

## Successful Treatment of Systemic Sarcoidosis with Tranilast

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### 2. Keywords

Systemic sarcoidosis; Tranilast;  
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### 1. Abstract

Although the effectiveness of tranilast in cutaneous sarcoidosis has been reported, its recorded adoption in systemic sarcoidosis is finite. We report a case of huge subcutaneous sarcoidosis with multiple organ involvement and systemic symptoms relieved quickly after the treatment of tranilast, suggesting that tranilast is expected to become the first-line therapy of sarcoidosis as for its less side effect.

### 3. Introduction

Sarcoidosis is a systemic disease of undetermined etiology, characterized by the presence of non-caseating epithelial granuloma involving multiple organs of the body, most frequently seen in lungs, lymph nodes, skin and eyes. Oral corticosteroid is a first-line treatment, but its long-term use may bring many side effects, especially in those with underlying diseases such as diabetes. There has been reports showing potential effects of tranilast in cutaneous sarcoidosis [1,2]. We present a case of a 64-year-old Chinese female with systemic sarcoidosis accompanied by systemic symptoms including chest pain, dry cough and dyspnea relieved significantly after the treatment of tranilast. So far, this is the first time to report a case of systemic sarcoidosis treated with tranilast,

and we hope the presentation will stimulate new investigations into this troublesome clinical problem.

### 4. Case Presentation

A 64-year-old Chinese female was referred to our dermatology clinic with subcutaneous nodules of 1 months' duration, large and firm on her both forearms, covered by normal-appearing skin, accompanied with systemic symptoms of chest pain, dry cough and dyspnea, which aggravated gradually for 1 months. She was not taking any oral medications before and the lesions of bilateral forearm did not experience trauma or injection. The findings of pulmonary CT scanning and ultrasound at different time point is compared in (Table 1).

**Table 1:** Examination results at different time points of therapy.

	At the beginning of therapy	Tranilast (0.3 g/day), 3 months later	Tranilast (0.3 g/day), 2 years later
Clinical Manifestation	large and firmly subcutaneous nodules on her both forearms	The skin turned soft and the nodules could not be touched.	normal
Skin Ultrasound	Ultrasonography indicated that the echo of the subcutaneous fat layer of bilateral forearms was not uniform ranging about 20'5'0.9cm in the left forearm and 20'5.9'0.7cm in the right.	The echo of the subcutaneous fat layer of bilateral forearms ranges about 20'3.5'0.6cm in the left and 20'2.6'0.5cm in the right.	normal
Abdominal Ultrasound	The abdominal ultrasonography revealed splenomegaly with a size of 14.8'4.4cm, smooth capsule and evenly distributed internal echo.	No obvious change.	The size of spleen was only 11.4'4.8cm, evidently smaller than before.
Pulmonary CT	Pulmonary CT scanning revealed multiple enlarged lymph nodes in the mediastinum and the largest of which under the tracheal protuberance was about 2.6cm in size.	No obvious change.	Pulmonary CT scanning revealed multiple enlarged lymph nodes in the mediastinum and the largest of which under the tracheal protuberance was about 1.0 cm in size.

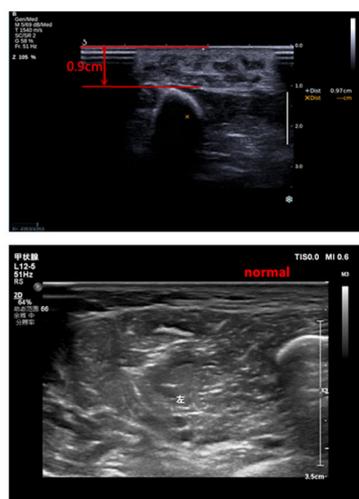
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Biopsy examination of a subcutaneous nodule of forearm revealed non-necrotizing epithelioid cell granulomas in the dermis, epithelioid cells, giant cells and cellulose were observed. Special stains for acid-fast bacilli and fungi were negative. The histopathology of intrathoracic lymph nodes revealed epithelioid cell granulomas. Ophthalmological examination indicated the age-related macular degeneration which is not associated with sarcoidosis. Laboratory tests including peripheral blood routine, hepatorenal function, angiotensin-converting enzyme (ACE), and anti-nuclear antibody (ANA), serum calcium were all normal. Tuberculin test was negative. The result of electrocardiogram was normal. His superficial lymph nodes were not enlarged (**Figure 1**).



**Figure 1:** Pulmonary CT revealed that the largest lymph node turned significantly smaller than before.

Based upon the clinical and histopathologic findings described above, the patient was diagnosed with subcutaneous sarcoidosis with systemic involvement. Oral administration of tranilast 300 mg per day was begun. The skin became soft and nodules could not be touched (still could be detected by ultrasound). Moreover, the symptoms of chest pain, dry cough and dyspnea disappeared entirely after 3 months of therapy (**Figure 2**).



**Figure 2:** Skin ultrasound indicated that after nearly 2 years of treatment, subcutaneous nodules returned to normal.

Two year later, ultrasonic manifestations of bilateral forearms returned to normal. At the same time, chest CT and abdominal ultrasound were reexamined and the lesions both become smaller than before. During these courses of treatment, no side-effect has been recognized and the patient continues taking tranilast 300mg per day. So far, the patient has been followed up.

The patient was then treated with 40 mg methylprednisolone along with anticoagulants (warfarin, low molecular heparin) and an antiplatelet (aspirin), which led to a dramatic reduction in his peripheral blood eosinophilia (at the absolute count of  $0.63 \times 10^9/L$ ) and clearance of his skin rash in the first week of treatment. Thus far, follow-up has been consistent.

## 5. Discussion

Sarcoidosis is a systemic disease characterized by the presence of non-caseating epithelial granuloma involving multiple organs of the body. There have been some reports showing the effectiveness of tranilast in treating cutaneous lesions in some cases of granulomatous disorders such as granuloma annulare, and sarcoidosis [1,2]. It has been demonstrated that tranilast decreases adhesion molecules such as ICAM-1 and LFA-1 expression on monocytes, inhibits the release of chemical mediators and affects the monocyte macrophage-lineage cells, resulting in resolution of the granulomatous lesions [3]. The major mode of the drug's efficacy appears to be the suppression of the expression and/or action of the TGF- $\beta$  pathway, inhibiting collagen synthesis in fibroblasts [4].

In this case, after the treatment of tranilast for 3 months, subcutaneous nodules could not be touched and symptoms of chest pain, dry cough and dyspnea disappeared completely, which suggests that tranilast is effective in treating systemic sarcoidosis and may improve clinical symptoms after three months. After nearly two years, the ultrasonic findings of subcutaneous nodules disappeared completely. But the manifestations of pulmonary lymph nodes and spleen, have not returned to normal. Treated with tranilast, subcutaneous nodules vanished ahead of internal organs, so it can be inferred that enlarged lymph nodes and spleen were as firm as subcutaneous nodules at the beginning but turned soft along with therapy, resulting in clinical remission. However, it takes a long time to observe all internal organs to return to normal and the time is up to the range of involvement. Our patient still needs further follow-up observation. Whether it will relapse after stopping the medicine is still a question. There has been no report of sarcoidosis involving several organs with systemic symptoms of fatigue and respiratory symptom treated successfully with tranilast. Although we report only a single case, tranilast may be a reasonable treatment option for not only cutaneous sar-

coidosis but can relief other sarcoidosis symptoms.

## 6. Compliance with Ethical Standards

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## 7. Conflict of Interest

We declare that there is no conflict of interest.

## 8. Ethical approval

This article does not contain any studies with animals performed by any of the authors.

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