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A 34-Year-Old Man from Thailand With Fever and a Papular Rash

JURI KATCHANOV AND HARTMUT STOCKER

Clinical Presentation

History

A 34-year-old man from Phuket, Thailand presents to a hospital in Germany with a 2-week history of fever. He has also noticed a papular rash affecting his whole body, particularly his face and trunk. When asked, he reports weight loss (7 kg in the last 3 months).

He lives in Thailand and arrived in Germany only 3 days previously to visit friends.

Clinical Findings

On examination, the patient is febrile with a temperature of 38.2°C (100.76°F). His conjunctivae are pale. He is very wasted, with a body mass index of 14 kg/m^2.

The patient has a generalized non-pruritic rash, predominantly on his face and trunk, which consists of small umbilicated papules (Fig. 17.1). There is generalized lymphadenopathy with visibly swollen lymph nodes in the left supraclavicular region; his inguinal and axillary lymph nodes are also enlarged. On abdominal examination, the spleen is palpable at two fingers below the left costal margin. The liver span is 15cm in the midclavicular line.

• **Fig. 17.1** Multiple umbilicated papular skin lesions on the neck.

Laboratory Results

Full blood count: WBC 2.1 $\times 10^9$/L (reference range 4–10), haemoglobin 9.8 g/dL (13–16), platelets 110 $\times 10^9$/L (150–350). C-reactive protein 150 mg/L (<5).

Questions

1. What is the single most important test to be done in this patient?
2. What is your differential diagnosis?

Discussion

A 34-year-old man from Thailand presents with a 2-week history of fever and a 3-month history of wasting. On examination, he has mild hepatosplenomegaly, generalized lymphadenopathy and a papular rash. The laboratory results reveal pancytopenia and an elevated C-reactive protein.

Answer to Question 1

What is the Single Most Important Test to be Done in This Patient?

The most important test to be done is an HIV serology. The patient presents with fever, unexplained weight loss, lymphadenopathy and a papular rash; his blood results show pancytopenia. Each of these conditions alone should warrant HIV testing.

Answer to Question 2

What is Your Differential Diagnosis?

Common causes of fever, generalized lymphadenopathy and hepatosplenomegaly are infectious diseases and neoplasms.

Apart from HIV, CMV and EBV infection should be considered. All three of these viral infections may present with fever, hepatosplenomegaly and a rash, but umbilicated papular lesions are not part of the clinical picture. However, in HIV-infected individuals, mollusca contagiosa are common, which resemble the lesions seen in this patient.

Disseminated tuberculosis and infections with atypical mycobacteria are important differential diagnoses. Both can also present with cutaneous manifestations. An infection that resembles mycobacterioses in many ways is melioidosis. Melioidosis is one of the leading causes of community-acquired septicaemia in Thailand. It may present with lymphadenitis and disseminated papular skin lesions.

Bartonella spp. (*B. henselae, B. quintana*) cause bacillary angiomatosis in immunosuppressed individuals. Bacillary angiomatosis presents with non-specific systemic symptoms and umbilicated papular skin lesions. However, these papules are usually erythematous.

Fungal infections to consider in this patient are cryptococcosis, histoplasmosis and talaromycosis (previously penicilliosis), which are all commonly associated with immunosuppression but may also rarely occur in non-immunosuppressed individuals. All three may also present with umbilicated, papular skin lesions. Visceral leishmaniasis causes fever, wasting, hepatosplenomegaly and pancytopenia. It does however not cause a papular rash. It has been reported from Thailand, but appears to be uncommon.

Neoplasms to consider include lymphomas and non-malignant neoplastic conditions such as HHV-8-associated Castleman's disease.

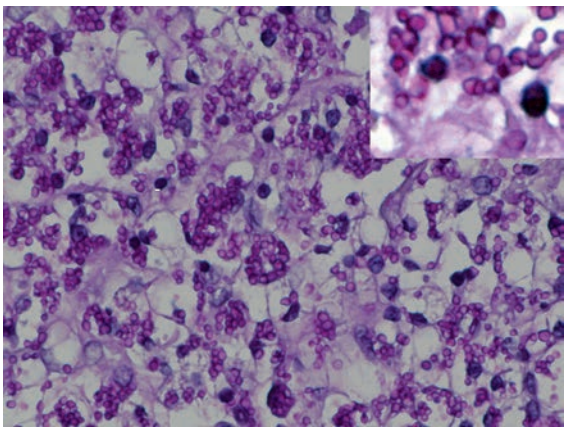
The Case Continued…

The HIV test came back positive. The patient was found to be highly immunosuppressed, with a CD4 cell count of 2/μL (normal range: 500–1000/μL).

Blood cultures were taken. A fine needle aspirate of the lymph node and a skin biopsy were performed, and the material was sent for microbiological and pathological work-up. Histopathology of the lymph node biopsy showed multiple yeast-like structures (Fig. 17.2). There were no acid-fast bacilli seen. The blood culture and cultures from the skin biopsy and lymph node all grew *Talaromyces (Penicillium) marneffei.*

The diagnosis of talaromycosis was made and the patient was started on a 2-week course of intravenous liposomal amphotericin B followed by oral itraconazole. On 3-week follow-up he was afebrile and gaining weight. Antiretroviral therapy (ART) was initiated.

Six months later the patient presented with a recurrence of his cervical lymphadenopathy. A talaromycosis relapse was suspected. However, this time an infection with atypical mycobacteria was found. His CD4 count had come up to 102/μL and the viral load was suppressed. This second infection within 6 months after starting ART was interpreted as an immune reconstitution inflammatory syndrome (IRIS) of the unmasking type.



• **Fig. 17.2** Histology of the supraclavicular lymph node showing multiple round-shaped yeast-like structures (PAS stain, × 400). *Inset:* Prominent septal wall ('septation') as a result of reproduction by fission. (Courtesy U. Zimmermann, M. Grünbaum and H. Herbst.)

SUMMARY BOX

Talaromycosis (Penicilliosis)

Talaromycosis (previously penicilliosis) is caused by *Talaromyces (Penicillium) marneffei,* a dimorphic fungus endemic to East and South-east Asia. Incidence of talaromycosis has increased in parallel with the AIDS pandemic. It is the third commonest AIDS-related opportunistic infection in Thailand and Vietnam after tuberculosis and cryptococcosis. Talaromycosis has also been reported in immunosuppressed travellers to endemic areas. Acquisition and transmission of talaromycosis, either by inhalation or by direct inoculation, have not been fully understood; the only known hosts are humans and bamboo rats.

Talaromycosis usually affects severely immunocompromised individuals who frequently have other concurrent opportunistic infections. Patients present with non-specific symptoms such as prolonged fever, fatigue, weight loss and diarrhoea. Clinical signs are lymphadenopathy, hepatosplenomegaly and anaemia. Generalized umbilicated papular skin lesions can help the clinician narrow down the differential diagnosis. The papules are often located on the face, on the chest and on the extremities. Lung involvement is common and chest radiography may reveal diffuse reticulonodular or alveolar infiltrates.

Diagnosis is made by identification of the fungus by microscopy and culture. Blood, bronchoalveolar lavage fluid, or biopsies of skin, lymph nodes or bone marrow are appropriate clinical specimens. Microscopical examination reveals extracellular and intracellular yeasts. The extracellular forms often have a transverse septum as a result of binary fission.

Treatment is with intravenous amphotericin B for 2 weeks followed by oral itraconazole. Secondary prophylaxis in HIV-infected patients with itraconazole (200 mg od) has been suggested until a CD4-count of ≥100 cells/μL has been maintained for at least 6 months.

Further Reading

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