Clinical Cases in Dermatology
Series Editor: Robert A. Norman

Fabio Arcangeli
Torello M. Lotti *Editors*

Clinical Cases in Early-Years Pediatric Dermatology

Springer

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Series Editor
Robert A. Norman
Tampa, FL, USA

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ISSN 2730-6178 ISSN 2730-6186 (electronic)
Clinical Cases in Dermatology
ISBN 978-3-030-89088-9 ISBN 978-3-030-89089-6 (eBook)
https://doi.org/10.1007/978-3-030-89089-6

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Contents

Chapter 1
5 Year Old with Fever and Perioral and Periorbital Erythema

Kenan Barut, Defne Özkoca, and Zekayi Kutlubay

A 5 years old male patient applied to the pediatric emergency department with the complaint of fever that has been persistent for 5 days and abdominal colic pain with a resultant diarrhea. The patient's past medical history and family history were unremarkable except for a SARS-CoV-2 infection in the family one-month ago. The patient was asymptomatic during the infectious period. At the time that the patient applied to the emergency department he was lethargic, tachycardic and tachypneic. His vitals were as follows: a body temperature of 38.9 degrees Celsius, a heart rate of 128 beats per minute, a respiratory rate of 30 per minute and a blood pressure of 60/40 mm mercury. Upon oscultation, the first and the second heart sounds were normal but a 2/6 systolic murmur was present. A hepatomegaly of 2 cm was present and the traube space was closed. Submandibular lymphadenopathies were palpated. A cutaneous rash, bilateral conjunctivitis and red strawberry tongue were observed. The laboratory examination revealed decreased white blood cells (5000/mm^3), decreased hemoglobulin (9.1 g/dL), decreased platelets (160,000/mm^3), decreased albumin (2.3 g/dL), increased ferritin (922 ng/mL), increased c-reactive protein (122.5 mg/L) and increased brain-natriuretic peptide (1894 pg/mL). The rest were normal. Echocardiography and cardiac enzymes were unremarkable.

The patient was consulted to dermatology due to the cutaneous findings. Upon the dermatologic examination the patient had a diffuse polymorphous eruption; perioral and periorbital erythema; and fissured lips (shown in Fig. 1.1). The tongue

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F. Arcangeli, T. M. Lotti (eds.), *Clinical Cases in Early-Years Pediatric Dermatology*, Clinical Cases in Dermatology,
https://doi.org/10.1007/978-3-030-89089-6_1

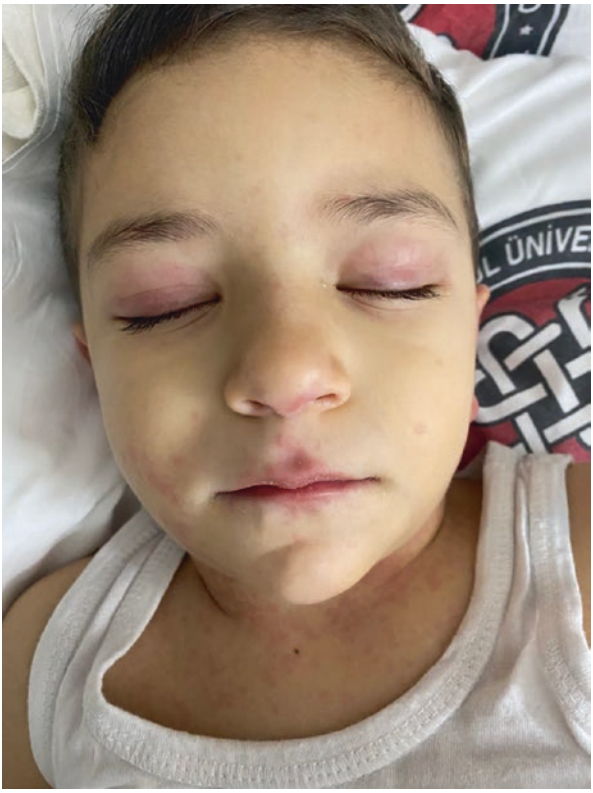

Fig. 1.1 Diffuse polymorphous eruption; perioral and periorbital erythema; and fissured lips

was bright red and edematous with the accentuation of the fungiform papillae (red strawberry tongue, shown in Fig. 1.2).

Based on the case description and the photographs, what is your diagnosis?

- Kawasaki Disease (MIS-C)
- Scarlet Fever
- Viral Exanthema
- Toxic Shock Syndrome

Diagnosis: Kawasaki Disease (MIS-C)

Given the increased C-reactive protein, leukopenia, increased ferritin, red strawberry tongue, bilateral conjunctival injection, submandibular lymphadenopathies, perioral erythema, fissured lips and polymorphous rash, the patient was diagnosed as Kawasaki Disease due to multisystem inflammatory syndrome in children (MIS-C), related to SARS-CoV-2 infection. Intravenous immunoglobulin, pulse corticosteroid, anakinra and wide spectrum intravenous antibiotherapy were initiated immediately upon the diagnosis. The fever and other symptoms subsided on

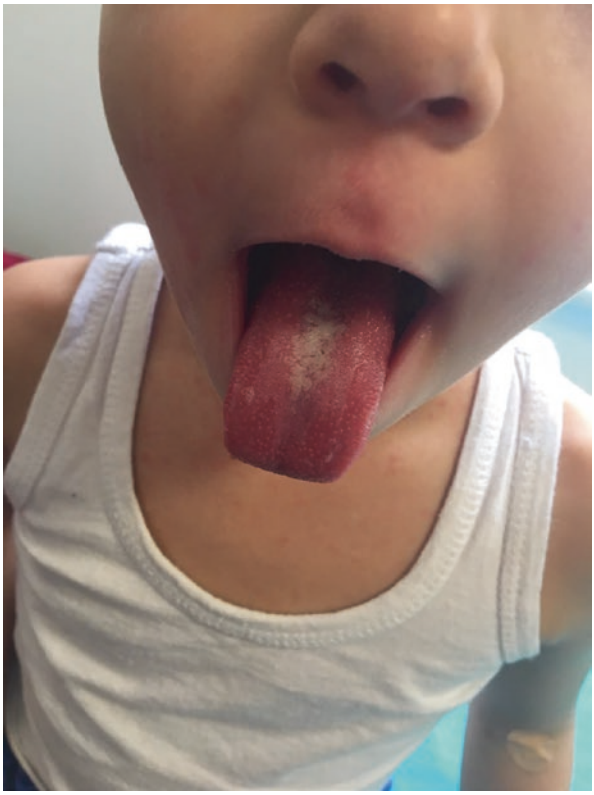

Fig. 1.2 Bright red and edematous tongue with the accentuation of the fungiform papillae (red strawberry tongue)

the fifth day of treatment and the patient was discharged on the 10th day of treatment.

Discussion

Kawasaki disease is a medium vessel vasculitis that is diagnosed by its cutaneous findings. It is the most common cause of acquired heart disease in children due to its affinity towards the coronary arteries. A typical patient has a persistent fever for at least 5 days and four of the following five principle manifestations [1]:

- Acute edema of hands and feet, acute erythema of palms and soles, subacute periungal peeling of the finger and the toes
- A polymorphous eruption (maculopapular, urticarial, erythema multiforme-like or erythrodermic, but not vesicular)
- Bilateral conjunctival injection
- Oral changes: Perioral erythema, fissured lips, strawberry tongue, diffuse injection of the oral mucosa
- Cervical lymphadenopaties (>1.5 cm, usually unilateral)

The main differential diagnoses of the disease are scarlet fever, toxic shock syndrome, measles, adenoviral infection or Steven Johnson's Syndrome [1].

The disease is important for its predilection to coronary arteries and may lead to coronary artery dilations or aneurysms. Rarely, macrophage activation syndrome can occur as a result of Kawasaki Disease [1, 2]. Recently, Kawasaki Disease has been linked with the MIS-C due to SARS-CoV-2 infection as well. The main treatment modality used in Kawasaki Disease is intravenous immunoglobulins. The aim of treatment is to overcome the acute systemic inflammatory process and its resultant possible coronary artery damage. In refractory cases, systemic corticosteroids, cyclosporine and anti-interleukin-1 biologic drugs may be used. Furthermore, aspirin is added to the regimen for its anti-platelet effects [2].

Strawberry tongue is the distinctive clinical picture that is observed due to the accentuation of the inflamed fungiform papillae on an erythematous background located on the dorsum of the tongue. It is a diagnostic criterion for the Kawasaki Disease and Scarlet Fever. This specific enanthema occurs due to the desquamation of the keratinized epithelium of the filliform papillae. Other diseases that may present with strawberry tongue are the toxic shock syndrome, group-A streptococcal pharyngitis, recurrent toxin-mediated perianal erythema, recalcitrant erythematous desquamating disorder, yellow fever and Yersinia pseudotuberculosis infection. This enanthema resolves with the treatment of the underlying disease [3].

Scarlet fever is an acute febrile exanthematous and respiratory infection that is caused by the Group-A streptococci (GAS), peaking during the winter and the spring. Streptococcal phayringitis is caused by the erythrogenic toxin of the GAS, which leads to vasodilation. Along with fever and pharyngitis, white followed by red strawberry tongue, a sand paper like rash most prominent at the flexures, circumoral pallor, pastia lines and the peeling desquamation of the hands and the feet are observed. The mainstay of treatment is antibiotherapy with penicillins [3, 4].

Key Points

- Kawasaki disease is a medium vessel vasculitis that is diagnosed by its cutaneous findings. A typical patient has a persistent fever for at least 5 days and four of the five principle manifestations.
- Kawasaki Disease can be seen along with the MIS-C due to SARS-CoV-2 infection.
- The main treatment modality used in Kawasaki Disease is intravenous immunoglobulins; and the aim of treatment is to overcome the acute systemic inflammatory process and its resultant possible coronary artery damage.
- Strawberry tongue is a distinctive clinical picture that is observed due to the accentuation of the inflamed fungiform papillae on an erythematous background; and it is a diagnostic criterion for the Kawasaki Disease and Scarlet Fever.
- Scarlet fever is an acute febrile exanthematous and respiratory infection that is caused by the Group-A streptococci; and it presents fever, pharyngitis, white followed by red strawberry tongue, a sand paper like rash most prominent at the flexures, circumoral pallor, pastia lines and the peeling desquamation of the hands and the feet.

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Chapter 2
A Child with High Fever, Rash, Chapped Lips and Conjunctival Injection

Alfonso Delgado Rubio and Fabio Arcangeli

A Child with High Fever, Rash, Chapped Lips and Conjunctival Injection

A three-year-old child came to our observation because he had had a high fever, intermittent vomiting and cough, for seven days. Five days earlier he had recived the diagnosis of acute bronchitis in an other clinic and was treated with amoxicillin, without any effect.

On clinical examination the child presented very irritable, with fever at 39.5 °C, mild rigidity of the neck and bilateral cervical lymphadenopathy. He also had a diffuse asymptomatic maculo-papular rash (Fig. 2.1), bilateral conjunctival injection without secretion (Fig. 2.2), dry, chapped lips (Fig. 2.3) and strawberry tongue.

Laboratory tests show several abnormal values: Hb 11.9 g/dl, leukocytes 19,820/mm^3. Erythrocyte Sedimentation Rate 95, C-reactive protein 17.5 mg/dl. The blood cultures were negative. The CSF examination showed a clear appearance with 55 cells/mm^3 (94% lymphocytes). The throat swab was negative. The serologies for CMV, EBV, Parvovirus B19, Toxoplasmosis and Rickettsia were negative. The ECG and the echocardiogram resulted normal.

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F. Arcangeli, T. M. Lotti (eds.), *Clinical Cases in Early-Years Pediatric Dermatology*, Clinical Cases in Dermatology,
https://doi.org/10.1007/978-3-030-89089-6_2

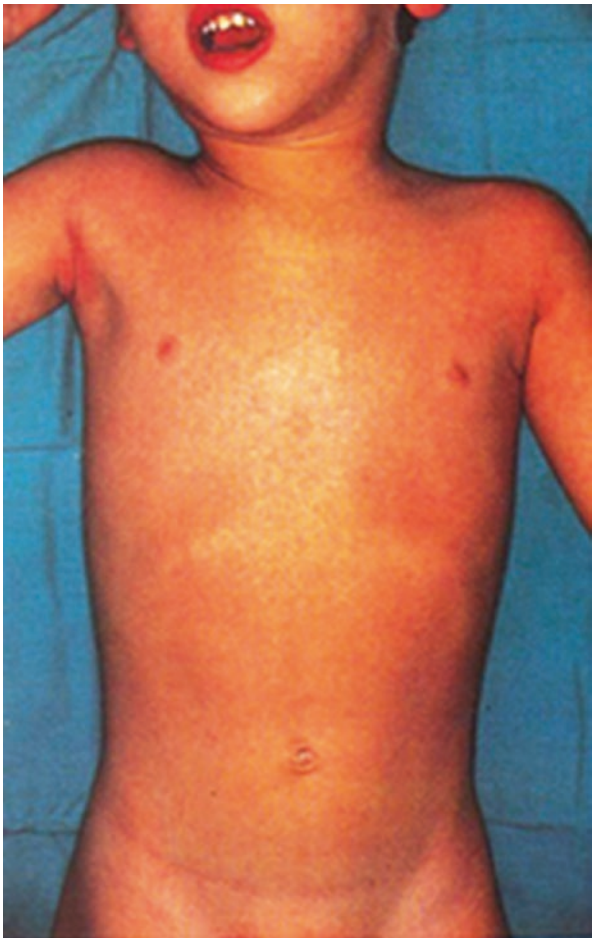

Fig. 2.1 Diffuse maculo-papular rash

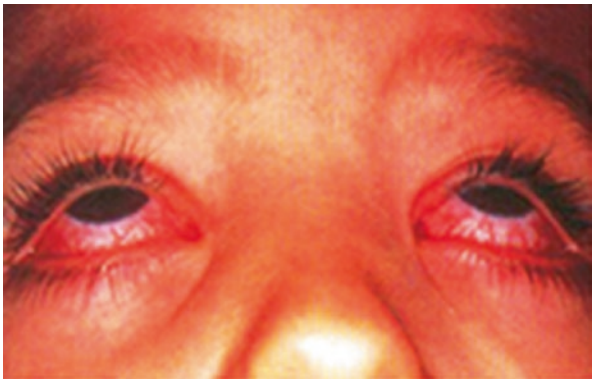

Fig. 2.2 Conjunctival injection without exudate

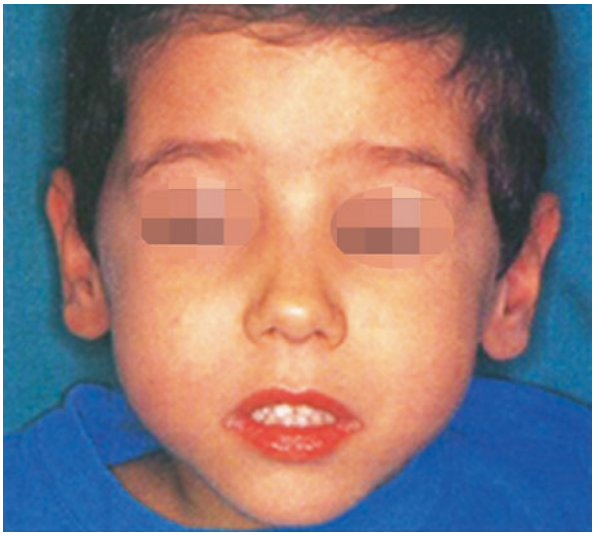

Fig. 2.3 Erythematous, dry, chapped lips

Based on the case description and the photographs, which diagnosis would you propose?

1. Classic exanthematous rash
2. Infectious Mononucleosis and Mononucleosis-like pictures
3. Drug reaction
4. Kawasaki disease

Diagnosis

Kawasaki disease (KD).

Discussion

Based on the clinical pictures and laboratory tests, we diagnosed Kawasaki disease and started therapy with aspirin (80 mg/kg/day) and intravenous gamma globulin (IVIG) at 2 g/kg in a single dose to prevent coronary artery abnormalities.

A few days later, hard edema of the hands and feet appeared, the exanthema improved, and after one week lamellar desquamation of the hands and the perineal region became evident.

The presence of a febrile syndrome and an exanthematous rash could have suggested a diagnosis of a classic exanthematous disease. However, our patient received the normal vaccinations. Furthermore, the clinical presentation did not point to any of the classic exanthematous diseases.

It should have been possible to think of a diagnosis of Mononucleosis or a Mononucleosis-like syndrome or even of an amoxicillin rash during of Mononucleosis. The clinical features and the serological investigations ruled out these diagnoses.

In the case of a drug hypersensitivity reaction, itching is frequently present, the fever is moderate and short. In addition, the laboratory tests show eosinophilia and an increase in transaminases, absent in our patient.

The appearance of an exanthematic eruption associated with a prolonged febrile syndrome that does not respond to antibiotics or antipyretics in a young child suggests a diagnosis of Kawasaki disease [1]. If bilateral conjunctival injection, oropharyngeal erythema, induration of the hands and feet, dry lips are present this diagnosis is more probable [1, 2].

In these cases, treatment with aspirin and IVIG should begin as soon as possible.

The diagnosis of Kawasaki disease is clinical and is based on defined criteria (Table 2.1) [3, 4].

In some cases, patients do not fulfill the classic criteria for Kawasaki disease and are classified as having incomplete (atypical) disease. This occurs in about 9.6% of cases. Atypical disease is suspected when patients have a fever for at least five days with only two or three of the principal clinical features [5, 6]. It is important to consider the diagnosis of Kawasaki disease and perform echocardiography in all infants younger than six months who have an unexplained fever lasting at least seven days with laboratory evidence of systemic inflammation [7] (Table 2.1).

Key Points

- Classic Kawasaki disease must be suspected in children with high fever of five days or more with at least four of five features: bilateral conjunctival injection, changes in the lips and oral cavity, cervical lymphadenopathy, polymorphous rash and extremity changes
- An early diagnosis of Kawasaki disease is very important because the treatment with aspirin and IVIG should begin as soon as possible.to prevent coronary abnormalities.

Table 2.1 Diagnostic criteria for classic Kawasaki disease [3, 4]

Diagnostic criteria for classic Kawasaki disease	Frequency (%)
Fever for at least five days and at least four of five principal clinical features listed below	100
1. Changes of the oral cavity and lips: cracked and erythematous lips, strawberry tongue	96.5
2. Polymorphous rash: maculo-papular, erythema multiforme–like or scarlatiniform rash, involving extremities, trunk, and perineal regions	96.0
3. Bilateral conjunctivitis, nonpurulent	89.0
4. Changes in the extremities (erythema of the hands and feet, desquamation of the hands and toes in weeks 2 and 3)	75.6
5. Cervical lymphadenopathy (> 1.5 cm in diameter), generally unilateral	62.7
Alternative diagnostic criteria for classic Kawasaki disease	
Fever for at least five days and two or three principal features; coronary artery abnormalities on transthoracic echocardiography	

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Chapter 3
A Five-Year-Old Girl with Erythematous Papules on Cheek

Xiangjin Song, Lihong Zhao, and Songmei Geng

A 5-year-old Chinese girl presented with erythematous papules located in her right cheek for six months. Her parents complained of tiny stab and wound occurred in site before. The papules gradually expanded and fused into erythematous plaques (Fig. 3.1).

Based on the case description and the photograph, what is your diagnosis?

1. Cutaneous Rosai-Dorfman disease
2. Cutaneous lupus erythematosus
3. Tinea Faciei
4. Majocchi granuloma

Physical examination demonstrated good general condition and no obvious abnormality of other internal organs. Routine laboratory work-up showed negative results or within normality limits. Biopsy from erythema papules on her cheek found that the epidermis was almost normal while granuloma consisting of histiocytes and plasma cells infiltrated around hair follicles in the dermis (Fig. 3.2). Gomori's methenamine silver staining (GMS) showed positive spores in granuloma. Based on clinical features and positive staining for fungi spores in tissues, the diagnosis of Majocchi granuloma was made. Oral terbinafine, 0.25 g per day, was prescribed to the patient. After 1 month follow up, the skin lesions were significantly improved and faded away.

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F. Arcangeli, T. M. Lotti (eds.), *Clinical Cases in Early-Years Pediatric Dermatology*, Clinical Cases in Dermatology,
https://doi.org/10.1007/978-3-030-89089-6_3

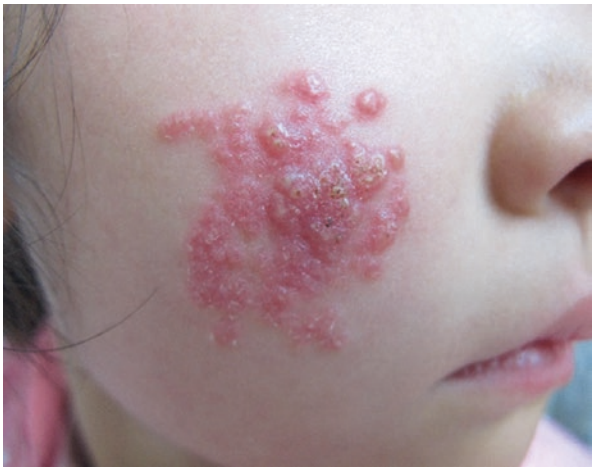

Fig. 3.1 Clinical manifestation of the patient. Red maculopapules on her right cheek

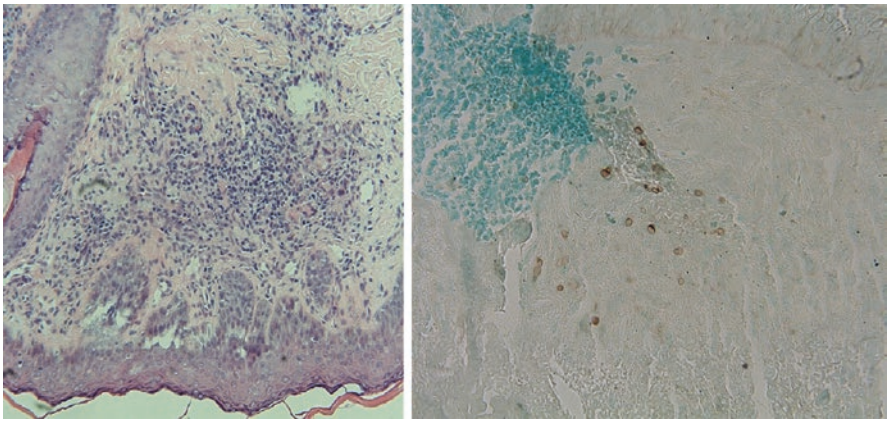

Fig. 3.2 Histopathology (HE×10) and GMS staining of the papules

Diagnosis

Mycotic Granuloma (Majocchi granuloma).

Discussion

Majocchi granuloma is a rare dermatophyte infection of dermis and subcutaneous tissues characterized by erythematous papules, stiffened plaques or granulomatous nodules [1]. Skin lesions usually presents on the extension of the thigh, some cases have reported groin, facial area and vulva may also be involved. The disease is

caused by infection of dermatophyte, especially trichophyton rubrum. Its risk factors include friction, trauma, and use of systemic immunosuppressants [2].

There are two clinical types of Majocchi granuloma: (i) small perifollicular popular form and (ii) deep subcutaneous nodular form [3]. The first type is usually secondary to trauma or the use of topical potent steroid, mainly occurs in healthy individuals. It's defined as a perifollicular infiltration and deep pustular type, erythema, papules and pustules on the smooth skin. Similarly to kerion celsii, scabs and purulent secretions can be seen in the local region. The second type is granulomatous secondary to immunosuppression and characterized by purplish red subcutaneous nodules, which can be fused into plaques. Nodules can be firm or fluctuant and usually present on the upper limbs.

Histopathological examination usually shows as a granulomatous folliculitis, ruptured hair follicle, hyphae and spores can be seen in the dermis. A large number of acute inflammatory cells on the basis of chronic inflammatory cell infiltration and podocytomatous granuloma are a characteristic change. Periodic acid-Schiff (PAS)and GMS methods are generally used to stain fungi. Molecular-base techniques fungal culture are helpful to define fungus [4].

For treatment, topical antifungal therapy usually is ineffective and systemic antifungal therapy is necessary. Terbinafine (250 mg/day), itraconazole (100–200 mg/day), griseofulvin (250–500 mg/day), voriconazole, and posaconazole were proved effective in treatment of Majocchi granuloma. [4] Treatment duration should be sufficient, usually takes 1–2 months, sometimes even as long as 6 months or longer until the lesions are completely cured and no mycology was detected repeatedly.

Cutaneous Rosai-Dorfman disease (CRDD) is an uncommon histiocytic disease with unknown etiology, often presents as solitary or numerous papules or plaques, mostly on facial area which is easily misdiagnosed as tinea. Histopathological examination is characterized by dense cellular infiltration in dermis. The infiltrating cells appear as large, eosinophilic histiocytes with abundant cytoplasm, lymphocytes and a few plasma cells can also be detected. Histiocyte's phagocytosis of lymphocytes and the proliferation of vasculars are features of CRDD. Histiocytes usually stained positive for S-100 protein and negative for CD1a.

Cutaneous lupus erythematosus (CLE) is a chronic autoimmune disease that encompasses a great variety of dermatologic manifestations such as discoid lupus or erythema annulare with papules and scales. The face is easily affected site and should be differentiated from infectious disease. The characteristic of histopathological examination are the presence of interface dermatitis with vacuolar changes of the basal keratinocytes and necrotic keratinocytes, mucin deposition, and variably dense lymphoid cell infiltrations [5].

Tinea Faciei is common superficial fungal infection manifested with red papules and scales. Most patients may have a history of using topical corticosteroids. Mycology direct microscopic examination is frequently used to make diagnose.

In this case, she presents with erythematous plaques and papules on her right cheek for 6 months after tiny stab. Histopathological examination with GMS stains confirmed the diagnosis and antifungal therapy was effective.