CLINICAL VIGNETTE

Granulomatous Mastitis: A Case and Implications on Management Strategies

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Case

A 42-year-old premenopausal female with hypothyroidism presented with a new right breast mass for 1 week. She had been seen in the Emergency Department (ED) the day prior. The lump was painful and was associated with overlying erythema and yellow and clear nipple discharge (Figure A). She denied any fevers or chills. She has never experienced similar symptoms before and did not have any family history of breast cancer or ovarian cancer. On exam, her vitals were normal. The breast mass was firm, with irregularly borders at the 4 o'clock position. There was no axillary lymphadenopathy. Labs were all normal, including cell blood count, comprehensive metabolic panel, erythrocyte sedimentation rate, and C-reactive protein. Breast ultrasound at the ED showed no discrete abscess, with heterogenous soft tissue without definite measurable mass.

She was prescribed amoxicillin-clavulanic acid twice a day for 7 days, which was extended to 14 days after patient noted some mild improvement after 1 week on the antibiotics, but persistent pain. Her mammogram and second breast ultrasound 2 weeks after presentation showed a 2 cm irregularly shaped mass with spiculated margins and phlegmonous changes with a possible early abscess, which was not fully formed. There was no definite fluid collection. She returned to the ED and was prescribed another 14 days of amoxicillin-clavulanic acid.

Breast core needle biopsy was performed 6 weeks after presentation and showed cystic neutrophilic granulomatous mastitis. There was no evidence of carcinoma. *Corynebacterium bovis* was detected on biopsy.

She developed persistent purulent discharge from the biopsy site, with a persistent fixed mass at least 4 cm long (Figure B). She was given trimethoprim-sulfamethoxazole twice a day for 2 weeks, which she felt helped improve her symptoms. She was then evaluated at Breast Clinic and prescribed doxycycline for 1 week and advised to apply warm compresses three times a day. After 1 week of doxycycline, her lump began to get warmer and more swollen again, and another week of doxycycline was prescribed. Pus started to drain out from a fistula that developed from the mass site (Figure C). A third week of doxycycline was prescribed and symptoms slowly started to improve.

Three weeks after finishing the doxycycline, her biopsy site healed and closed, and the palpable mass was significantly smaller and softer (Figure D).

Discussion

Granulomatous mastitis (GM) is a rare, benign chronic inflammatory breast disorder characterized by relapsing inflammation which can be difficult to treat. There is a higher prevalence of GM in women of Asian, Hispanic, and Arabic descent.[1] Clinical presentation often resembles that of breast mastitis, abscess or malignancy, which can lead to delayed diagnosis. Most commonly, it presents as a palpable firm mass that tends to spare the subareolar region and is often painful. Other symptoms may include erythema, edema, skin or nipple retraction, ulceration, discharge from a sinus or fistula, and lymphadenopathy.[1,2] Imaging with ultrasound and mammography often finds an irregularly shaped mass, classified as suspicious, and a histologic diagnosis via core needle biopsy is necessary to rule out malignancy.[3]

The etiology of GM is unclear but it has been associated with autoimmune conditions, and infections and elevated hormonal states including oral contraceptives, pregnancy, and breastfeeding.[4] While much of the literature reports the autoimmune hypothesis is the most common, a strong correlation has been found with *Corynebacterium* after the bacteria was identified in the lipid-filled vacuoles within the granuloma. Some suggesting a causal link.[1,4] This GM variant, cystic neurotrophilic granulomatous mastitis (CNGM) has neutrophilic and granulomatous inflammation surrounding clear cystic spaces, which can harbor *Corynebacterium* species.[5]

Many reports established an association between GM and different species of *Corynebacterium*, including *C. kroppenstedii, C. tuberculostearicum*, and *C. freneyi*.[1] Our case is the first association with *C. bovis* in humans. Furthermore, given the presence of Corynebacterium in this case and our patient's response to certain antibiotics, it is supportive of recent literature that suggests antibiotics may be more effective than initially thought.

The treatment for GM is still controversial, with variable strategies used, including observation, oral antibiotics, oral and intralesional corticosteroids, and immunosuppressives such as methotrexate. Surgical interventions including incision and

drainage, limited or wide surgical excision, mastectomy are now less favored.[3] Empirical antibiotics alone were previously felt to be effective treatment for GM. Immunosuppressives such as corticosteroids were reported to have higher success rates.[1,3] However, more recent literature has postulated that if CNGM is histologically determined and *Corynebacterium* species are found, antibiotics alone may be a viable treatment, specifically if an extended course of a lipophilic antibiotic is used.[6,7] Better clinical responses were reported with lipophilic antibiotics able to penetrate into breast tissue.[6,7] Examples of lipophilic antibiotics include doxycycline, trimethoprim-sulfamethoxazole, clarithromycin, rifampicin, and clindamycin.[7,8] Penicillins and cephalosporins, which are often the first-line antibiotics used for breast soft tissue infections, are not lipophilic.

Our patient, represented the first reported case of *Corynebacterium bovis*-associated human GM in the literature. She only mildly improved after her initial one-month treatment with amoxicillin-clavulanic acid. After lipophilic antibiotics trimethoprim-sulfamethoxazole and doxycycline were started, her symptoms significantly improved, supporting the argument for extended courses of lipophilic antibiotics as treatment in GM and especially CNGM.

Figures

(*from top and left). Figure A: on initial presentation. Figure B: discharge from biopsy site. Figure C: discharge from breast mass site. Figure D: after 5 weeks of lipophilic antibiotics.*

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