Syphilitic Alopecia in HIV Infected Homosexual Men: Case Reports

INTRODUCTION

Hair loss is an uncommon manifestation of secondary syphilis. Its clinical manifestations include diffuse effluvium or patchy ‘moth-eaten’ pattern of alopecia. Although syphilitic alopecia is non-scarring hair loss often associated with other mucocutaneous lesions of secondary syphilis, it might well be the only presenting symptom of syphilis.

Secondary syphilis was diagnosed in ten homosexual men who attended the City Institute for Skin and Venereal Diseases in Belgrade from January to October 2010, among them three patients were HIV positive. Syphilitic alopecia was detected in two of these three patients, both HIV positive receiving antiretroviral therapy and with the ‘moth-eaten’ pattern of hair loss, presented herein.

CASE REPORTS

**Case 1.** A 33-year-old homosexual man was referred to the City Institute for Skin and Venereal Diseases, complaining of reddish patches involving the penile shaft and scrotum, which had appeared two weeks before. Examination revealed a few red papulosquamous lesions with flat surfaces on the penis and scrotum and non-tender bilateral regional lymphadenopathy with no other skin lesions. Further examination also revealed a mucous patch on the tongue and patches of ‘moth-eaten’ alopecia in the parieto-occipital scalp regions (Fig. 1). These areas of alopecia were free from other cutaneous lesions and the hair pull test was negative.

The patient had several sexual experiences with different partners during the previous six months, and he practiced unprotected receptive anal intercourse. However, he denied any previous anogenital or other skin lesions.

Serologic test results included positive nontreponemal reaction; the Venereal Disease Research Laboratory (VDRL) test titer was 1:64, with specific *Treponema pallidum* Hemagglutination Assay (TPHA) test being positive as well.

Five months before, HIV infection was detected and the patient was receiving treatment with abacavir, lamivudine and efavirenz. At that time, his CD-4 lymphocyte count was 185 per mm$^3$.

The patient was treated with 3 consecutive doses of penicillin G benzathine, 2.4 million units intramuscularly at 1-week intervals (total 7.2 million units). He experienced dramatic hair regrowth within 3 months of treatment, VDRL titer declined (1:8) and CD-4 T lymphocyte count was 362 cells/mm$^3$.

**Case 2.** A 30-year-old homosexual man presented to our Institute complaining of genital ulcers. Examination revealed erosions on the prepuce, non-tender bilateral regional lymphadenopathy and the ‘moth-eaten’ pattern of alopecia. Genital lesions appeared one month before, and had already been treated by a dermatologist with topical antibiotic cream, but the lesions remained unchanged.

This patient also had several sexual partners during the previous six months, and he practiced unprotected insertive oral intercourse.

Nontreponemal VDRL test titer was 1:256, with positive TPHA test. The patient was detected as being HIV positive one year before and was receiving lamivudine, zidovudine and efavirenz. His CD-4 lymphocyte count was 295 per mm$^3$. The patient was treated with penicillin G benzathine (total 7.2 million units). All syphilitic lesions resolved within 3 months after
treatment, VDRL test titer declined to 1:64 and CD-4 level was 863 cells/mm³.

The patient refused to be photographed.

**DISCUSSION**

Alopecia syphilitica is not a common feature of secondary syphilis. The prevalence of syphilitic alopecia ranges from 2.9% (1) to 3.9% (2), with the highest reported rate of 11% (3). In these studies, the HIV status of syphilitic patients was not specified, since they originate from the initial era of the HIV pandemic. The course of syphilis in an HIV-infected patient may differ from the natural history of the disease (4).

In the case series of secondary syphilis among homosexual men in our Institute from January to October 2010, seven (70%) patients presented with rash on the trunk, one with syphilitic hepatitis (5) and two with alopecia (20%), both HIV infected. Similarly, in one Brazilian study, 15 of 24 HIV infected patients with syphilis had secondary syphilis and 3 (20%) patients presented with patchy alopecia (6).

Moreover, the HIV infection rate is high in patients with syphilis. Studies conducted in the United States revealed that the median HIV seroprevalence in men and women infected with syphilis was 15.7%, and seroprevalence among men who have sex with men and injecting drug users ranged from 64.3% to 90% and 22.5% to 70.6%, respectively (7). These facts along with the current data raise the question whether the prevalence of alopecia syphilitica differ between HIV negative and HIV positive patients, nevertheless, it could not be deducted herein because of small number of patients.

The pathogenesis of alopecia syphilitica has not been completely elucidated. In the study by Nam-Cha et al., *Treponema pallidum* was detected in the hair follicle in syphilitic alopecia, suggesting that alopecia may be caused directly by spirochetes (8).

There are two types of secondary syphilitic alopecia: uncommon ‘symptomatic’ type where hair loss is associated with an actual secondary lesion on the scalp, and ‘essential’ alopecia without visible syphilitic scalp lesions (9). Essential syphilitic alopecia could be present in a diffuse pattern with generalized thinning of the hair, as localized pattern called ‘moth-eaten’ alopecia, or as a combination of both. Of these, the ‘moth-eaten’ pattern is most frequent (10). Even though syphilitic alopecia predominantly affects scalp, hair loss can involve any body area including eyebrows, chest and legs (11).

Clinically, the ‘moth-eaten’ pattern of alopecia may mimic trichotillomania and traction alopecia. The chief clinical and histologic differential diagnosis includes alopecia areata because both alopecias are inflammatory and non-scarring types and are mediated by a peribulbar lymphocytic infiltrate (12). On the other hand, clinical conditions that mimic diffuse syphilitic alopecia include telogen effluvium and androgenic alopecia (13).

The treatment of choice for secondary syphilis is a single dose of penicillin G benzathine, 2.4 million units intramuscularly, however, our HIV positive patients were treated with 3 consecutive doses at 1-week intervals (total 7.2 million units). Alopecia usually resolves within three months of treatment (11), as described in our patients.

Syphilitic alopecia should not be overlooked in patients with localized non-scarring hair loss. Complete examination of the skin and mucous membranes to detect the lesions of secondary syphilis as well as serologic tests for syphilis are mandatory to confirm the diagnosis in patients with localized non-scarring hair loss.

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**References**


Milan Bjekić1, Milica Marković1, Dubravka Salemović2, Sandra Šipetić3

1City Institute for Skin and Venereal Diseases; 2Institute for Infectious and Tropical Diseases, Clinical Centre of Serbia; 3Institute of Epidemiology, School of Medicine, Belgrade University, Belgrade, Serbia

Corresponding author:
Marković Milica, MD
City Institute for Skin and Venereal Diseases
Džordža Vašingtona 17
11000 Belgrade
Serbia
mipopovi@eunet.rs

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Unusual Presentation of Dermatofibrosarcoma Protuberans in Deep Skin over the Breast – Imaging Findings

INTRODUCTION
Dermatofibrosarcoma protuberans (DFSP) is a rare locally aggressive tumor of the dermis and subcutaneous tissue that commonly appears on upper extremities and on the trunk. There is a slight male predominance and the lesion is commonly seen between the second and fifth decades of life. The tumor grows slowly over years and rarely metastasizes; however, local recurrence is frequent. The most common sites for metastasis are lymph nodes and the lungs. The treatment of the tumor is resection with wide margins (1,2).
Here we present radiologic findings of DFSP with unusual presentation located in the deep skin over the breast, which was excised successfully and without local recurrence during a 36-month follow-up period.

**CASE REPORT**

A 36-year-old female with a palpable right breast mass located in the upper inner quadrant and change in skin color without a significant history was admitted to surgery department. She claimed that the mass had first appeared two years before and was slowly growing. She had no history of recent trauma or surgical operation. On inspection, a well circumscribed, plaque type lesion was observed, along with a violet-purple change in color of the skin over the right breast (Fig. 1). The patient reported neither systemic disease or known illness nor continuous drug usage. Physical examination was unremarkable except for a well-defined non-tender mass on the right breast. The left breast and bilateral axillaries were normal. The patient was referred for radiologic examination to exclude a primary breast tumor. Bilateral breast ultrasound (US) and color Doppler ultrasound (CDUS) was performed with a Toshiba, Powervision 6000 SSA-370A (Tokyo, Japan) with 6-11 MHz high frequency linear transducer. US demonstrated a 3.5x1.5 cm sized solid, hyperechoic lesion with sharp margins in the subcutaneous fat tissue, without marked vascularity on CDUS (Fig. 2). The left breast and both axillaries were unremarkable. The right mammography (HFXPlus-Fischer Imaging, Denver, USA) on mediolateral oblique (MLO) projection showed a well-defined bilobulated density with irregular margins and no calcifications (Fig. 3). Based on the mammography and sonography findings, the mass was considered suspect of malignancy and breast magnetic resonance imaging (MRI) study was planned for further examination. A contrast-enhanced breast MRI was performed using a 1.5 tesla MR unit (Somatom Vision Plus, Siemens, Erlangen, Germany) at our institution. Unfortunately, the mass could not be demonstrated on either T1, T2 or postcontrast subtracted images (Fig. 4).

The patient was referred to surgery department and wide excision of the mass was performed. On pathologic evaluation, spindle cells were seen to be arranged in a storiform pattern, with minimal pleomorphism (Fig. 5). Immunohistochemical stain with CD34 was positive (Fig. 6) and definitive histologic diagnosis was DFSP.

On follow-up, 36 months after surgical treatment, the patient continued to be symptom free, with no signs of tumor recurrence.

**DISCUSSION**

Dermatofibrosarcoma protuberans is a rare fibrous tumor of the soft tissue, commonly arising from dermis and subcutaneous tissue, which was first described by Darier and Ferran in 1924 (3). It ac-
counts for 0.1% of all malignant tumors and 1% of all soft tissue sarcomas. The tumor is mostly located on the trunk skin (50%-60%) and is more common in men than women. The majority of these tumors are less than 5 cm in diameter. It can be seen at any age but it is much more common between ages 20 and 50, however, there are few cases reported in early childhood. DFSP has an indolent growth pattern and its symptoms are mostly long lasting, spanning over months and years (1,2,4).

DFSP poses a diagnostic challenge as the clinical symptoms and the radiologic signs are nonspecific. The tumor usually causes a red-purple change of color on the overlying skin on inspection, and if it presents with a red and irregular bordered lesion, it can mimic a hemangioma. When DFSP is located in the breast, it can be mistaken for primary breast tumor and the accurate diagnosis is difficult to reach. Usually after clinical evaluation, US is the first choice for imaging and CDUS is very helpful for vascular situation but neither of the modalities is specific for diagnosis. Shin et al. report that a diagnosis of DFSP should be

Fig. 3. Mammogram on mediolateral oblique projection showing a well-defined mass with irregular margins, bilobulated density without any calcifications.

Fig. 4. The tumor could not be demonstrated on postcontrast subtracted axial image. The examination was normal.

Fig. 5. Photomicrograph demonstrating the presence of hypercellular spindle cells, located within the dermis with minimal pleomorphism, in a storiform pattern. Note that the epidermis is spared. (HE, X100)
considered if US reveals an oval mass in the subcutaneous tissue that is abutting against the skin and has a focal lobulated margin with hypoechogenicity or an irregular margin with mixed echogenicity (5). Although an echogenic macrolobulated oval mass located over the breast lying in the deep dermis and the subcutaneous tissue without marked vascularization was demonstrated, an exact diagnosis could not be made in the present study. Unfortunately, mammography was also found to be nonspecific, with macrolobulated density on MLO projection. Considering mammography and sonography findings, a primary breast tumor could not be excluded and the present case was classified as BI-RADS category 4.

Computed tomography is not indicated unless bony invasion or pulmonary metastasis is suspected in some occasional cases. Although MRI is also nonspecific for the exact diagnosis of DFSP, it is useful for identifying the extent and location of the mass, especially in large recurrent tumors. In addition, the areas of hemorrhage within the tumor may be demonstrated by use of MRI and can suggest the diagnosis (6,7). Another current imaging modality, multivoxel proton [1H]) MR spectroscopy (MRS), is accepted as an adjunctive method to breast MRI on differential diagnosis of benign versus malignant tumors. A recent case study of DSFP located on the breast, reported by Ivanovic et al., did not show significant cholin peak on [1H] MRS (8). In the present case, the mass could not be demonstrated on either T1 or T2 weighted images, and there was no significant enhancement on post-contrast subtracted images on breast MRI examination. It is considered that the discrimination failed both on pre- and post-contrast images as the mass was probably carrying similar signal characteristics of the adjacent subcutaneous fat tissue in which the lesion developed.

Complete surgical resection is accepted as the optimal treatment for primary or recurrent DFSP. Studies have shown that resection with wide margins is essential and recurrence rates after local resection are reduced while the excision margins are widened. The combination of adjuvant radiotherapy before or after the surgery is a treatment option, particularly in those who cannot undergo wide surgical excision for several reasons. In addition, there are some successful clinical reports on imatinib, a tyrosine kinase inhibitor, which can induce regression in patients with unresectable or metastatic DFSP (1,2,4).

Proper follow-up seems critical since the most significant characteristic of the tumor is recurrence, and local recurrence generally occurs in the first 3 years after surgery. Sonographic evaluation and re-biopsy is advisable if suspicion occurs. In addition, mammography might be helpful in the diagnostic work-up in breast located tumors for periodic control of recurrence.

In conclusion, DFSP is a rare soft tissue tumor of cutaneous origin that mostly occurs on the trunk and might be rarely seen on the breast skin and can be confused with primary breast tumors. We believe that the importance of the present case is to upgrade the awareness of this soft tissue tumor while keeping in mind the differential diagnosis of other breast tumors.

References
Cardiac Arrhythmia as a Side Effect of Ketanserin Therapy in a Patient with Systemic Scleroderma

INTRODUCTION

Systemic scleroderma (SS) is a systemic disorder of the connective tissue, of obscure etiology and characterized by fibrosis of the skin, visceral organs and vascular walls. Clinically, it is a heterogeneous disorder characterized by high collagen deposition into the connective tissue, microcirculation abnormalities, and immune system impairment (1). It may be localized to the skin and show a mild clinical course, or may involve visceral organs, kidneys, lungs, heart and gastrointestinal organs, assuming a malignant course (1). The pathophysiology of SS is complex. Environmental, genetic, vascular and immune factors, fibroblasts and matrix substances seem to be implicated in the pathogenesis of the disease, thus SS is classified in autoimmune diseases, or generally in connective tissue disorders (2).

Immune fibroblast stimulation occurs due to some unknown reason, which is followed by an enhanced collagen production, vascular endothelial lesions and fibrosis (2). Raynaud’s phenomenon is pronounced in SS, found in 90%-98% of cases (1,2); however, pulmonary and renal vessels may frequently be involved, resulting in considerably more severe sequels. Some observations imply serotonin as the possible pathogenetic factor in the development of microvascular disease (2,3). Serotonin may lead to digital ischemia or constriction of digital arteries alone. In patients with Raynaud’s phenomenon, serotonin infusion leads to abnormally long vasoconstriction. Serotonin antagonists alleviate these symptoms and improve blood flow in digital arteries as well as clinical signs of SS. Nearly all circulating serotonin is found in specific platelet granules and is released on platelet aggregation. Platelet activation has been clearly demonstrated in SS. Besides kidneys and lungs, SS may also involve the heart. Cardiac involvement in SS may frequently be underestimated because the symptoms are attributed to pulmonary, musculoskeletal or esophageal lesions.

Cardiac manifestations in SS may vary, may be primary or secondary, due to pulmonary hypertension or renal crisis (4). Systemic scleroderma may involve


Emine Ozturk¹, Cüneyt Yücesoy¹, Begum Demirler¹, Demet Yilmazer², Baki Hekimoğlu¹

¹Department of Radiology, ²Department of Pathology, Ministry of Health, Ankara Diskapi Yildirim Beyazit Education and Research Hospital, Ankara, Turkey

Corresponding author:
Dr. Cüneyt Yücesoy
Mutluköy Sitesi 12. Sok. No.17 Ümitköy
06530 Ankara
Turkey
yucesun2000@yahoo.com

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the myocardium, coronary arteries, conduction system, or pericardium (4). Clinically, it may present with left heart failure, cardiac congestion, chest pain due to myocardial ischemia, syncope, and sudden death due to arrhythmia. Recent studies indicate that clinical signs of myocardial lesion are present in 20%-25% of SS patients (4,5).

In a study that included 54 patients, electrocardiogram abnormalities, pericardial effusion, elevated systolic pressure in the right ventricle, or left atrial dilation were recorded in 69% of patients (4). Besides structural changes, arrhythmias and conduction system abnormalities were verified by 24-h ambulatory monitoring (4).

Heart involvement is an adverse prognostic sign in SS (6,7). Medsger and Masi demonstrated the clinically present heart involvement in SS to be associated with 70% 5-year mortality (6). Myocardial fibrosis and pericardial disease are the most common and typical autopsy findings. Arrhythmias and conduction impairments are relatively frequent in SS patients and are considered consequential to cardiac conduction system fibrosis or ischemia.

The treatment of SS is focused on the prevention and alleviation of endothelial lesions, collagen overproduction, and suppression of immune reaction. Many agents have been tried in the treatment and prevention of vascular manifestations, however, mostly with disappointing results (1,2). Patients are advised to avoid cold and stress exposure, and to quit smoking. Calcium antagonists, e.g., nifedipine in a dose of 30-60 mg/day, are used with limited success and frequently have to be discontinued due to side effects. Angiotensin II receptor antagonists have proved more efficient than calcium antagonists in Raynaud's phenomenon, losartan 50 mg/day led to reduction of body weight and frequency of vasoconstrictions. Prostaglandins, e.g., iloprost and cisaprost, as potent vasodilators, were not superior to placebo in a controlled study (8). Prasosine proved only partially efficient, whereas ketanserin and cyclophenyl were inefficient.

Ketanserin is a serotonin receptor blocker. Serotonin can cause peripheral vasoconstriction, especially in SS, platelet aggregation and pulmonary hypertension (3). In some studies, the use of ketanserin led to inhibition of platelet aggregation and of vasoconstriction (3,9,10).

**CASE REPORT**

A female patient N. M., born in 1959, was diagnosed with SS according to the American College of Rheumatology criteria (1). Clinical picture was predominated by the symptoms and signs of Raynaud's syndrome, and therapy with nifedipine, a calcium antagonist, aspirin and ketanserin was prescribed. The patient was followed-up at regular intervals, with complete work-up every 6 months to verify the possible changes involving parenchymal organs.

Despite therapy, hand and foot lesions progressed, with the occurrence of ulcerations, necrosis and contractions. The patient had difficulties with food mastication and deglutition. In 2000, she was treated for pneumonia; in 2004, she was diagnosed with cryoglobulinemia and a corticosteroid was introduced in therapy. In 2007, ultrasonography of the heart revealed frequent extrasystoles (ES), which were not noticed by the patient; therefore, ambulatory ECG monitoring (Holter) was used to record an array of cardiac rhythm abnormalities (supraventricular or ventricular ectopic beats, sinus bradycardia, sinus tachycardia, sinus pauses, paroxysmal supraventricular tachycardia, and ventricular tachycardia, fortunately without hemodynamic and subjective discomforts).

The conduction system impairments due to the underlying disease were considered to be the cause of these abnormalities. As the patient reported no subjective discomforts and no hemodynamic sequels were recorded, we decided to postpone additional cardiologic examinations and therapy for some time. Instead, we reconsidered the medicamentous therapy she had taken by then and raised doubts about side effects of the drugs taken by the patient, first of all ketanserin. Indeed, all heart rhythm abnormalities disappeared upon discontinuation of ketanserin therapy. The follow up Holter finding was normal.

**CONCLUSION**

Systemic scleroderma may involve almost every parenchymal organ or system, including cardiovascular, myocardium, pericardium, and conduction system of the heart. Although the impact of SS on cardiac function has long been known, its prevalence and prognosis have only recently been more extensively investigated and better understood. In most patients, cardiac involvement is subclinical; however, the prognosis is very poor in those that develop overt symptoms and complications. Development of a number of novel noninvasive and invasive techniques in cardiology has certainly contributed to these new insights. Of the currently available screening methods, annual echocardiographic examination and assessment of the N-terminal segment of the pro-B natriuretic peptide (NT-pro-BNP) concentration is recommended to anticipate the development of cardiac symptoms (5).

The true cause of SS remains unknown, and thus the treatment remains quite inefficient. Therefore, the
aim of therapy is to prevent and reduce vascular lesions, fibrosis and/or immune response suppression. Numerous agents, including ketanserin, have been tried to prevent and reduce vascular lesions. Ketanserin proved efficient in some studies, but not in others. However, all these drugs are associated with potential side effects.

Therefore, in case of complications in SS patients, differential diagnosis is very broad; yet, prior to introducing extensive diagnostic work-up with both non-invasive and invasive examinations, therapy taken by the patient should be carefully explored, with special reference to its possible side effects. In our patient, drug side effects were the main culprit, fortunately without clinical sequels, and recognizing it we obviated the use of invasive procedures.

References


Božena Coha, Pejo Samardžić, Ivica Dundjer, Marijana Knežević-Praveček

Department of Medicine, Dr Josip Benčević General Hospital, Slavonski Brod, Croatia

Corresponding author:
Božena Coha, MD
Andrije Štampara 42
HR-35000 Slavonski Brod
Croatia
bozena.coha@sb.t-com.hr

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