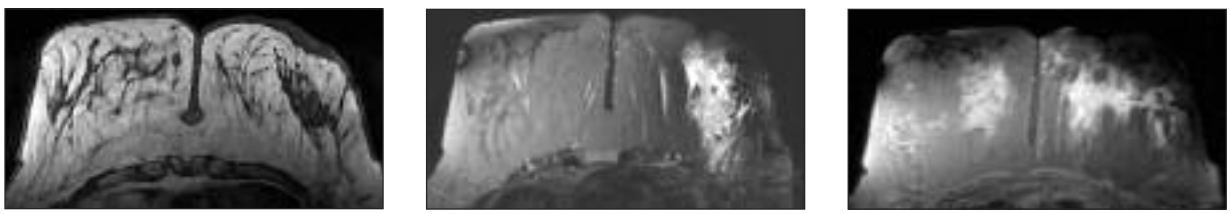

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FIGURE 7: MRI images of the patient with IGM of the left breast **a.** Asymmetrical tissue of low signal intensity on the lateral aspect of the left breast is seen on axial T1 weighted image **b.** On axial T2 weighted fat suppressed images the lesion is seen as heterogeneously hyperintense. **c.** Axial fat suppressed T2 weighted image of a different patient demonstrates increased segmental heterogeneity of both breasts.

spiculated; therefore contrast enhanced images are required. Dynamic contrast enhanced MRI of the breast has been proposed to increase the specificity for the diagnosis of breast lesions. Specific patterns of enhancement have been defined as persistent (type 1), plateau (type 2), and washout (type 3).[14] Type 1 (persistent) contrast enhancement which is characterized by a monotonic increase has been shown to be suggestive of a benign lesion, whereas type 3 (washout) contrast enhancement is highly associated with malignancy. However, a type 2 plateau enhancement pattern can be seen in both benign and malignant lesions.[14] MRI examination of IGM usually demonstrates focal or diffuse asymmetrical signal intensity and enhancement. Mostly recognized pattern is segmental heterogeneity, heterogeneously enhanced irregular lesion that is hypointense on precontrast T1- weighted images and hyperintense on T2-weighted sequences (Figure 7). Nodular lesions and abscess formation which is always in aseptic form can also be seen.[4,7,10,12] Different imaging appearances reflect the different stages and histopathologic findings such as the degree of inflammatory reaction and fibrotic content in IGM patients. A possible autoimmune mechanism is attributed for aseptic abscesses, which can be seen in a phase of the IGM.[10] On postcontrast dynamic T1-weighted scans, usually a benign type 1 time-signal intensity curve from both lesions and abscess walls are seen (Figure 8a). However, occasionally heterogeneously contrast enhanced areas with a malignant washout type 3 time-signal curve

can also be seen (Figure 8b). Heterogeneously enhancing areas, diffuse enhancement, nodular enhancement or ring-like enhancement of abscesses can be also seen (Figure 9).[4,7,10]

DIFFUSION MRI AND MR SPECTROSCOPY

Diffusion MRI and MR spectroscopy are new techniques being used in differential diagnosis of the breast lesions. Diffusion imaging depends on the local tissue environment and detects Brownian motion of water protons, thus reflecting the biologic character of the tissue.[13] Increased cellularity of malignant lesions can restrict water motion in a reduced extracellular space resulting in lower ADC values.[13] Diffusion is also restricted in an abscess due to the pus consistency itself, and therefore high diffusion-weighted imaging signal intensity with low ADC values are seen.[15] Diffusion MRI of breast

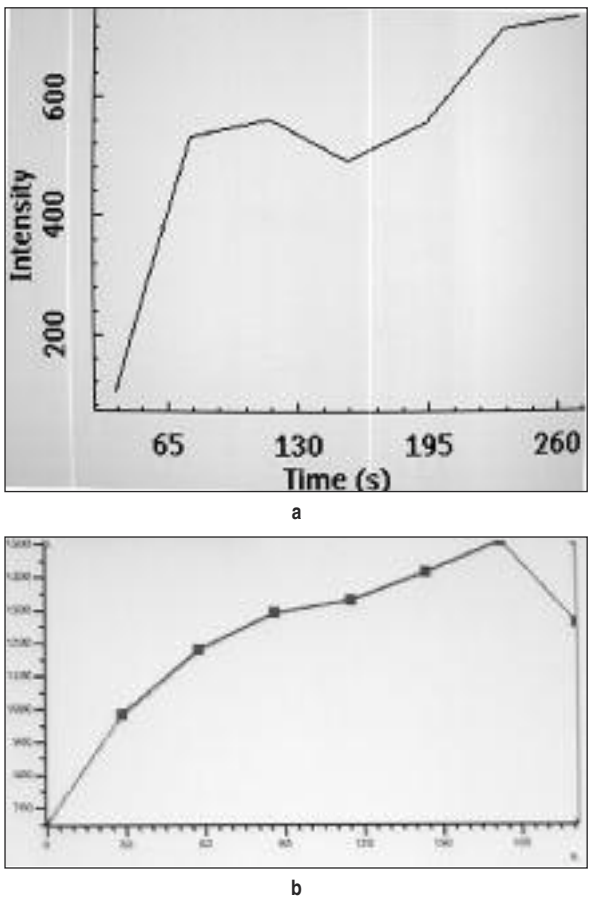

FIGURE 8: Dynamic signal intensity time graphs **a.** Benign type curve is gradual and progressive enhancement without washout from the lesion **b.** Malignant type time-signal curve is seen as early peak enhancement and washout.

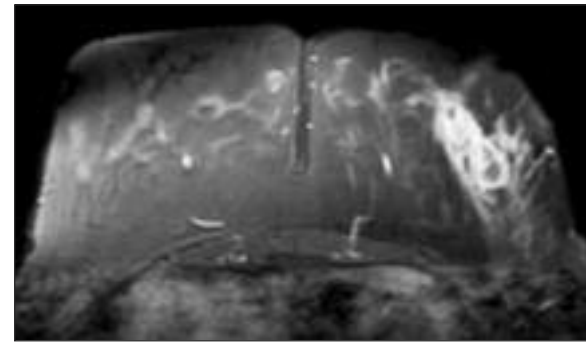

FIGURE 9: Heterogeneously enhancing areas and ring-like enhancement of abscess are seen on postcontrast MRI of the patient in Figure 7a.

lesions are being increasingly used for differentiating benign lesions from malignancy, but diffusion findings of IGM has not yet been defined to our knowledge. Diffusion is restricted and the ADC of IGM lesions are found to be low mimicking a malignancy. The lowest ADC values are obtained from the abscess cavities (Figure 10). Proton MRS findings are reported to be valuable in differentiating malignant lesions from benign ones. Choline (Cho) is reported to be detected in breast cancers, generally undetectable in normal breast tissue and benign lesions via in vivo proton MRS.[16] A statistically significant correlation between Cho concentration and early contrast washout is reported in malignancy. It was supposed to be based on two factors; firstly Cho is associated with active cell replication, and secondly tumor growth requires active angiogenesis, resulting in leaky immature vessels (e.g., with wide endothelial junctions).[17] Cho peak is not seen in breast abscesses.[18] Although IGM lesions demonstrate restricted diffusion mimicking malignancy, Cho peak is not encountered (Figure 11). Therefore MRS seems more helpful than diffusion imaging in IGM diagnosis.

RADIOLOGICAL DIFFERENTIAL DIAGNOSIS

Differential diagnosis of IGM includes inflammatory breast conditions such as inflammatory breast carcinoma, abscess, and fat necrosis.[4,19-21] Abscesses cannot be differentiated from some patterns of IGM. Fat necrosis which may occur as a result of radiation therapy, trauma, or some surgical interventions also demonstrates a wide spectrum of MG,

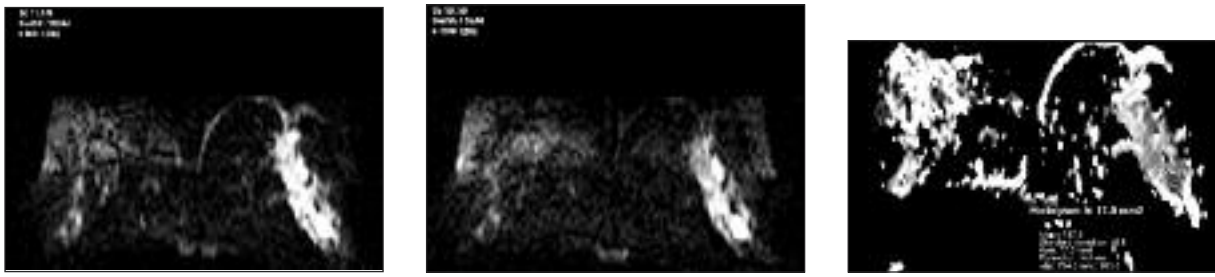

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FIGURE 10: Diffusion weighted MRI of the same patient in Figures 7 and 9 with diffusion sensitivities as **a.** b= 500s/mm^2 and **b.** b= 1000s/mm^2 images demonstrate high signal intensity due to restricted diffusion. Note that the highest signal is obtained from the abscess cavity. **c.** ADC mapping demonstrates low signal intensity of the IGM lesion. ADC value of the abscess is very low, measured as 797x10^{-6} mm^2/s.

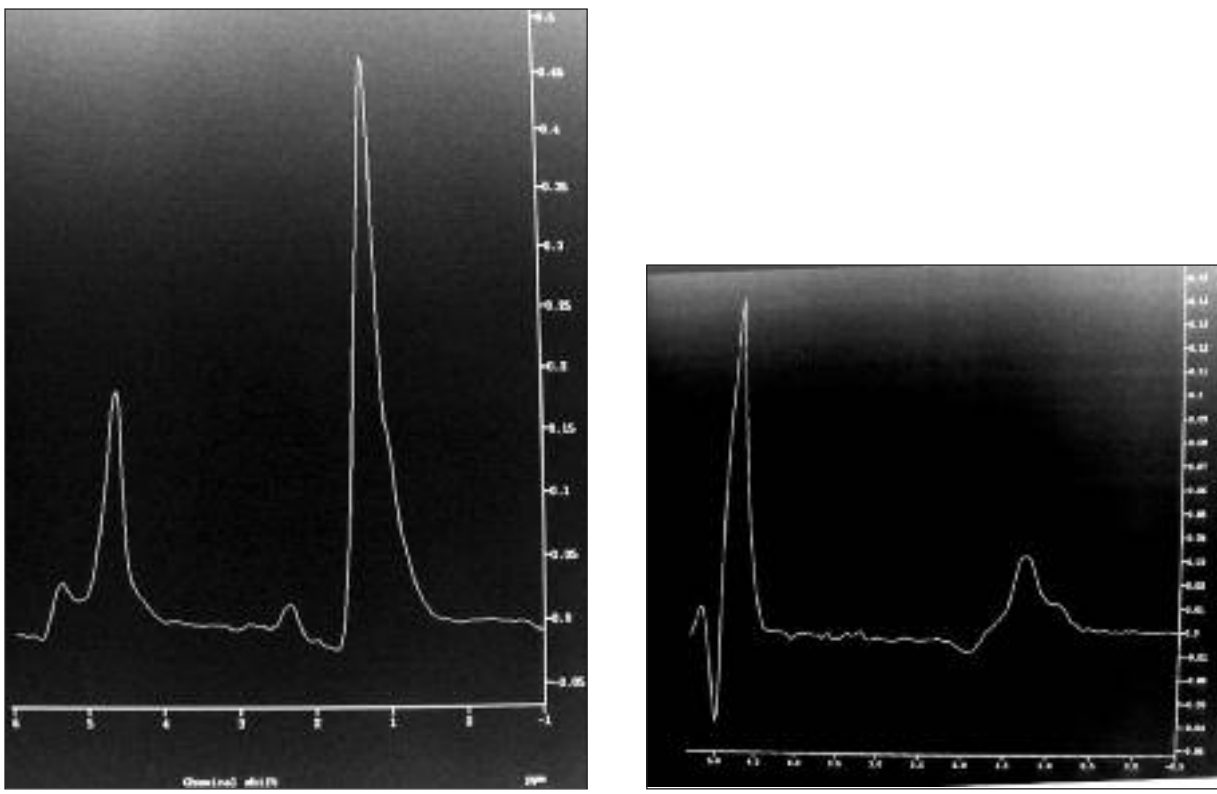

FIGURE 11: Single voxel proton MRS of different patients with IGM are shown. Note that none of them demonstrate choline peak.

US and MR imaging findings including irregular and early enhancement, spiculated enhancement, and ring-shaped enhancement without washout.[19] Without a clinical history, it is difficult to differentiate IGM from fat necrosis. The differential diagnosis of IGM from inflammatory breast carcinoma is also a diagnostic dilemma. Breast edema, enlargement, and skin thickening have been reported as common clinical and imaging features of inflammatory breast carcinoma.[20] Time-signal intensity curves in inflammatory breast carcinoma may be type 2 or type 3. Demonstration of an abscess formation is a sign for benign lesiens since the possibility of an abscess harboring malignancy is rare and abscess formation in inflammatory breast carcinoma has been reported as 10%.[21]

Diagnosis of IGM is actually a diagnosis exclusion; all known infectious and noninfectious causes

of granulomatous inflammations, chronic inflammatory breast diseases such as mammary duct ectasia, fat necrosis, foreign body reaction, Wegener granuloma, sarcoidosis, tuberculosis and histoplasmosis, carcinoma and carcinomatous mastitis must be excluded.[2,3] Biopsy still remains the only method for definitive diagnosis. IGM is histologically characterized by a chronic, noncaseous, necrotizing granulomatous lobulitis with or without abscess formation.[1,2,9]

TREATMENT AND COMPLICATIONS

There is no definite treatment for IGM. Wide local excision with or without steroid therapy is the most preferred method.[4,5] There is a strong tendency for persistence or recurrence; relapse after treatment has been reported in approximately 38% of the cases. Complications such as fistula and abscess formation may also develop as a result of the disease and/or surgical interventions. The prognosis is generally favorable.[2] Recurrence, fistula formation and secondary infections are the most common complications.[22]

In conclusion, radiological diagnosis of IGM is difficult. MRI is a promising diagnostic tool, type 1 dynamic contrast enhancement pattern and absence of Cho peak in MRS show the benign nature of the disease.

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