GRANULOMA TRICHOPTHYTICUM MAJOCCHI: A CASE REPORT*

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INTRODUCTION

Granuloma trichophyticum, as a chronic granuloma due to fungal infection in dermis, was first described by MAJOCCHI\(^1\) in 1883. From 1883 to 1926, he and other Italian investigators made minute studies of a long series of cases\(^1\) of this condition, which, they believed, should be distinguished, both clinically and pathologically, from common tinea profunda occurring as acute suppurative mycoses, namely, kerion celsi, sycosis parasitaria, and folliculitis aguminata parasitaria. However, the pathogenesis and classification of granuloma trichophyticum have not yet been satisfactorily determined.

In Japan, all of the cases reported as granuloma trichophyticum have been complicated with tinea generalisata, and no case of the localized type has yet appeared in the Japanese literature.

In this report, a case of granuloma trichophyticum Majocchi will be represented and the pathogenesis also will be discussed.

REPORT OF CASE

J. A., a Japanese man, aged 34, was first seen at our Hospital on June 4, 1968.

There was no family history of tinea or similar skin lesions. The past history was negative but for gastric neurosis.

The patient had suffered tinea pedis since 1961 and tinea inguinalis et glutaealis since 1965. In spite of the local application of various fungicidal preparations, these lesions would not heal well.

In August 1967, he noticed firm asymptomatic nodule on the dorsal aspect of the right first toe. A diagnosis of callus was made by his physician. The

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nodule, however, gradually grew and became slightly tender on pressure. Further, within a few months, he noticed new small nodules on the dorsal aspects of the right fourth and fifth toes.

I. Description of the lesions

There was a large, round, firm, highly elevated, keloid-like tumor on the first phalanx of the right first toe (Fig. 1). The surface of the tumor was flat, brown, and approximately 1.5 cm in diameter; there were scales, crusts, and some dilated hair-lost follicular orifices on the surface, from which a serous purulent fluid could be pressed out. Branching mycelia were demonstrated in this fluid by direct microscopic examination (Fig. 3). The skin in the vicinity of the tumor was intact.

On the dorsa of the right fourth and fifth toes, there were some groups of small nodules which were similar to the lesions on the first toe (Fig. 2). However, these small nodules were surrounded with scaly lesions and the 2nd, 3rd and 4th interdigital webs were scaly. From these scales, mycelia could be demonstrated under direct microscopic examination and culture. The nail of the fifth toe was thickened and turbid, but no fungus-elements could be demonstrated in wet preparation and in culture.

Samples taken from the scaly lesions of the inguinal folds and the glutaeal region, revealed numerous branching mycelia in wet preparation (Fig. 4).

One of the crural lymph nodes was swollen up to

FIGURE 1 Granuloma trichophyticum Majocchi on the right foot of a 34-year-old Japanese man. Large highly elevated tumor on the first toe, and small grouped nodules on the fourth and fifth toes. The skin in the vicinity of the large tumor is intact, although the skin surrounding the small nodules is scaly.

FIGURE 2 High magnification of Fig. 1. Nodules on the fourth and fifth toes. A dilated hair-lost follicular orifice is seen on the surface of each nodule.

FIGURE 3 Mycelia in fluid obtained from the dilated follicular orifice on the tumor. (Wet preparation ×400)
II. Histopathologic findings

Specimens were biopsied from the center of the tumor on the first toe and one of the nodules on the fifth toe. The right crural lymph node also was biopsied. These specimens were serially sectioned and stained with hematoxylin-eosin stain, WEIGERT-van GIESON stain, PAS stain, and PAP's silver impregnation method for histopathologic studies.

1. The tumor on the first toe (Figs. 5 to 13):

The epidermis was hyperkeratotic, parakeratotic, acanthotic, and showed pseudocarcinomatous hyperplasia (Figs. 5, 6). In the upper dermis, there were a few small microabscesses containing leucocytes, and some inflammatory infiltrations of leucocytes, lymphocytes, plasma cells, and histiocytes (Figs. 5, 6). In the middle and deeper dermis, granulomatous reactions, resembling sarcoïd or tuberculoid formations, were found consisting of epitheloid cells, giant cells, plasma cells, and leucocytes (Figs. 7, 8). At the peripheral parts of the specimens there were a few destroyed hair follicles, but in the infiltrative and granulomatous areas there were no hair follicles, sebaceous glands, hair arrector musculi, or eccrine sweat glands to be found (Figs. 5, 6, 7, 9, 10). Collagen and elastic fibers were few or absent in these areas, but the reticulum fibers had abundantly increased to form a network around the granulomas,
FIGURE 7  Granulomatous reaction in the middle and deeper dermis. Numerous giant cells are present. (Hematoxylin-eosin stain $\times 20$)

FIGURE 8  Granulomatous reaction resembling tuberculoid formation. Proliferation of the reticulum fibers is predominant. (Pap’s silver impregnation method $\times 20$)

FIGURE 9  The hair follicle at the periphery of a section. Granulomatous reaction is seen near the hair follicle (PAS stain $\times 40$)
which contained numerous fungus-elements (Figs. 8, 11). These fungus-elements could be easily demonstrated with PAS stain and Pap's silver stain.

Numerous mycelia and spores were found in the granulomas, foreign body giant cells, microabscesses, and in the deeper hair canals of the remaining hair follicles (Figs. 10, 11, 12, 13).

2. The nodule on the fifth toe (Figs. 14, 15):

As compared with the above-mentioned tumor, this nodule revealed nearly the same histological pictures, but the cell infiltration was more non-specific, and the granulomatous reactions were scanty and tended to lie in form of scattered islands (Fig. 14). Fungus-elements were seen even within the giant cells (Fig. 15).

3. The lymph node (Fig. 16):

The capsule of the lymph node was well preserved. The lymph follicles had increased in size but were partially destroyed. Numerous inflammatory cell infiltrations composed of lymphocytes, neutrophils, eosinophils, and plasma cells were seen, but no fungus-element was found in the sections of the lymph node.

III. Mycologic findings

Pressed-out fluid and tumor fragments from the first toe, scales from the glutaeal region and the fifth toe, and the turbid nail of the fifth toe were used for culture on Sabouraud's glucose agar.

1. The fluid and fragments obtained from the
tumor on the first toe:

The colonies were round, slightly elevated, short-cottony and white in color, but these reverses showed no pigment production after three weeks (Figs. 17, 18). Pigment production became prominent when cultures from the first colony had been done three times on SABOURAUD's media. Slide culture preparations stained with lactophenol cotton blue revealed that the fungi were undifferentiated from trichophyton shoenleini, because “favic chandeliers” were present, pectinate hyphae were suspected, microconidia were few, and macroconidia were absent in the preparations (Fig. 19). However, these strains were later found to be trichophyton rubrum.

2. The scales on the toe and the glutaeal region:

The colonies were gypsic, cerebriform or radial, and white. The reverse sides did not produce pigment after three weeks (Figs. 20, 21). However, the pigment production did become rather good after five months. Slide culture preparations showed numerous grape cluster-, pear- and club-shaped microconidia as well as sausage-shaped macroconidia, but no spiral or nodular bodies and no racquetts hyphae could be observed (Fig. 22).

From the above findings, these strains were identified as trichophyton rubrum.

**FIGURE 15** High magnification of Fig. 14. Short branching mycelium is seen within a giant cell. (PAS stain ×400)

**FIGURE 16** Lymph node. Enlargement and destruction of lymph follicles. Inflammatory infiltrations are seen, but no fungus-elements could be found in sections stained with PAS reaction. (Hematoxylin-eosin stain ×40)

**FIGURE 14** Nodule on the fifth toe. Some scattered granulomas showing no typical tuberculoid reaction. (PAS stain ×40)
FIGURE 17 The colony cultured from serous puruleut fluid obtained from the tumor on the first toe. The surface is short-cottony and white in color. (Sabouraud’s glucose agar; after three weeks)

FIGURE 18 The reverse of Fig. 17. No pigment production.

FIGURE 19 Slide culture preparation, produced from the colony shown in Fig. 17. “Pseudochandelier” formation. (Lactophenol cotton blue stain ×400)

FIGURE 20 The colonies cultured from scales on the fifth toe. The surface is gypsic, cerebriform or radial and white in color. (Sabouraud’s glucose agar; after three weeks)

FIGURE 18 The reverse of Fig. 17. No pigment production.
FIGURE 21  The reverse of Fig. 20. No pigment production.

3. The turbid nail:

From the materials obtained from the turbid nail, no fungi could be cultured on SABOURAUD's media.

IV. Laboratory findings

Intradermal tests with trichophytin and sporotrichin were negative. The intradermal test with tuberculin was positive and all the serologic tests for syphilis were negative.

Blood sedimentation rate 2 mm. in 1 hr., 6 mm. in 2 hrs.; Red cell count 4,730,000/cc. mm.; White cell count 5,600/cc.mm. The white cell analysis was as follows:

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The hemoglobin percentage was 94%, and the mean hematocrit was 43.5%. Color index 0.99; Volume index 1.01.

The urinary analysis showed no abnormal findings.

The fasting blood glucose showed normal range (85 mg/100 cc).

Liver function tests were as follows: S-GOT 21 u., S-GPT 14 u., Icterus index 5, CCF 3+, TTT 2 u., ZST 7 u., Serum cobalt reaction R3.

The serum protein analysis was as follows:

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<td>7.3g/dl</td>
<td>4.93</td>
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X-ray examinations of the chest and the gastrointestinal canal showed no abnormal findings.

V. Treatment

The patient orally received 750 mg of griseofulvin (6 tab. of fulvistatin F. P. daily). All of the granulomatous lesions gradually became small and soft, and three months later, the small nodules had completely disappeared while the large tumor had decreased to one third in size. The tinea pedis and the tinea inguinalis et glutaealis had become completely healed.

DISCUSSION

According to MAJOCCHI12) and many other authors9,14,23), granuloma trichophyticum usually occurs on the scalp and beard, but the
hands, scrotum, buttocks, and glabrous skin also have been involved. This condition is characterized by chronic intra- or subcutaneous nodules which arise in the area of superficial trichophytosis. It has been usually found in childhood, while many cases have occurred at all ages. The nodules are discrete or grouped, and show no acute suppurative inflammatory reaction. Therefore, they are not painful and never result in pustulation or abscess formation. The nodules frequently excrete viscid and turbid fluid in which fungus-elements usually lie free.

Our case clinically showed the same features as that of the granuloma trichophyticum reported by MAJOCCHI. Although, the tumor on the first toe was a single, very large lesion and the surrounding skin was intact, the vicinity of the tumor suggested a prior superficial trichophytosis. Perhaps the granuloma trichophyticum occurring as a single tumor may be a rare manifestation.

MAJOCCHI\(^1\) pointed out that granuloma trichophyticum could be divided into two types, namely, fibroid and degenerative. The former is firm and keloid-like and the latter is soft and pseudofluctuate. The difference between two types depends upon whether or not necrobiotic changes occur in the nodules during the course. Our case resembled the fibroid type clinically.

It is not yet clearly determined whether the regional lymph node is involved or not. In the first case of BRAUN-FALCO et al.\(^3\), the lymph node in the neck swelled and was painful on pressure. Our case showed an asymptomatic swelling of the crural lymph node, but the histologic findings revealed non-specific inflammatory cell infiltrations and no fungus-elements.

In general, generalized disseminated granuloma trichophyticum seems to be complicated with tinea generalisata and usually numerous swollen superficial lymph nodes are palpable. NAKAHIRA\(^17\) (1954) emphasized that "generalized disseminated granuloma trichophyticum" should be considered a clinical entity which is composed of numerous trichophytic granulomatous lesions, generalized trichophytosis, and swellings of superficial lymph nodes.

In 1954, WILSON et al.\(^24\) first described "nodular granulomatous perifolliculitis of the legs caused by trichophyton rubrum". WILSON et al. described a series of 14 cases of this mycosis in which all nodules composed of a chronic granulomatous infiltrate surrounding infected hair follicles occurred within the confines of plaques of scaly erythematous trichophytosis usually distributed unilaterally on the lower portions of the legs of dark-haired adult women in California. Clinically and histopathologically, the process closely resembled MAJOCCHI's granuloma trichophyticum in many respects, but the location and distribution of the disease and the causative organisms were different.

GÖTZ\(^9\) (1962) described Wilson's nodular granulomatous perifolliculitis in JADAS-SOHN's Handbuch (Erganzungswerk) and used the term "tinea granulomatosa nodularis cruris". He suggested that the term tinea granulomatosa nodularis should be used for the chronic granulomatous type of tinea, because he believed that granuloma trichophyticum and nodular granulomatous perifolliculitis must share the same pathogenetic process. BRAUN-FALCO et al.\(^9\) (1962) insisted that the term granuloma trichophyticum should be used for chronic infiltrative trichophytosis since it is based on granulomatous reaction.

In our opinion, generalized disseminated trichophytic granuloma and Wilson's nodular granulomatous perifolliculitis should both be categorized as granuloma trichophyticum Majocchi.

As to the causative organisms of granuloma trichophyticum, various dermatophytes were isolated from materials of the skin lesions; those which were most frequently isolated were Trichophyton violaceum, T. mentagrophytes, T. rubrum, and T. tonsurans.

According to WILSON et al.\(^24\), trichophyton ruhrum was isolated from the fluid or the
fragments of the deeper portion of the nodules in all his 14 cases.

In our case, the dermatophyte cultured on SABOURAUD'S media from the fluid and the tumor fragments from the first toe was at first misconceived as trichophyton schoenleini, but was later discovered to be trichophyton rubrum. Trichophyton rubrum was also isolated in the scales of superficial tinea. It was interesting to find that the features of the colonies and slide culture preparations of the above-mentioned two types of trichophyton rubrum should be so different in character. Our interpretation was that this difference might be due to the various patho-physiologic conditions of the involved locations, which interpretation brings up the important problem of the host-parasite relationship.

In regard to the intracutaneous test with trichophytin, the reaction in granuloma trichophyticum cases is usually negative, or at least less positive, than in commn tinea profunda cases. Our own case was negative. However, the first case of BRAUN-FALCO et al.3) was strongly positive. Among the 14 cases of WILSON et al.24), the reaction was variable, i.e., 8 cases were negative and 4 cases were positive.

Because granuloma trichophyticum shows varying grades of reaction to the trichophytin test, it is suggested that in this condition there should be no strong allergic condition caused by trichophyton.

Except for MORIKAWA's case10), all the cases of generalized disseminated granuloma trichophyticum reported in the Japanese literature were negative in the trichophytin test. The reason for this reaction may be that these cases were unable to produce a strongly allergic condition, because of the existence of systemic diseases complicated by such conditions as anemia (TAKAHASHI23), FUKUSHIRO5), INABA11), hypoalbuminuria (INABA11), NOHARA20), liver function disturbances (FUKUSHIRO et al.9), HIDANO10), NOHARA et al.20), and malignant lymphoma (NOGUCHI et al.19).

As to the histopathologic findings, granuloma trichophyticum Majocchi demonstrated the same pictures as those of Wilson's nodular granulomatous perifolliculitis and generalized disseminated trichophytic granuloma (WILSON et al.24), BRAUN-FALCO et al.3), MONTGOMERY15). The histopathologic findings have been studied and explained in detail by MAJOCCHI12), SABOURAUD21), MIESCHER14), GANS7), GÖTZ9), BRAUN-FALCO et al.3), and others.

The characteristic findings are as follows:

1. The granuloma formation in dermis is polymorphous. However, massive disseminated or confluent granulomas, in which a central necrobiosis is demonstrated, have been frequently found. The tuberculoid formation was emphasized by SABOURAUD21).

2. The granulomas are composed of epitheloid cells, giant cells, histiocytes, lymphocytes, neutrophils, and eosinophils.

3. Destruction of hair follicles and sebaceous glands are seen in the granulomatous areas, but eccrine sweat glands and hair arrector musculi are strongly resistant.

4. Numerous fungus-elements are demonstrated in the granulomatous areas and also in the giant cells. It is most important to note that fungus-elements are also found within the remaining hair follicles and in the peripheral part of the hairs.

In our case, the histopathologic findings for the tumor on the first toe were observed as massive, disseminated or confluent granulomas in dermis, which were characterized by tuberculoid formations with central necrobiotic changes; numerous branching hyphae and spores were found in the granulomas. These fungus-elements could be seen not only in the granulomas but also in the giant cells and microabscesses. At the peripheral part of the lesions, there were a few remaining hair follicles including fungus-elements. One of nodules on the fifth toe revealed some scattered granulomas showing no typical tuberculoid formation. However, a few short branching
hyphae and spores could be found within the giant cells in granulomatosus islands. The infiltrations around the granulomatosus areas and non-specific infiltrations in dermis were composed of numerous lymphocytes, plasma cells, histiocytes, and a few leucocytes. GOTTRON stated that such infiltrations were lympho-reticular hyperplasia and presumed them to be a reactive expression. Our own case showed predominant proliferations of reticulum fibers within the non-specific infiltrations where no fungus-elements could be found.

On the pathogenesis of granuloma trichophyticum, many papers have been published. Recently, BRAUN-FALCO et al. described the pathogenesis of two of his cases.

Undoubtedly this granuloma occurs on a superficial trichophytosis and may develop from an infected hair follicle. It has been recognized by many authors that fungus-elements penetrate the dermis through hair canals, and then form granulomatous changes in dermis.

In our case, dilated, hair-lost, follicular orifices were found on the surface of the tumor or nodules, and fungus-elements were seen in the hair canals as well as in the granulomatosus areas. Further, granulomatosus areas were observed around the deeper portion of the infected hair follicles.

From these findings, it is suggested that granuloma trichophyticum may arise from follicular infection due to trichophyton.

The mechanism how fungus-elements grow in dermis still remains unknown. From this point of view, the problem of the host-parasite relationship in this condition becomes important, because only a few patient with superficial trichophytosis suffer from granuloma trichophyticum. In our case, the mycologic examination of the trichophyton rubrum obtained from the superficial trichophytosis and that obtained from the granuloma trichophyticum yielded different findings in the colonies and slide cultures, in spite of the fact that both samples must belong to the same strain. The problem of patho-physiologic conditions caused by trichophyton in affected locations may also be involved.

SUMMARY

1. Reported here is a granuloma trichophyticum Majocchi occurring on the right toe of a 34-year-old man, the first Japanese case of this localized type of granuloma.
2. It is suggested that both generalized disseminated trichophytic granuloma and WILSON's nodular granulomatous perifolliculitis should be categorized as granuloma trichophyticum Majocchi, as all three conditions share the common histopathological findings.
3. Two types of trichophyton rubrum were isolated from the granuloma and the superficial trichophytosis. Their culture findings were different both on SABOURAUD'S glucose agar and on slide culture preparation.
4. The pathogenesis of granuloma trichophyticum is discussed, and the importance of the host-parasite relationship is brought up.

REFERENCES

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