CASE REPORT

Granulomatous Lobular Mastitis Following Drug-Induced Galactorrhea and Blunt Trauma

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Abstract: We report a single case of chronic granulomatous lobular mastitis following metoclopramide-related galactorrhea and a blunt trauma in a young parous woman who underwent two conservative operations before becoming symptom-free. We have found only two other literature cases associated with hyperprolactinemia, and our case could be another of this etiologic group. The absence of well-formed granulomas in the first histology specimen in the present case was misleading; it was reinterpreted as granulomatous mastitis only after the second specimen was examined. Reinterpretation was based on the lobular distribution of a lymphoplasmocytic infiltrate (nonspecific chronic lobulitis) and the presence of epithelioid cell sheets and neutrophils in the absence of well-formed granulomas. The case lends further support to the theory of a local immune response initiated by the secreted material or by one of its components in the formation of granulomas. However, contributory factors such as the trauma in this case (a blow from a shovel handle) or systemic disease in others may play a role in the development of the disease, which in some instances may represent a pattern of tissue reactions to different noxious agents.

Key Words: breast abscess, diagnosis, galactorrhea, hyperprolactinemia, idiopathic granulomatous lobular mastitis, treatment

Diabetic granulomatous lobular mastitis (GLM) is a rare, but well-defined and readily recognized entity characterized by the formation of noncaseating granulomas in a lobular distribution and an inability to demonstrate any infective agent at presentation. Since Kessler and Wolloch (1) documented the first cases under this heading in 1972, several others have been reported in the literature.

GLM characteristically appears in young women in the postpartum period and has on rare occasions been related to hyperprolactinemia or systemic disease. We report here a case presenting as a recurrent abscess following drug-related galactorrhea and trauma which healed after two conservative operations.

CASE REPORT

A 38-year-old woman presented with a painful swelling of the left breast on January 23, 1996. She had taken oral contraceptive pills since the age of 20. She had given birth to three children, the first in 1988 and the third in 1993. The breastfeeding of her children lasted 3.5 months, 2 weeks, and 10 days, respectively. In April 1993, gastroesophageal reflux disease was diagnosed and she started a long course of ranitidine (1 year) and
metoclopramide. The latter was discontinued after 6 months because of the presenting galactorrhea, which ceased after the drug was withdrawn. The serum prolactin level was not investigated. In January 1996, she reported a severe blunt trauma to the left breast caused by the handle of a shovel.

On physical examination, her breasts exhibited mastopathic changes. The periareolar area of the left breast was erythematous, and a tender, slightly hardened mass was observed. The axilla displayed palpable, nontender lymphadenopathy. General symptoms were absent except for subfebrility. A mammogram on January 31 was interpreted as negative for malignancy and suggestive of mastopathic changes. The results of routine laboratory tests were within normal ranges, with a leukocyte count of $10.5 \times 10^9/L$ and an erythrocyte sedimentation rate (ESR) of $30 \text{mm/hour}$. The patient was operated on because of the clinical diagnosis of abscess on February 7. Excision and drainage of the $4 \text{cm} \times 5 \text{cm} \times 6 \text{cm}$ “abscess” was carried out via a subareolar incision. The impression of the operating surgeon was that the abscess was atypical. Instead of discharging pus from a preformed lumen, the breast contained some kind of fibrous debris and no preformed lumen was identified. Tissue was sampled for culture and histology. On histology, fibrous breast tissue predominated, but there were many neutrophils at one edge of the specimen, with cellular debris at the borders. A considerable number of mononuclear cells were visible in foci at some distance from the lesion. Seemingly intact lobules were also present. A few epithelioid cells arranged in sheets and giant cells were observed, but these were interpreted as part of the granulation tissue surrounding the abscess. The slides did not include well-formed granulomas. No bacteria grew from the specimen. A short parenteral course of antibiotic (cefamandole) was started. The patient was discharged without symptoms on February 11.

She returned on March 4 because of an infiltrate in the operated breast. A mammogram was recorded (Fig. 1) and an ultrasound examination was carried out (Fig. 2). These revealed a compact central area and two circumscribed lesions $2.5$ and $0.7 \text{cm}$ in diameter. The chest X-ray and abdominal ultrasound examinations were negative. Of the routine laboratory findings, only a slightly elevated ESR ($28 \text{mm/hour}$) need be mentioned. The patient underwent reoperation on March 6, with a diagnosis of recurrent abscess. The inner upper quadrant containing necrotic tissue was debrided and an incision was made for drainage of the central part. A washing-draining system was inserted and continuous lavage with aseptic physiologic saline solution was begun. Tissue samples for histology and culture were again obtained. A course of metronidazole and amoxicillin + clavulanate was then started.

**Figure 1.** Mammogram of the lesion in March. A central compact area and skin reaction missing from the first mammogram are discernible.
On histology, the specimen clearly showed well-formed noncaseating granulomas with Langhans’ and foreign body-type giant cells within fibrous background tissue (Figs. 3 and 4). These exhibited a distribution mainly respecting the lobules, but at some sites completely destroying these structures. Not only acini, but also some terminal ductules were involved. Certain of the lesions displayed a high number of neutrophils, while others had no such feature. Coalescing suppurating granulomas forming abscesses were also present. A number of apparently intact lobules could be demonstrated, while some of the lobules exhibited a mononuclear infiltrate (lobulitis) without epithelioid cells (Figs. 5 and 6). Auramine staining (2) did not reveal acid-fast bacilli. Special stains (Grocott’s methenamine silver, PAS, and tissue Gram’s) likewise failed to demonstrate other bacteria or fungi. No refractile foreign bodies could be demonstrated with polarized light, and the specimen also lacked Schaumann or asteroid bodies.

In retrospect, the same lobular distribution of mononuclear cells (lobulitis) was present in the specimen examined in January. This inflammatory response, coupled with the epithelioid cells and neutrophils, the negative culture, and the special stains for an infective cause, led to a reinterpretation as GLM.
No bacteria grew from the two consecutive specimens sent for microbiology under aerobic and anaerobic conditions. The lavage drainage system was changed once under aseptic conditions. The discharge through the drains gradually decreased and no further abscess formation was noted. The draining system was gradually evacuated and the patient was once again discharged without symptoms on March 20.

Because of the diagnosis of GLM, steroid treatment was suggested. However, the patient concomitantly had rosacea and there was a strong suspicion that this was related to previous local steroid treatment. There was no evidence of other dermatologic disorders. Accordingly the patient was carefully followed and only a course of oral antibiotic (ofloxacin) was instituted in order to prevent subsequent infections. The patient is well more than 1 year after the second operation. No infections complicated the disease, even in the reconvalescence stage.

**DISCUSSION**

The clinical importance of GLM is that it often simulates carcinoma, although it may present as an abscess, as in this case. Carcinoma is by no means the most important possibility necessitating a clinical differential diagnosis. GLM can simulate a neoplasm not only by giving a hardened mass and microcalcification, but also by adhering to the skin, producing the “peau d’orange” sign, ulceration, and nipple inversion, and sometimes leading to axillary lymphadenopathy (3). The mammo-gram and/or biopsy suggest a malignant diagnosis in some cases (1,4), which emphasizes the need for an adequate tissue sampling biopsy for a firm diagnosis.

The disease has been coupled with the use of contraceptive pills and breastfeeding, but Going et al. (5) found no relation between the development of GLM and these clinical data. GLM is clearly associated with pregnancy, since the affected women are parous and in most of them only a short time has elapsed since their most recent pregnancy.

We believe that the lesions observed on histology represent different steps of a pathogenetic process. One step might be the chronic nonspecific lobulitis seen in many lobules, demonstrating a reactive lymphoplasmocytic infiltration. Destruction of the lobules could be identified in some cases. This might subsequently lead to secretion leakage and the formation of granulomas, which on occasion display a central suppuring necrosis. Coalescence of such foci can lead to the formation of more definite abscesses. The secretion present in some intact acini could be the precipitating cause in most cases that are associated with the previous, or rarely (6) the current pregnancy, or the two cases associated with hyperprolactinemia of other etiology (5,7). Oral contraceptive pills could similarly play a role in stimulating secretion in the breast (8). Postparturn and post-oral contraceptive pill galactorrhea are recognized entities with a similar suggested etiology: the increased sensitivity of the breast to normal circulating prolactin levels (9). Galactorrhea is often overlooked, because patients do not think it worth mentioning, but galactorrhea is not necessarily needed: a minor secretion might be enough to initiate GLM. Galactorrhea ceased in our patient 27 months prior to the manifestation of GLM, but a PAS-positive secretion could still be demonstrated in both specimens. Trauma may also be a contributing factor in our case.

Certain of the pathogenetic steps mentioned here were earlier suggested by Kessler and Wolloch (1), who drew attention to the similarity between GLM and “idiopathic” granulomatous inflammation of the testis and thyroid. Besides De Quervain’s thyroiditis, which is presumed to result from a primary viral infection, we must mention the resemblance with palpation thyroiditis, where mechanical factors lead to the development of granulomas in the thyroid gland. This analogy suggests that trauma cannot be neglected as a possible contributor in the present case. Multiple operations could also correspond to trauma, and this is why vigorous surgical interventions should be avoided as much as possible.
A central, but probably not unique role is attributed to the extravasated secretion in the development of a granulomatous response. Most cases were seen within a few years after the most recent pregnancy. Besides the present case, which was associated with previous galactorrhea, two literature cases were associated with hyperprolactinemia (5,7). However, other factors may also play a role in the generation of this disease, as evidenced by a normoprolactinemic case starting 15 years after the last pregnancy, or an unreported postmenopausal case seen by Howell et al. (3). Many studies report the lack of serologic abnormalities relating to a systemic autoimmune mechanism, again favoring a localized immune response, probably of allergic type IV, to an as yet uncharacterized antigen, which must be present in the mammary secretion. However, the fact that GLM has been associated with chronic granulomatous disease (a case presented by Dr. J. L. Peterse at the XXIst International Congress of the International Academy of Pathology in Budapest on October 25, 1996) or with erythema nodosum and/or polyarthralgias in a minority of cases (5,10) suggests that GLM can also be a manifestation of systemic disease. Some authors are skeptical about the noninfective nature of the disease, but it seems reasonable to regard the disease as an immune-mediated one. No epidemiologic data are indicative of an infective origin, and the lesions do not involve any identifiable primary microorganisms, although they do predispose to secondary infections (3,11).

There is no generally accepted treatment and no apparent optimal treatment for the disease, which follows a troublesome course. A wide excision has often been used (1,12–14), but such surgical treatment has been associated with a high rate of recurrent lesions and the need for reoperations. Secondary infections and sinus formation can complicate surgical excisions (3). The number of operations required can be as high as four (14). The mechanical factors outlined earlier (vigorous palpation and surgical manipulation) might be the cause of the recurrent lesions associated with surgery. Radical surgical treatment has been challenged by others, who suggest a more conservative approach, with incision and drainage (15). Since DeHertogh et al. (16) first suggested steroid treatment for the disease, a number of therapeutic successes have been documented (4,5,17,18). However, other cases did not respond definitively to steroid treatment (5,14,17). We believe that this may be explained in part by the short duration or the low dose of the treatment regimen. We would have treated our patient with a high dose (1 mg/kg body weight) of prednisone for several months after the diagnosis was made, but the probability that the patient’s rosacea was steroid-related led us to wait for some time before initiating the drug treatment. Fortunately, conservative surgery was sufficient. Since data strongly supporting the effectiveness of prednisone are not available, and relapse has also been documented with steroids (17), the advantages and possible disadvantages of relatively long-term corticotherapy must be seriously considered. We are aware of a case that seemingly healed spontaneously without any specific treatment (6), and the “Natura sanat” effect cannot be excluded in our case. Special cases associated with hyperprolactinemia deserve further attention and diagnostic effort. The case reported to be associated with a prolactinoma was successfully treated with bromocriptime (7).

CONCLUSIONS

Granulomatous lobular mastitis is now a well-known entity, but it causes differential diagnostic problems. The diagnosis seems to require some kind of biopsy, since the diagnosis has practically never been suggested without this procedure. In most cases an excision biopsy should be performed, but fine needle aspiration can also give an adequate diagnosis (6). Exclusion of an infectious origin is essential, particularly when steroid treatment is considered. If surgery forms part of the treatment, a conservative approach seems to be most adequate. This could prevent the contribution of mechanical factors to the pathogenesis of the disease. Besides parity and a suggested increased responsiveness of the breast to normal prolactin levels or hyperprolactinemia, additional contributing factors such as trauma and systemic disease (arthralgia and erythema nodosum or chronic granulomatous disease) must be considered in the etiology of some cases. In this way, GLM might be viewed not only as a distinct clinicopathologic entity, but also as a pattern of tissue reactions to different noxious agents.

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