Breast inflammation: Clinical examination, aetiological pointers

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Abstract  Red, hot, and painful breast inflammation can have a large number of causes. The history of the condition and clinical observations usually give a pointer to the aetiological diagnosis, which is based on the classic triad of clinical, radiological and histopathological examinations, and guide the choice of additional investigations for rapid therapeutic management of this breast emergency. In breastfeeding women, the cause is often mastitis or, more rarely, an abscess; in non-breastfeeding women, the problem may be mastitis or a peri-areolar abscess, inflammatory lesions sometimes with secondary infection, or more rarely a real abscess, regardless of a catalogue of various causes. In all cases, the possibility must be considered of inflammatory breast cancer.

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Breast inflammation is a clinical condition, which can express a wide spectrum of aetiologies ranging from infection after nipple piercing to dreaded inflammatory cancer.

Confronted with this situation, the clinicians, such as the radiologist and all the others who will be managing the patient, must keep in mind all the possible causes. Fortunately, the history of the condition and clinical observations will usually provide rapid aetiological guidance, but the possibility of quickly revising first impressions, if initial management is unsuccessful, must never be ignored. Diagnosis of breast inflammation must be made as soon as possible and depends on the classic triad of clinical, radiological and histopathological examinations. It is a perfect example of the necessary multidisciplinary nature of senological practice.

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Clinical examination

The expression “breast inflammation” is not specific and does not differentiate between an infectious and a non-infectious process [1].

The clinical examination of a patient with an inflamed, red, hot and painful breast follows the well-known classic rules [2]: questioning will reveal the history of the condition and the personal and family medical history, and is followed, as always, by inspection and palpation of the mammary glands and lymph node areas, firstly at rest with the patient standing or sitting then lying down, then made more sensitive by active or passive movement, with a general examination to finish.

In this way, the context in which the inflammatory reaction has arisen and how and where it has occurred can be defined, and the clinical observations, including a diagram, which will be of use for monitoring its evolution, will be recorded in the medical file.

Aetiological pointers

After questioning and the clinical examination, two distinct situations will immediately become apparent, depending on whether the patient is breastfeeding or not.

Breast inflammation during lactation

According to the WHO [3], mastitis is defined as an inflammatory disease of the breast, which may or may not be accompanied by an infection. When associated with breastfeeding, it is known as lactational or puerperal mastitis. An abscess, a collection of pus located in the breast, is a complication of mastitis, but an abscess is not necessarily preceded by symptomatic mastitis [3].

Lactational mammary inflammation occurs with a frequency of between 2% and 33% depending on the series [4], but is generally below 10% [3].

In pregnant women it is difficult to distinguish between infectious and non-infectious mastitis, at least when the symptoms begin to appear.

When simple milk stasis occurs, whatever the cause, release of inflammatory cytokines may cause fever, muscle pain and shivering, producing a pseudo-infectious picture, and of course the milk stasis itself may also develop a secondary infection [3–5].

Irrespective of whether the mastitis is infectious or not, it will classically present as an indurated, swollen, hot, red and painful area of part of the breast [3]. Mastitis usually occurs during the first 6 weeks of breastfeeding [6], in general affecting only one breast. While infectious mastitis typically presents a fever of more than 38.5 °C and flu-like symptoms, non-infectious mastitis can be diagnosed when the symptoms rapidly decrease in 12 or at most 24 hours of giving corrective treatment for the milk stasis [4]. If the treatment fails, or sometimes even if it does not, an abscess may occur, with redness and pain increasing. Mammary abscesses in breastfeeding women usually appear in the first 6 weeks post-partum [3] and 0.4% to 11% of women with breast inflammation will develop an abscess, although in breastfeeding women they can appear independently of any previous infection [6,7]. The classic entry point for infection is an erosion of the skin or the nipple but this is sometimes not found on careful examination, even with a magnifying glass.

The clinical picture of a formed abscess is of a hot, red, extremely painful swelling covered by skin with an oedematous appearance. Palpation, which must take into account the pain, usually reveals a more or less fluctuating mass, with fever, possibly accompanied by adenopathy, particularly for superior-lateral locations. In the absence of treatment, the mass fluctuates and the skin may become necrotic, with possible fistulation.

In most cases, the microorganism concerned is Staphylococcus aureus. Staphylococcus epidermidis and alpha-haemolytic, beta-haemolytic and non-haemolytic streptococci are also found, more rarely Escherichia coli, Candida and Cryptococcus, an anaerobic flora, and exceptionally Mycobacterium tuberculosis [3,4,8].

An inflammatory reaction, in isolation or associated with a mass, which does not subside within 10 days of apparently suitable treatment, should bring to the clinician’s mind the possibility of a malignant lesion or even an inflammatory cancer [3,6,9].

Foxman et al. [5] analysed the frequency and management of breastfeeding-related mastitis in 946 women. The significant predictive factors for the appearance of these mastitis, the frequency of which was 9.5% in this series, were a history of mastitis during a previous pregnancy (OR = 4 [2.64–6.11]), nipple erosion or pain (OR = 3.4 [2.04–5.51]), the use of an antifungal cream on the nipple during the previous 3 weeks (OR = 3.4 [1.37–8.54]) and the use of a manual breast pump (OR = 3.3 [1.92–5.62]). In this paper, there was mammary pain in 98% of cases, fever in 82%, a feeling of malaise in 87%, shivering in 78%, redness and a localised hot and painful area in one breast in 78% and 62% of cases respectively.

The cumulative risk for mastitis occurring was 7.3% in women who had never previously breastfed, and 10.8% for those who had [5].

Breast inflammation in non-breastfeeding women

Other than during breastfeeding, and even if a great variety of other aetiologies are more frequent, breast inflammation should, in principle, always raise the question of inflammatory breast cancer (IBC). While it represents only 1 to 5% of all mammary cancers, it is a very aggressive form with a severe prognosis, and requires urgent treatment [10].

The other causes of breast inflammation in non-breastfeeding women may be infectious or non-infectious [1,6–9,11].

Inflammatory breast cancer

The clinical picture should produce a diagnosis of IBC, but its rarity means that few practitioners immediately think of it, since they have never encountered it [10,11].

Unlike most patients with breast cancer who usually present with a painless mass, a patient with IBC frequently describes the breast as feeling heavy, with a burning sensation or pain, even before any clinical symptoms appear.
By definition the disease progresses in these patients very rapidly and between these first symptoms felt by the patient and the appearance of the first clinical observations is short [10]. Either of the two breasts may be involved, the left breast more frequently according to certain authors [10]. Patients affected seem to be younger and more frequently pre- or perimenopausal than those with breast cancer with secondary inflammatory conditions, a differential diagnosis which is sometimes difficult [12,13].

Changes in the skin covering the breast is usually the first sign of IBC, the colour and distribution depending on the degree of evolution at the time of the consultation. At an early stage, there is erythema, which may vary from pale to deep pink, sometimes approaching pinkish-purple (Fig. 1). This coloration of the skin affects at least one third of the breast [10–13]. It may not be uniform and may be more marked on the lower half of the breast affected [10–14]. The breast is often hot or warm. At a more advanced stage, the pinkness becomes decidedly red or purple and may affect the whole breast, which may take on a marbled appearance and look bruised without an obvious cause, either over the whole surface or in particular areas [10–14]. This colour change is obviously not specific and, particularly at the beginning, may mislead diagnosis towards an inflammatory or infectious condition for which anti-inflammatory and/or antibiotic treatment is prescribed, and possibly repeated. This treatment delays correct diagnosis and of course does not stop the erythema from evolving, which, in addition, may misleadingly briefly fade. It should be emphasized as a warning that, unlike a breast infection, there are normally no general symptoms in IBC, such as fever or hyperleukocytosis, since there is no true inflammatory reaction [10–13].

The appearance of these skin colour changes may be more difficult to detect on black skins.

A rapid increase in volume of the breast affected, appearing almost simultaneously with skin changes, is highly suggestive of IBC [10–14] (Fig. 2). The woman may need to change bra size within a few weeks and the volume of the breast may double or triple. This rapid increase in volume, usually in less than 10 weeks, associated with skin colour changes affecting more than one third of the breast, clinically distinguishes true IBC from a neglected evolved cancer, which might have developed a secondary inflammatory reaction over time [10–14].

According to the classic description, there is no nipple discharge [15] and usually during IBC there is no breast ulceration, which is seen much more frequently, on the other hand, in cases of neglected advanced breast cancer. Clinically, careful palpation of the breast will find no palpable mass in the majority of cases of IBC [13]. It is precisely the absence of an underlying mammary lesion, which should catch the attention and lend weight to suspecting IBC. The associated cutaneous symptoms are also very evocative. The skin becomes thick and oedematous and appears infiltrated [14], producing the classic ‘orange peel’ look. Since this orange peel appearance depends on the oedema, in advanced forms it may cover the entire breast. The nipple may also be affected, with erythema, retraction, blisters and scabs, although this is not part of the typical form [10–15].

Careful palpation of the axillary, sub- and supra-clavicular lymph nodes is very important. Involvement of the axillary and supra-clavicular lymph nodes is very frequent, and reported in 55% to 85% of cases [13], and in up to 100% of cases in certain series [10]. A third of patients may already have remote metastases at the time of diagnosis and a general clinical examination will do its utmost to locate them, but, of course, it will be the additional investigations performed during staging which will find them and reveal their characteristics.

Evolved forms of IBC have been described in which the opposite breast was involved, and contralateral axillary invasion may also be seen [10]. Although forms affecting both breasts from the outset are rare, they have been described, as have lymphoedemas through massive lymph node invasion.

Diagnosis of IBC thus requires a combination of observation, careful chronological recording of the medical history, clinical examination (with photographs if possible) and, very rapidly to avoid erroneous diagnosis, a biopsy to detect obstruction of the lymphatics by emboli of carcinomatous cells, which are considered to be responsible for the clinical picture [15].

Inflammatory breast cancers are classed as T4d in the TNM classification. The Institut Gustave-Roussy has
suggested adding the idea of 'poussée évolutive' or evolving inflammatory signs (PEV stages). When inflammatory signs affect part of the breast the disease is classed as stage PEV2, while involvement of the entire breast is stage PEV3, or classic carcinomatous mastitis [14,16].

Other causes of breast inflammation
Inflammation and infection of the mammary glands are presented in the literature in a very varied manner depending on the classification used. According to Dixon et al. [6], distinctions should be made, depending on the location, between central, retroareolar or subareolar lesions, and peripheral lesions away from the nipple-areolar complex, returning in fact to the conventional separation between superficial and deep lesions [1].

Periareolar mastitis and periareolar abscesses
Inflammatory periareolar mastitis is the commonest condition encountered in young women, with a mean age of 32 years [6]. It consists, clinically, in the first instance, of rapidly arising, painful, localised, periareolar redness (Fig. 3 a, b), sometimes with slight areolar retraction on the side of the duct affected. There may be a discharge from the nipple. Ninety percent of patients with this lesion are smokers [6]. Evolution is very capricious [17]. The redness spreads, associated with oedema which is usually discrete and may appear as a small painful superficial swelling, sometimes fluctuating, producing an aseptic periareolar abscess, which usually finishes by forming a fistula along the area of least resistance, usually at the areola/skin junction (Fig. 4) [1,6,8,9,17]. There is a strong tendency for periareolar abscesses, which form the majority of non-puerperal mammary abscesses, to recur, with the possibility of secondary infection by cutaneous microorganisms. The pathogenic hypothesis is that this inflammatory lesion is the result of the evolution of a galactophorous secretting ectasia, with obstruction of the terminal subareolar galactophorous ducts – possibly by squamous metaplasia of the epithelium – rupture and inflammatory reaction, whose result is plasma cell mastitis [17,18], possibly with secondary infection [6–9,11]. Its evolution is often unpredictable, "alternating regression and recurrence, variable over time and from one woman to another" [17].

Tobacco is a factor significantly associated with this condition, with a relative risk of 6.2 (2.9–13.4) [19] to 14.73 (3.18–68.22) [20] depending on the authors, and up to 26.4 (9.9–70.2) for heavy smokers [21].

Peripheral or deep abscesses
True peripheral or deep abscesses are much less common in non-breastfeeding women and are found in particular situations, notably in diabetic women, immunosuppressed subjects, those receiving immunosuppressive treatment or following trauma [6,8,10]. The breast rapidly increases in volume, becomes red, hot, heavy and very painful with a piecing throbbing pain, with shiny skin or even cutaneous oedema with the classic ‘orange peel’ appearance [1]. The onset of this type of abscess is quite specific and will become evident during questioning. It starts abruptly: the patient can very often state the exact time. It is associated with erythema, sometimes a purulent galactophorous discharge, oedema, deformation, general symptoms and, on gentle palpation, a mass with possibly homolateral painful adenopathy which is generally axillary. An abscess is a rare
breast emergency but it requires very rapid management, remembering the frequent involvement of anaerobic organisms.

Occasionally, an in situ ductal carcinoma can develop a secondary infection and present as infectious inflammatory mastitis [14], or an abscess [6].

In a patient, particularly one over 35 years of age, who presents with inflammation, an infection or an abscess—particularly where there is no detectable aetiological factor—it is wise to perform appropriate additional examinations once the infection has subsided. The risk of finding a cancer in the wall of a formed abscess has been assessed to be 4.37% (9/206) [22].

Gollapalli et al. analysed the risk factors for the appearance of a primary breast abscess and its possible recurrence [20]. Classifying breast abscesses depending on location—central (subareolar and retroareolar), or distal relative to the nipple-areolar complex—they found several statistically significant risk factors. Tobacco is significantly associated with the development of a subareolar abscess: the risk of this type of infection is 11 times greater in smokers than in non-smokers, with the risk of recurrence being 15 times greater than in non-smokers. Univariate analysis indicated that smoking, relative to not smoking, (OR = 8 [3.4—19.4]), obesity, defined as a body mass index equal to or greater than 30 kg/m², (OR = 3.6 [1.5—9.2]), diabetes (OR = 5.7 [1.1—54.9]) and nipple piercing (OR = 10.2 [1.3—454.4]) are all risk factors for a breast abscess. Multivariate analysis confirmed that smoking is a significant factor (OR = 6.15 [2.65—14.29]) as is nipple piercing in the sub-group of sub-areolar abscesses (OR = 20.26 [2.01—204.28]). As far as the recurrence of breast abscesses is concerned, multivariate analysis found smoking (OR = 14.73 [3.18—68.22]) and a history of surgical treatment (OR = 11.94 [1.08—131.72]) to be the main risk factors. Despite the relatively wide confidence intervals, due to the small size of the series published (cases, n = 68, controls n = 68), and any possible bias, these results show smoking to be a major factor in mammary infection and recurrence, while nipple piercing is associated with considerable risk of subareolar abscesses [20].

Granulomatous mastitis
Granulomatous mastitis is an inflammatory lesion, which evolves unpredictably and for which the aetiology is still hypothetical. It can present as an inflammatory mass, which may sometimes mimic an abscess, with or without ulceration of the overlying skin, or a cancer [6]. The cause of this peripheral rather than periareolar lesion [17], which can recur and form fistulae, is as yet unknown [6] and should be compared with that of plasma cell mastitis [17].

Other situations
A number of other inflammatory breast pictures may also be more rarely encountered, such as an inflammatory reaction when there is mammary tuberculosis (rarely primary) [23], herpes, syphilis or actinomycosis [8]. Secondary infection of sebaceous cysts, hidradenitis, an infectious complication after plastic surgery or radiotherapy may also be encountered [6]. In certain cases, inflammatory reactions can be observed, which may be of infectious or mycotic origin [6], affecting the sub-mammary folds or the inferior half of the breast, often exacerbated by obesity and diabetes.

It should also be remembered that exceptionally there are situations, particularly in a psychiatric environment, where the patient self-inflicts breast wounds, which can develop a secondary infection, not so much by linear cuts which are easily recognisable, as by pricking with a pin, needle, paperclip etc., which may produce recurring abscesses with an aetiology which is particularly difficult to determine [8,9].

Equally exceptional cases have been reported of mammary metastases of an ovarian cancer presenting as IBC [24].

Many other situations may occasionally be expressed as an inflammatory breast reaction and it is not possible to list them all here [25,26]. We will however mention Mon dor’s disease, mammary trauma, cytosteatonecrosis, certain forms of diabetic mastopathy [25,27], Lyme disease [17], phyllode tumour, giant adenofibroma and even juvenile breast hypertrophy or gigantomastia [7,11,17,25,26].

Conclusion
The clinical examination is essential as the moment for aetiological diagnosis of breast inflammation. Based on questioning and careful breast, lymph node and general examination, which must be adapted to what is often a painful condition, it is decisive in guiding the aetiological diagnosis towards the choice of additional investigations, in the forefront of which are imaging examinations, and in allowing rapid therapeutic management of this breast emergency.

As an example of the transdisciplinary nature of sonology, the diagnosis and management of an inflamed breast means the doctor must keep in mind all the possible causes, without ever forgetting the possibility of a cancer when the picture persists despite rapid, initial and apparently appropriate treatment.

**TAKE-HOME MESSAGES**
- The inflamed breast is red, hot and painful, and is a clinical condition, which may have many causes. From questioning and the clinical examination two different situations will arise, depending on whether the woman is breastfeeding or not. When the woman is breastfeeding, lactational mastitis needs to be distinguished from an abscess. Lactational mastitis is primarily inflammatory, linked to milk stasis, and it is the absence of regression within a maximum of 12 to 24 hours after correcting the stasis that may indicate an infection. An abscess presents the classic picture. In non-breastfeeding women, we can find periareolar mastitis and periareolar inflammatory abscesses with or without secondary infection, and true peripheral or more rarely a real abscess, regardless of a long list of various causes. Whether the woman is breastfeeding or not, the possibility of a cancer must always be borne in mind, particularly inflammatory breast cancer, the cardinal clinical signs of which associate an inflammatory reaction with a very rapid increase in the volume of the breast affected.
• The aetiology based on the clinical observations is only hypothetical and must be rapidly supported by the result of additional investigations, and immediately revised in the event of failure of an apparently perfectly appropriate initial treatment.
• The diagnosis and management of a patient with breast inflammation is an urgent situation and an example of the necessary multidisciplinary nature of senological practice.

Clinical case

Case No. 1

This 37-year-old patient has undergone tumourectomy and axillary node dissection for an infiltrating ductal carcinoma SBR3 of 20 mm, RH -, Her2 -, 10 N -, and had six courses of adjuvant chemotherapy (Figs. 5 and 6). The clinical examination shows breast inflammation. What is your diagnosis?

Answer

These photographs were taken during the fifth week of radiotherapy, at the end of 50Gy, before the beginning of a boost to the tumour bed.

The diagnosis was of acute radiodermatitis. Inflammatory breast reactions during radiotherapy are common [25] and may be accompanied by diffuse redness, oedema or an exudative reaction. A sharp boundary without any transition between the healthy skin and the irradiated skin is characteristic. The principle differential diagnosis is breast cellulitis after treatment of a breast cancer, where on examination there is erythema and fever (often 39°), with sudden onset. A clinical example of this differential diagnosis [28] is available free of charge on line on the site of the New England Journal of Medicine at the address: http://www.nejm.org/doi/full/10.1056/nejmicm065836.

Case No. 2

A 57-year-old patient, with no hormonal treatment of the menopause, consults as an emergency for sudden onset right breast pain, with no fever.

Patient is standing, hands on her head (Fig. 7). What diagnosis do you suggest?

Answer

Examination found periareolar redness, with no abscess, umbilicated nipple or visible excoriation. Dynamic
inspection, with the patient standing with her hands on her head, found a small deformation of the inferior quadrants of the right breast, a little more marked than on the contralateral side (Fig. 7). In the lying position, where the breast spreads out well, the right periareolar redness is more clearly seen, without cutaneous oedema (Fig. 8). Gentle palpation, with the patient first standing then lying, found no mass or real cutaneous retraction and there was no discharge, nipple or areolar retraction, or adenopathy. Contralateral breast was clinically normal. With anti-inflammatory and antibiotic treatment given because questioning had produced the fact that periareolar hair had been pulled out during the previous days, the lesion regressed completely in 10 days.

A mammogram and ultrasound examination was undertaken after the clinical recovery, in case there was an underlying neoplastic lesion. This proved normal and the patient, who was clinically monitored but with no recurrence, returned for the organised screening programme. The diagnosis was of periareolar mastitis.

Disclosure of interest
The author declares that he has no conflicts of interest concerning this article.

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