DOI: 10.1515/sjdv-2015-0004

Majocchi's Granuloma in a Healthy Adult Man – a Case Report

Milan BJEKIĆ[1*], Jasna GAJICA BASARA[1,2]

[1]City Institute for Skin and Venereal Diseases, Belgrade, Serbia
[2]Department of Laboratory Diagnosis – Microbiology Laboratory, Serbia

*Correspondence: Milan Bjekić, E-mail: milinkovski@gmail.com

DE GRUYTER
OPEN

UDC 616.5-002.828-07/-08

Abstract

Majocchi's granuloma was first described by Domenico Majocchi in 1883, as a deep chronic dermatophyte infection of hair follicles, in which dermatophytes penetrate the dermis through hair canals, forming granulomatous changes in the dermis and/or hypodermis. Majocchi's granuloma has two different clinical variants: the first is a small perifollicular papular type, seen in otherwise healthy individuals, that occurs secondary to trauma (e.g. in women with chronic tinea pedis that extends to the legs and who shave their legs); the second is a type with deep plaques or nodular lesions in immunocompromised hosts. The diagnosis is primarily made using direct microscopy of unstained specimens and fungal cultures, while additional diagnostics (histology, PCR) are generally not necessary. It is most commonly caused by Trichophyton rubrum.

We present a 26-year-old otherwise healthy man exhibiting blue erythematous patches over the skin of his abdomen on clinical examination, which agglomerated to form slightly raised plaques with irregular ovoid contours, spreading from umbilicus to the pubic region; they were covered with multiple red-blue, erythematous partly coalescing scales, eroded, firm papules and nodules. On pressure, some nodules excreted viscid and turbid sero-purulent content. The lesions were slightly itchy. The patient was previously unsuccessfully treated during at least 4 weeks with a topical steroid cream prescribed by his physician. Direct microscopy for fungi of skin scrapings and pus mounted in potassium hydroxide was negative. Cultures of the contents and scrapings were performed on Sabouraud's glucose agar and Trichophyton rubrum was isolated. The diagnosis of Majocchi's granuloma was made, and the patient was treated with itraconazole (200 mg daily) for eight weeks, when all lesions resolved and fungal culture was negative.

Misapplication of topical corticosteroids over a long period, as in our case, can produce Majocchi's granuloma. When assessing skin lesions of unusual appearance, especially if aggravated by corticosteroids, dermatologists and general practitioners should consider tinea incognito, which may appear in its invasive form of Majocchi's granuloma. The available world literature shows that Majocchi's granuloma presenting as tinea incognito caused by topical corticosteroids has been reported extremely rarely.

Key words

Granuloma; Skin Diseases; Trichophyton; Tinea; Anti-inflammatory Agents + adverse effects; Treatment Outcome; Itraconazole; Case Reports

Dermatophytes are fungal pathogens that commonly infect the outer keratinized layer of the epidermis, therefore causing mainly superficial infections of the skin, hair and nails, termed dermatophytoses. Subcutaneous infections due to dermatophytes are usually limited to immunosuppressed hosts (1, 2, 3). However, in immunocompetent individuals, deep or inflammatory forms of dermatophytoses are usually acute suppurative forms such as kerion, or e.g. much less often chronic granulomatous infiltrates surrounding the hair follicles. The latter was first described in 1954, by Wilson et al. as "nodular granulomatous perifolliculitis of the legs caused by *Trichophyton rubrum*", where nodular lesions are within the plaques of scaly erythematous trichophytosis (4). Much earlier, in 1883, Domenico Majocchi described granuloma trichophiticum, a deep chronic granulomatous infection in the dermis caused by *Trichophyton* spp. now known as Majocchi's granuloma. He believed that both clinically and

pathologically, this condition should be distinguished from common tinea profunda, an acute suppurative condition which usually occurs as kerion celsi, sycosis parasitaria, and folliculitis aguminata parasitaria (5). Though the pathogenesis and classification of trichophytic granuloma have not yet been satisfactorily explained, it has widely been suggested that Wilson's nodular granulomatous perifolliculitis should be categorized as Majocchi trichophytic granuloma (6).

Majocchi's granuloma has two different clinical variants (1): the first are small perifollicular papular lesions seen in healthy individuals, and the second are deep plaques or nodular lesions in immunocompromised hosts. It is most commonly caused by *Trichophyton rubrum* (1).

Topical agents are usually ineffective, because of the deep location of infection, and thus oral antifungal agents are generally required.

Herein we present a case of an otherwise healthy, immunocompetent male, who developed Majocchi's granuloma on the abdominal wall after a prolonged application of a potent topical corticosteroid.

Case report

A 26-year-old man with a 1.5 month history of expanding abdominal lesions was referred to the City Institute for Skin and Venereal Diseases in Belgrade by his physician who had unsuccessfully treated the lesions as eczematous with a topical steroid cream (betamethasone dipropionate) during the least 4 weeks. On physical examination he exhibited blue erythematous patches over the skin of his abdomen, which agglomerated to form slightly raised plaques with irregular ovoid contours, spreading from the umbilicus to the pubic region, covered with multiple red-blue, erythematous partly coalescing scaled, eroded, firm papules and nodules. On pressure, some nodules excreted viscid and turbid sero-purulent content (Figure 1). The plaques were erythematous and sharply demarcated. However, some satellite papules and pustules were noticed on his trunk and in the inguinal area. The patient complained of mild pruritus. He was otherwise healthy, not receiving any medications and had an unremarkable medical history.

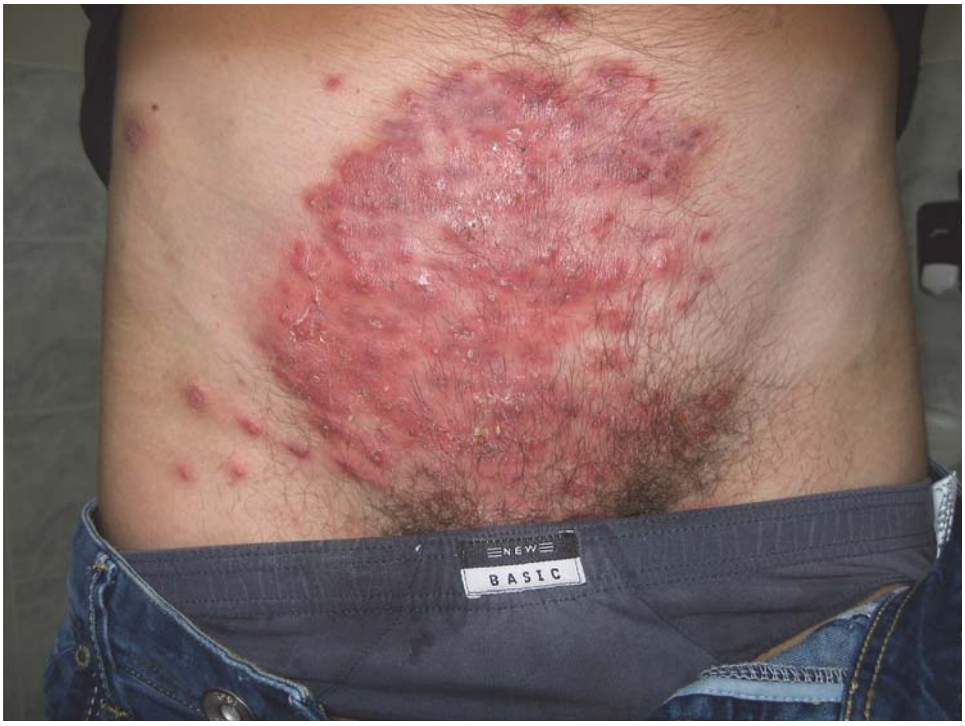

Figure 1. Multiple livid and red bluish papules and firm nodules coalescing into sharply demarcated plaques. On pressure, some nodules excreted viscid and turbid serous or purulent content. There are also some satellite papules and pustules on the trunk and in the inguinal area.

Full blood count and routine biochemistry, including bacteriological examination of smears from swabs taken from the lesions, were normal. The patient denied any history of trauma, like shaving the abdomen or previous cutaneous fungal infections, such as athlete's foot, onychomycosis or fungal infections on other regions. Direct microscopy for fungi of skin scrapings and pus mounted in potassium hydroxide was negative. Cultures of the content and scrapings were performed on Sabouraud's glucose agar and *Trichophyton rubrum* was isolated. The diagnosis of Majocchi's granuloma was made and the patient was treated with itraconazole, 200 mg daily, for eight weeks. After four weeks of therapy, a marked improvement of lesions with significant reduction in erythema, lack of pustules and flattening of the papules and nodules was recorded (Figure 2). Over the next four weeks, the papules and nodules disappeared, leaving postinflammatory hyperpigmented macules. The potassium hydroxide examination and fungal cultures were negative. No relapse was observed in the 9-month follow up.

Discussion

Majocchi's granuloma was first described by Domenico Majocchi in 1883, as a deep dermatophyte infection of hair follicles, in which dermatophytes penetrate the dermis through hair canals, forming granulomatous changes in the dermis and/or hypodermis (5). Undoubtedly, this granuloma occurs in the background of superficial trichophytosis, and may develop from an infected hair follicle. *Trichophyton rubrum* is the most common cause and it is most frequently associated with the potential for tissue invasion (2). Other dermatophytes associated with Majocchi's granuloma are as follows: *Trichophyton mentagrophytes*, *Trichophyton epilans*, *Trichophyton violaceum*, *Microsporum audouinii*, *Microsporum gypseum*, *Microsporum ferrugineum*, and *Microsporum Canis* (7).

There are two types of Majocchi's granuloma: the first represents a small perifollicular papular form in otherwise healthy individuals that occurs secondary to trauma (e.g. in women with chronic tinea pedis that extends to the legs, and in those who shave their

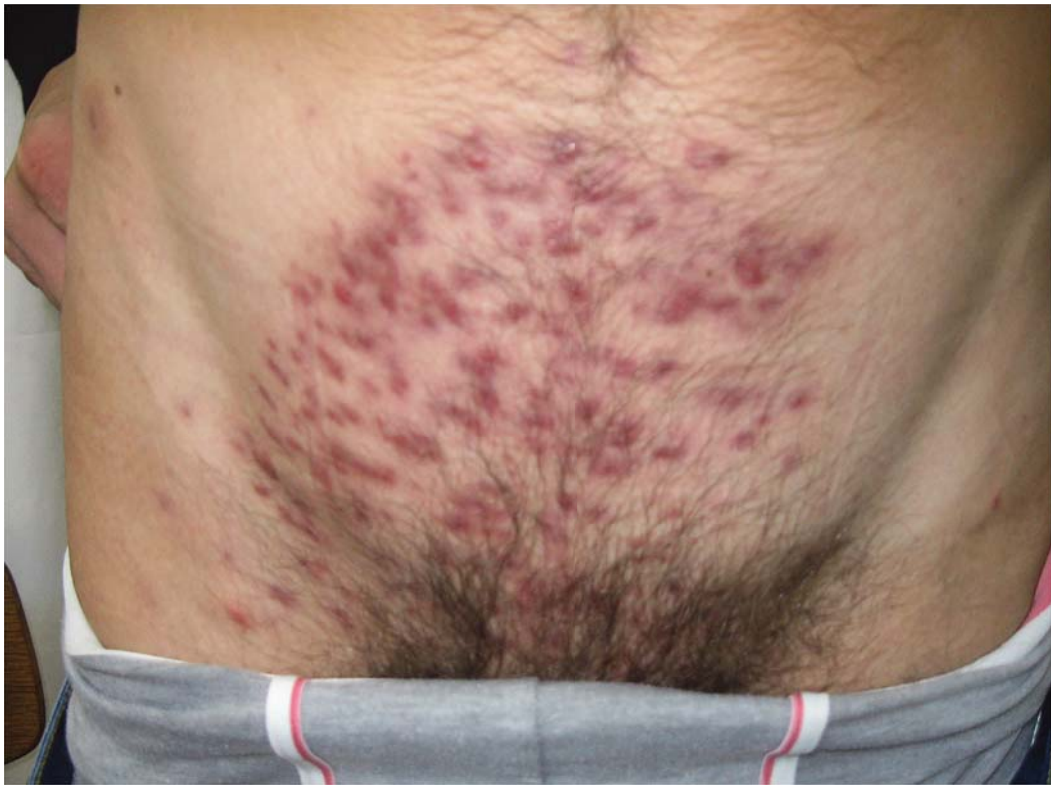

Figure 2. After four weeks of therapy, there is a marked improvement of lesions with reduced erythema, lack of pustules and flattening of the inflamed papules and nodules

legs), and the second is a deep type with plaques or nodules that affects severely immunosuppressed patients (3, 8, 9, 10, 11, 12, 13). Apart from trauma, previous inappropriate and prolonged use of topical steroids, prescribed as a result of incorrect diagnosis, as in our case, masks the early clinical manifestations of dermatophytic infection and can lead to local immunosuppression and promote the development of Majocchi's granuloma (7, 9, 10, 12). In immunocompromised patients, due to impared cell-mediated immunity and the inflammatory response, cutaneous fungal infections may penetrate deep into the skin and induce a pronounced inflammatory reaction resulting in granulomatous skin disease (2). Moreover, several studies have reported Majocchi's granuloma among solid organ transplant recipients, due to immunosuppressive drug regimens (14, 15, 16). In immunocompromised hosts, clinical features may be similar to those in healthy individuals, or characterized by groups of firm or fluctuant subcutaneous nodules and abscesses (nodular granulomatous perifolliculitis) located mostly on the scalp, face, hands or forearms (3, 17). In exceptional cases, systemic dissemination occurs (18).

The diagnosis is primarily made with direct microscopy of unstained specimens and fungal cultures, while additional diagnostics (histology, PCR) are generally not needed. Direct microscopy for fungi of skin scrapings and pus mounted in potassium hydroxide is often negative, as in our case (2), and the most commonly recovered pathogen is *Trichophyton rubrum,* like in our patient. Moreover, *Trichophyton rubrum* is the most common cause of Majocchi's granuloma worldwide (19). Trauma may induce follicular disruption with passive invasion of dermatophytes and keratinous material into the dermis. The latter can provide a substrate for the organism (7). It has been suggested that keratin is carried by a severe inflammatory response into the dermis (5). Even in severe immunosuppression, deeper hematological invasion does not happen because dermatophytes need keratin found in the hair, skin, or nails. Despite its ability to adapt to environmental conditions, as well as its capability of deep infiltration, it seems that *Trichophyton rubrum* cannot infiltrate and survive in human blood and lymph vessels (15).

In differential diagnosis, other eruptions that are more traditionally associated with deep cutaneus and/or systemic infections than dermatophytes, e.g. mycobacteria or nondermatophyte fungi, must be rulled out. In contrast to fungal suppurative folliculitis or Majocchi granuloma, these deep dermatophyte infections are typically found in immunosuppressed hosts, they are more sudden in onset, may be more aggressive, larger, or more deep-seated in location, and should not necessarily be associated with hair follicles (2). Regarding tinea profunda, a common inflammatory (deep) dermatophytosis, as previously mentioned, even Majocchi believed that both clinically and pathologically (absence of keratin or hair elements, the scarcity of foreign-body giant cells), these conditions, (e.g., kerion celsi), should be distinguished from Majocchi's granuloma, as more acute, suppurative and painful conditions which usually occur as sycosis parasitaria and folliculitis aguminata parasitaria (5). Nevertheless, though the pathogenesis and classification of trichophytic granuloma have not yet been satisfactorily explained, whether or not deep or locally invasive deramtophyte infections are sufficiently unique to support their classification as a distinct entity, remains to be determined. It is possible that both types of infection represent a single pathologic process, with a broad spectrum of clinical presentations different in severity, from mild localized to severe widespread disease, where Majocchi granuloma may represent the most indolent form of dermatophytosis involving the dermis (2). In our patient, lesions were only slightly itchy.

The treatment of Majocchi's granuloma with topical antifungals is usually ineffective (20). Systemic antifungal treatment is preferred in both patients who are immunocompetent and in those who are immunocompromised, and should last at least 4 - 6 weeks. There is no standard regimen for the treatment. According to the literature data, griseofulvin, ketoconazole, terbinafine and itraconazole have been used (20, 21, 22). Although griseofulvin and ketoconazole have each been used successfully, terbinafine and itraconazole and fluconazole (the newer azoles) have been used in recent cases with good results (2). Several studies have shown that oral terbinafine, 250 mg daily for six weeks, was effective in the treatment of this condition (21, 23). Our

patient was successfully treated with itraconazole, 200 mg daily, for eight weeks. However, Gupta et al. (20) have shown that itraconazole pulse therapy (three pulses – 200 mg twice daily for one week, followed by two weeks off, between pulses) is also effective in the treatment of Majocchi's granuloma. However, due to possible interactions between antifungals and immunosuppressants, since terbinafine involves fewer risks of drug interactions, it is preferable to azole antifungals in Majocchi granuloma (Majocchi 1) (22).

Conclusion

We present a case of an otherwise healthy, immunocompetent male, who developed Majocchi granuloma on the skin of his abdominal wall after prolonged application of a potent topical corticosteroid. When assessing skin lesions of unusual appearance, especially if aggravated by corticosteroids, dermatologists and general practitioners should consider tinea incognito, which may appear in its invasive form as Majocchi's granuloma. The available world literature shows that Majocchi's granuloma presenting as tinea incognito caused by application of topical corticosteroids has been reported extremely rarely.

Acknowledgement

This study was supported by the Ministry of Science and Technology of Serbia, Contract No. 175042 (2011 - 2014).

References

1. Radentz WH, Yanase DJ. Papular lesions in an immunocompromised patient. Arch Dermatol 1993;129:1189-90.
2. Chastain MA, Reed RJ, Pankey GA. Deep dermatophytosis: report of 2 cases and review of the literature. Cutis 2001;67:457-62.
3. Gupta S, Kumar B, Radotre BD, Rai R. Majocchi`s granuloma trichophyticum in an immunocompromised patient. Int J Dermatol 2000;39:140-1.
4. Wilson JW, Plunkett OA, Gregfersen A. Nodular granulomatous perifolliculitis of the legs caused by Trichophyton rubrum. AMA Arch Derm Syphilol 1954;69:258-77.
5. Majocchi D. Sopra una nuova tricofizia (granuloma tricofitico), studi clinici e micologici. Bull R Acad Med Roma 1883;9:220-3.
6. Yasuhara M, Fukaura H, Hashimoto T. Granuloma trichophyticum Majocchi: a case report. Skin Res 1968;10(5):643-54.
7. Bae BG, Kim HJ, Ryu DJ, Kwon YS, Lee KH. Majocchi granuloma caused by *Microsporum canis* as tinea incognito. Mycoses 2010;54:361–2.
8. Gill M, Sachdeva B, Gill PS, Arora B, Deep A, Karan J. Majocchi's granuloma of the face in an immunocompetent patient. J Dermatol 2007;34:702-4.
9. Jacobs PH. Majocchi's granuloma (due to therapy with steroid and occlusion). Cutis 1986;38:23.
10. Elgart ML. Tinea incognito: an update on Majocchi granuloma. Dermatol Clin 1996;14:51-5.
11. Lourdes LS, Mitchell CL, Glavin FL, Schain DC, Kaye FJ. Recurrent dermatophytosis (Majocchi granuloma) associated with chemotherapy-induced neutropenia. J Clin Oncol 2014;32(27):e92-4.
12. Meehan K. A growing, pruritic plaque on the thigh. Majocchi's granuloma with secondary tinea incognito. JAAPA 2002;15:16, 65.
13. Mayser PA. Majocchi granuloma**.** Advantages of optical brightener staining in a case report. Hautarzt 2014;65:721–4.
14. Burg M, Jaekel D, Kiss E, Kliem V. Majocchi's granuloma after kidney transplantation. Exp Clin Transplant 2006;4:518-20.
15. Brod C, Benedix F, Röcken M, Schaller M. Trichophytic Majocchi granuloma mimicking Kaposi sarcoma. J Dtsch Dermatol 2007;5:591-3.
16. Steiner UC, Trueb RM, Schad K, Kamarashev J, Koch S, French LE, et al. Trichophyton rubrum – induced Majocchi's granuloma in a heart transplant recipient. A therapeutic challenge. J Dermatol Case Rep 2012;6(3):70-2.
17. Gong JQ, Liu XQ, Xu HB, Zeng XS, Chen W, Li XF. Deep dermatophytosis caused by Trichophyton rubrum: report of two cases. Mycoses 2007;50:102-8.
18. Hironaga M, Okazaki N, Saito K, Watanabe S. Trichophyton mentagrophytes granulomas. Unique systemic dissemination to lymph nodes, testes, vertebrae, and brain. Arch Dermatol 1983;119:482-90.
19. Seebacher C, Bouchara JP, Mignon B. Updates on the epidemiology of dermatophyte infections. Mychopathologia 2008;166:335-52.
20. Gupta AK, Groen K, Woestenborghs R, De Doncker P. Itraconazole pulse therapy is effective in the treatment of Majocchi's granuloma: a clinical and pharmacokinetic evaluation and implications for possible effectiveness in tinea capitis. Clin Exp Dermatol 1998;23:103-8.
21. Elgart ML, Warren NG. The superficial and subcutaneous mycoses. In: Moschella SL, Hurley HJ, editors. Dermatology. 3rd ed. Philadelphia: WB. Saunders Company; 1992. p. 869-912.
22. Gupta AK, Prussick R, Sibbald RG, Knowles SR. Terbinafine in the treatment of Majocchi's granuloma. Int J Dermatol 1995;34:189.
23. Bressan AL, Silva RS, Fonseca JC, Alves Mde F. Majocchi's granuloma. An Bras Dermatol 2011;84:797-8.

Majocchis granulom kod zdravog odraslog muškarca – prikaz slučaja

Sažetak

Uvod. Majocchis granuloma je prvi opisao 1883 Domenico Majocchi, kao dermatofitima izazvanu duboku hroničnu infekciju dllačnog folikula u kojoj dermatofiti invadiryju dermis putem penetracije dlačnog kanala i izazivaju granulomatozne promene u dermisu i/ili hipodermisu. Oboljenje se retko javlja, a može se klinički ispoljiti u dva morfološki raličita oblika, površni i duboki: prvi se pretežno manifestuje sekundarno kao posledica traume kod inače zdravih, imunokompetentnih osoba u vidu malih perifolikularnih papula (najčešće kod žena koje imaju hroničnu tineu na stopalima kada posle brijanja dlačica na donjim ekstremitetima dolazi s jedne strane do do širenja infekcije na podkolenice,a s druge srane do utiskivanja delova keratina iz epidermisa neophodnog za rast dermatofita u dermisu; duboki oblik se manifestuje plakovima i nodusima kod imunosuprimiranih osoba, koji dobijaju imunosupresivnu terapiju, npr posle transplantacije organa. Dijagnoza se postavlja na osnovu anamneze, kliničke slike i izolacije uzročnika, a potvrđuje identifikacijom uzročnika iz kulture s obzirom da mikroskopski pregled nativnog preparata može biti negativan; u protivnom potrebno je uraditi dodatne analize dokazivanja uzročnika kao što je patohistološka analiza PAS-bojenog preparata ili PCR. Najčešći ali ne i jedini dermatofit uzročnik Majocchi granuloma je *Trichophyton rubrum*.

Prikaz slučaja. U ovom radu prikazujemo slučaj dvadesetšestogodišnje osobe muškog pola, inače dobrog opšteg zdravlja, koja je upućena od strane izabranog lekara na pregled dermatologa u Gradski Zavod za kožne i venerične bolesti u Beogradu. Iz anamneze se saznalo da su se promene zbog kojih se javio na pregled počele javljati pre više od mesec i po dana. Potom se pacijent javio na pregled kod svog izabranog lekara koji je preporučio lokalnu aplikaciju potentnog kortikosteroida u obliku masti, jer je sumnjao da je priroda promena ekcemska. Tokom više od četiri nedelje pacijent je svakodnevno redovno aplikovao mast na obolelo područje kože. Promene su bile lokalizovane na koži prednjeg trbušnog zida ispod pupka,da bi se tokom lečenja pošele povećavati, slivati u veće čvorovei širiti sve do stidnog predela. U momentu pregleda, na koži prednjeg trbušnog zida, celom širinom i dužinom od umbilikusa do pubične regije, uočavale su se brojne numularne indurirane površine lividne i tamno eritematozne boje, koje su većim delom međusobno konfluirale čineći jasno demarkirani ovoidni plak tamno eritematoze boje sa čije su se površine izdizale brojne promene tipa papula i nodusa razne veličine, od zrna graška do manjeg oraha zagasito lividno eritematozne boje. Pojedine promene su bile čvrste konzistencije dok se iz drugih na pritisak mogao istisnuti židak, viskozan serozan do seropurulentan sadržaj; 0ko centralnog plaka, nalazilo se nekoliko satelitskih promena u vidu pojedinačnih papula, nodusa i plakova numularnog oblika i veličine, Iz anamneznih podataka se saznalo da niti je sam pacijent niti je bilo ko iz njegove porodice imao oboljenja kože, kose i noktiju. Svi laboratorijski nalazi kako hematološki tako i osnovni biohemijski bili su u granicama normale; iz brisa uzetog sa površine promena i na pritisak istisnutog sadržaja iskultivisana je normalna bakteriološka flora. U nativnom mikroskopski pregledanom preparatu nisu nađeni gljivični elementi, ali je uzet materijal zasejan na Sabouraud-ov glukozni agar a iz kulture je izolovan i identifikovan *Trichophyton rubrum.*

Dijagnoza i diferencijalna dijagnoza. Na osnovu kliničke slike i mikološke analize, postavljena je dijagnoza Majocchi granuloma. U diferencijalnoj dijagnozi bitno je isključiti druge uzročnike na koje se u praksi češće pomišlja kada su duboke inflamatorne nodularne lokalne i/ili sistemski invazivne dermatoze u pitanju, kao što su atipične mikobakterije i nedermatofitne gljive. Za razliku od mikotičnog hroničnog supurativnog Majocchi granuloma, ove duboke infekcije ukoliko su izazvane dermatofitima, imaju mnogo akutniji početak, agresivniji tok, dostižu veće dimenzije, smeštene su dublje, ne moraju obavezno zahvatati dlačne folikule i skoro po pravilu javljaju se kod osoba sa visokim stepenom imunosupresije. Kada je *tinea profunda* u pitanju, ona predstavlja primer inflamatornih (dubokih)

dermatofitoza koje se relativno često dijagnostikuju u dermatološkim ordinacijama: još i sam Majocchi je verovao da njih treba razlikovati od njegovog granuloma, kako klinički (značajno akutniji nastanak, jača supuracija, bolnost, npr. *sycosis parasitaria* i *folliculitis aguminata parasitaria*), tako i histološki (odsustvo keratina, delova dlake, mali broj džinovskih ćelija tipa oko stranog tela, zavatanje dubljih slojeva. Imajući sve navedeno, možemo zaključiti da patogeneza i klasifikacija trihofitičnog granuloma i dalje ostaje predmet novih istraživanja, koja treba da odgovore na pitanje: da li se lokalno invazivne dermatofitoze dovoljno jasno međusobno razlikuju da bi se klasifikovale kao posebni entiteti. Vrlo je moguće da se u osnovi sve tri gore navedene grupe dermatofitoza nalazi isti patogenetski mehanizam sa širokim spektrom kliničkih manifestacija, od blagih lokalizovanih do agresivnijih diseminovanih, u kome Majocchi granulom predstavlja najmanje bolnu dermatofitiju koja zahvata dermis/hipodermis i ima hroničan ili hronično-recidivirajući tok.

Terapija. Lečenje je započeto peroralno sa itrakonazolom u dozi 200 mg dnevno: nakon četiri nedelje lečenja, došlo je do značajnog, kliničkog poboljšanja, a nakon 8 nedelja do potpuno kliničkog i mikološkog izlečenja.

Diskusija. Direktan uzrok Majocchi granuloma može biti neopravdana lokalna aplikacija kortikosteroidnih preparata tokom dužeg vremenskog perioda, kao što je to bio slučaj kod našeg pacijenta, U svakom slučaju u kome su promene zadobile neuobičajen izgled i agravaciju nakon primene kortikosteroidneih preparata za lokalnu primenu, svaki lekar, ne samo dermatolog koji leči takvog pacijenta, treba da u diferencijalnoj dijagnozi isključi *tineu incognito* koja može zadobiti invazivni tok, u formi Majocchi granuoma.

Zaključak: U radu prikazujemo sučaj inače zdrave muške osobe kod koje je Trichophiton rubrum izazvao Majocchi granulom u formi *tinea incognito.* U nama dostupnoj literaturi ovakvi slučajevi su u izuzeno retko objavljivani.

Ključne reči

Granulom; Kožne bolesti; Trihofiton; Tinea; Anti-inflamatorni lekovi + neželjena dejstva; Ishod lečenja; Itrakonazol; Prikazi slučajeva