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A CASE REPORT OF SIMULTANEOUS DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS AND BREAST CANCER AND LITERATURE REVIEW

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Abstract: Objective To improve the alertness and diagnosis and treatment of systemic lupus erythematosus (SLE) combined with breast cancer through case report and review of related literature. Methods To review the diagnosis and treatment of a patient diagnosed with both systemic lupus erythematosus and breast cancer, summarise the clinical features and follow up the changes in her condition after treatment, and summarise her diagnosis and treatment. Results The patient was admitted to the hospital with arthralgia accompanied by fever, with a past history of breast hyperplasia, and a complete examination suggesting leukopenia, positive anti-double-stranded DNA antibody and antinuclear antibody, and low complement, which was in line with the classification criteria of systemic lupus erythematosus of the American College of Rheumatology (ACR) of 2019, and the examination of breast ultrasound suggesting a category 4C (the classification of Breast Imaging Reporting and Data System)nodule in the right side of the breast, and puncture pathology suggesting infiltrating carcinoma in the breast, the patient was subsequently treated for both SLE and breast cancer. Conclusion:The onset of SLE is insidious, and after diagnosis of SLE, patients should be aware of the need for regular breast cancer screening, and individualised treatment for both diseases can be carried out.
Keywords: Systemic lupus erythematosus; Breast cancer; Case report

1 INTRODUCTION

Systemic lupus erythematosus (SLE) is a complex autoimmune disease, and breast cancer is one of the most common malignant tumors in women. With the progress of medical research, the diagnosis and treatment of SLE are becoming more standardized, and the prognosis of patients with SLE is getting better and better, and there are many domestic and international reports of SLE in breast cancer, but most of them are diagnosed after breast cancer [1].The coexistence of SLE and breast cancer faces a special challenge in diagnosis and treatment. In this article, we report on a young woman who was diagnosed with SLE and breast cancer at the same time, summarize the diagnosis and treatment of this patient, and review the relevant literature, so as to provide a certain reference for the subsequent diagnosis and treatment of patients with SLE combined with breast cancer.

2 CASE REPORT

The patient is a 37-year-old woman, who was admitted to the hospital because of recurrent joint pain for 5 months and fever for 3 days. 5 months ago, the patient experienced swelling and pain in the right knee joint, which made it difficult for her to walk, and was diagnosed as synovitis in the orthopedic department of the local hospital, and she was given Erythroxib, synovitis granules, and pain-eliminating plasters, and then she still suffered from recurrent pain, which she did not pay much attention to; she developed a fever without any obvious triggering cause 3 days ago, and the maximum temperature was 38.5 degrees Celsius. The maximum temperature of 38.5 degrees Celsius, fear of cold, no cough and sputum, no chills, no runny nose, headache, to the outpatient department of the community hospital to consider acute upper respiratory tract infection, oral ibuprofen, Lotus Clearance Granules, phenol qaifengmin still recurring fever, and before the scattered erythematous rashes on the torso, accompanied by the wrist joints, knuckle joints, knee joints, swim persistent mild dull pain, obvious after activity, finger movement is unfavorable, obvious morning wake up! The patient was admitted to the department of general practice on May 25, 2023 with arthralgia and fever for further treatment, accompanied by numbness and weakness of the limbs. Past history: breast hyperplasia was detected 5 years ago in an outside hospital. Menstrual history, personal history, family history are not specific.
Admission examination: temperature 37.3℃, pulse 69 times/min, respiration 20 times/min, blood pressure 111/68mmHg. Scattered maculopapular rashes were seen on the trunk and lower limbs, no cyanosis on the lips and mouth, pale conjunctiva, symmetry of respiratory movements bilaterally, clear respiratory sounds in both lungs, no dry or wet rales were heard; heart rhythm was unanimous, and no murmur was heard in the valvular auscultation area; abdomen was soft, with no pressure and rebound pain in the whole abdomen, and abdominal mass was not palpated, and liver and spleen were not palpated under the rib cage; kidney area was not palpated. No subcostal mass was

detected; no percussion pain in the renal region; no edema in both lower limbs; mild swelling of the right knee joints of both hands and knuckles with moderate pressure pain.

Auxiliary examination: blood routine: leukocyte count 2.01×10^9/L, neutrophil absolute value 1.03×10^9/L, hemoglobin 101 g/L; erythrocyte sedimentation rate measurement 27mm/h, nuclear antibody measurement (ANA) titer 11:320, anti-SSA antibody positive , anti-Sm antibody positive, anti-double-stranded DNA antibody (dsDNA) 428.3IU/ml, C3 0.348g/L , C4 0.0308/L; Direct Coombs test was positive; antieutrophil cytoplasmic antibody, anticardiolipin antibody assay, tuberculosis infection T-cell assay, influenza viral antigens,COVID-19 nucleic acid detection, tumor markers did not show any abnormality. MR scanning of the right knee joint showed no obvious abnormality.

The patient had unexplained arthralgia with fever, antinuclear antibody (ANA) titer ≥1:80, decreased complement, leukopenia, fever >38.3°C, accompanied by limb rashes, and appeared to have swelling and pressure pain in more than two joints, which was in accordance with the 2019 ACR classification criteria for systemic lupus erythematosus.After the diagnosis was clarified, the patient was referred to the Department of Rheumatology for further treatment on May 29, 2023, where he was given rehabilitation physiotherapy and methylprednisolone 40mg ivgtt qd anti-inflammatory, supplemented with gastric protection, calcium supplementation, vitamin D supplementation, anti-allergy and other symptomatic supportive treatment.

The patient had a past history of breast hyperplasia, and on May 30, 2023, a perfect breast ultrasound showed a right-sided breast lesion, BI-RADS category 4C, and ultrasound-guided puncture biopsy was recommended. The patient then underwent ultrasound-guided coarse needle aspiration biopsy of the right breast mass under local anesthesia.Pathology results on June 1, 2023: (right breast) invasive carcinoma of the breast, combined with HE morphology and immunohistochemistry results, the lesion was consistent with (right) invasive ductal carcinoma of the breast. Immunohistochemistry: the cancer cells were about 90% strong (+) for ER, 95% strong (+) for PR, 90% strong (+) for AR, HER2 (2+), about 80% (+) for P53, about 50% (+) for Ki67, E-cadherin (+), and P120 membranes (+), and CK5/6 and P63 showed myoepithelial deletion around the invasive carcinoma .The fluorescence in situ hybridization of HER2 test suggested that the HER2 gene was not amplified. Bone scan did not show clear signs of bone metastasis on systemic bone imaging on June 5, 2023. The patient's symptoms gradually improved, and he was discharged from the hospital on June 6, 2023 with the following medications: prednisone acetate 25mg qd, hydroxychloroquine 0.1g tid. The patient's oral hydroxychloroquine was discontinued after the aggravation of skin itching, and oral cyclosporine treatment was added.

On June 14, 2023, the patient was admitted to the Department of Breast and Nail Surgery for breast cancer and underwent modified radical surgery for right breast cance rand blue dye tracer biopsy of right axillary anterior sentinel lymph node under general anesthesia on June 15, 2023; postoperative pathology was performed on June 21, 2023, in which a right breast mass was found to have a large, deeply stained nucleus with tumor cells arranged in the form of nests or beams, and the nuclei were easily visible, and acne was seen. The image was easy to see, and acne-like necrosis was seen, which was consistent with invasive carcinoma of the breast, non-specific type (invasive ductal carcinoma), and 14 anterior sentinel lymph nodes in the right axilla, of which 2 metastatic carcinomas were seen (2/14). Discharge diagnosis: right breast invasive carcinoma pT1cN1M0 stage ,IIA grade, III luminal B1 type, axillary lymph node metastasis, systemic lupus erythematosus. The patient was admitted to the Department of Nail and Breast Surgery for inpatient infusional port implantation on June 23, 2023.Between July 2 and August 13, 2023, the patient underwent 3 adjuvant chemotherapy treatments with the TC (docetaxel 100mg and cyclophosphamide 0.8g) regimen. The patient was treated with goserelin and letrozole endocrine therapy after chemotherapy. On August 23, 2023, the patient was admitted to the Department of Rheumatology and Immunology with a right foot wound ulcer for 2 weeks and was discharged with ceftriaxone 2.0g ivgtt QD for 7 days to fight infection. Between September 6 and October 18, 2023, the patient continued TC program of adjuvant chemotherapy every 21 days, chemotherapy process had IV degree of myelosuppression, be given to enhance the leukocyte treatment and improved.

On August 31, 2024, there was no sign of recurrence of breast and axillary lymph node ultrasound at the outpatient clinic of the Department of Nail and Breast Surgery, and the arthralgia could be controlled.

3 DISCUSSION

SLE is a chronic autoimmune disease with multisystem involvement, characterized by the immune system attacking its own tissues, leading to inflammation and tissue damage [2]. The clinical manifestations are diverse and include joint pain, skin rash, kidney lesions, and hematologic abnormalities. Breast cancer is one of the most common malignant tumors in women worldwide, and its occurrence has been linked to a variety of factors such as genetics, environment, and lifestyle [3]. Whether patients with SLE have an increased risk of developing breast cancer is still controversial. Canadian scholar Mruganka Kale found that SLE patients had an increased risk of hematologic, lung, thyroid, liver, cervical, and vulvovaginal cancers, and a decreased risk of breast and prostate cancers, which was hypothesized to be related to the presence of lupus autoantibodies and the down-regulation of certain proteins in systemic lupus erythematosus [4]. However, it has recently been suggested that this population-based cohort study shows that women with SLE are not at a lower risk of developing breast cancer than women without SLE. Women with SLE should follow routine breast cancer screening recommendations for this age group to avoid delayed diagnosis, as the presence of SLE may influence the choice of early breast cancer therapies [5]. A Mendelian randomization study from China suggested a causal association between SLE and breast cancer in an East Asian population, and the SLE prognostic scoring system

consisting of five SLE-related genes, RACGAP1, HMMR, TTK, TOP2A, and KIF15, could be used to categorize patients with breast cancer into high-risk and low-risk groups based on their survival rates, which is a good predictor [6]. The case reported here had a past history of breast hyperplasia, and the correlation between SLE and breast cancer needs to be confirmed by further studies.

The diagnosis of SLE combined with breast cancer requires a combination of the patient's clinical manifestations, laboratory tests and imaging. For SLE patients with suspected breast cancer ,mammography, ultrasonography and puncture biopsy should be performed as early as possible to clarify the diagnosis [7]. At the same time, attention needs to be paid to the impact of SLE disease activity on breast cancer diagnosis and prognosis. During the diagnostic process, other autoimmune disease-related complications that may cause breast lumps need to be excluded.

The goals of treatment for SLE are to control disease activity, reduce organ damage, and improve quality of life. The treatment plan should be based on the patient's clinical presentation, laboratory tests, imaging tests, and disease activity. Therapeutic drugs include glucocorticoids, immunosuppressants, and biologics. Among them, hydroxychloroquine plays an important cornerstone role in the treatment of SLE, and the domestic SLE guidelines recommend hydroxychloroquine as a long-term basic treatment for all SLE patients except those with contraindications [8]. It is worth noting that the use of hydroxychloroquine may cause adverse reactions, including rash, gastrointestinal symptoms, fundus retinal damage, neurological reactions, and other adverse effects, and the case reported in this paper had a more serious rash and was discontinued, so the regimen for SLE needs to be individualized. Glucocorticoids are the basic drugs for SLE treatment, with powerful anti-inflammatory and immunosuppressive effects. However, long-term use of glucocorticoids can bring about a variety of adverse effects, such as infection, osteoporosis, and hypertension. Chien-Chih Chen [9], a Taiwanese scholar, studied and compared the incidence of infections in 174 breast cancer patients with autoimmune diseases with that of 4,429 patients without autoimmune diseases, and multivariate analysis showed that autoimmune diseases were an independent factor in the incidence of infections. The patients in the case report developed skin infections and were hospitalized to fight the infection before proceeding to the next step of treatment. Therefore, the dose and duration of glucocorticoid use should be strictly controlled and gradually tapered to the lowest effective dose. The goals of breast cancer treatment are to eliminate the tumor, prevent recurrence, and improve survival and quality of life. The treatment plan should be formulated according to the patient's pathological type, stage, age, physical condition and personal wishes. Treatment methods include surgery, radiation therapy, chemotherapy, endocrine therapy and targeted therapy [10].

The treatment of SLE combined with breast cancer requires comprehensive consideration of SLE disease activity, breast cancer stage, and overall patient condition. For patients with early-stage breast cancer, surgical treatment is still the first choice, but attention should be paid to the effect of surgery on SLE disease activity. Endocrine therapy and targeted therapies have significant efficacy in some breast cancer patients, but drug-drug interactions and possible adverse effects should also be noted. However, attention should be paid to the effect of drugs on the immune system of SLE patients and possible complications. Some studies have shown that anastrozole, an endocrine therapy drug for breast cancer, and abciximab, an immunotherapy drug, cause subacute cutaneous lupus erythematosus [11, 12]. Radiotherapy and chemotherapy play an important role in breast cancer treatment. Cyclophosphamide is recommended as postoperative adjuvant chemotherapy for both HER-2 positive and negative breast cancer patients, and is usually combined with an anthracycline or paclitaxel drug at a recommended dose of 600 mg/m2, and is also the most commonly used first-line drug for the treatment of SLE nephritis, as reported by the European League Against Rheumatism (EULAR) and the Kidney Disease Prognostic Organization Worldwide (KDIGO) have both developed relevant treatment guidelines, but there are differences in the recommended dose for treatment, with the KDIGO and ACR guidelines recommending a high-dose intravenous cyclophosphamide regimen (750-1000 mg/m2 once a month for 6 months), whereas the EULAR guidelines recommend only a low-dose intravenous cyclophosphamide regimen (500 mg every 2 weeks for 6 consecutive doses for 3 months, not to exceed 3g) as the preferred regimen. Hydroxychloroquine (HCQ), a well-known antimalarial drug, has been successfully used in the treatment of autoimmune diseases, and recent evidence suggests that HCQ has a positive role in oncology research because it can inhibit autophagy by deacidifying lysosomes, and that the combination of HCQ with 2-deoxyglucose (2-DG) further inhibits the viability and migration of breast tumor cells and induces the induction of breast tumor cells, as compared to other drugs alone [13-16]. cell viability and migration and induce apoptosis. Radiotherapy is controversial in the treatment of SLE-combined breast cancer, and some experts would consider the lethal post-radiotherapy reactions in SLE patients due to autoimmune disorders and hard-to-heal wounds [17], but there are also individualized radiotherapy regimens that have benefited patients, proving that radiotherapy is not an absolute contraindication to the treatment of SLE-combined breast cancer [18].

4 CONCLUSION

Looking forward, research on SLE combined with breast cancer needs to further focus on the following aspects: first, in-depth exploration of the potential links and mechanisms between SLE and breast cancer; second, optimization of treatment protocols for patients with SLE combined with breast cancer, to improve therapeutic efficacy and reduce complications; third, strengthening of interdisciplinary cooperation, to improve early diagnosis and therapeutic efficacy of patients with SLE combined with breast cancer; Fourth, we should pay attention to patients' psychological health and social support to improve their quality of life. With the continuous progress of medical technology and the in-depth

development of interdisciplinary cooperation, it is believed that the therapeutic effect of patients with SLE combined with breast cancer will be significantly improved.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

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