Metastatic melanoma masquerading as disseminated sporotrichosis

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The incidence of melanoma in the United States has increased between 1975 and 2010 with an estimated 76,100 new cases in 2014. While reasons behind this are controversial, increased recreational exposure to ultraviolet radiation is believed to be an important factor. Although most patients present at an early stage, some present with metastatic disease. The clinical presentation of metastatic melanoma is variable and depends on disease site, burden, and systemic effects. Diffuse melanosis is a rare manifestation of metastatic melanoma that is characterized by diffuse slate-gray discoloration of the skin and mucous membranes as a result of pigment deposition and is associated with poor prognosis. Here, we present a rare case of metastatic melanoma with diffuse melanosis that was initially diagnosed as disseminated sporotrichosis based on a false-positive serologic test and discuss the possible mechanism behind this observation.

Case presentation

In November 2013, a 66-year-old man presented with lethargy and confusion, which had been ongoing for 2 weeks. The results of a physical examination showed a striking diffuse slate-gray discoloration of the skin and mucous membranes, distended abdomen, and bilateral lower extremity edema. His urine was black in color. Laboratory work-up revealed a white blood cell count of 16.8 x 10^3/µL (normal, 4.5-10.9 x 10^3); hemoglobin, 9.9 g/dL (normal, 13.5-17); platelet count, 70 x 10^3/µL (normal, 140-400 x 10^3); creatinine, 2.6 mg/dL (normal, 0.6-1.3); bilirubin, 3.9 mg/dL (normal, 0.3-1.2); prothrombin time, 30 s (normal, 12.3-14.8); and partial thromboplastin time, >200 s (normal, 22-34).

A computerized tomography scan of the abdomen and pelvis showed multiple lytic bone lesions in the lumbarosacral spine and pelvis and multiple heterogeneous splenic lesions. Diagnostic work-up was expanded to include malignancy and invasive infection. A biopsy could not be performed in a timely manner because of the rapid deterioration in the patient's mental and respiratory status and associated high procedural risk. Serum and urine protein electrophoresis did not show a monoclonal protein. His prostate specific antigen level was 10 ng/mL (normal, 0-4). Blood stains and cultures for bacteria, acid-fast bacilli, and fungi were negative. Serologic assays for aspergillosis, coccidioidomycosis, histoplasmosis and blastomycosis were negative. Finally, the laboratory reported a positive Sporothrix schenckii latex agglutination test with a very high titer (1:4096) that was repeated and confirmed. Diagnosis of disseminated sporotrichosis was made and treatment was immediately initiated with intravenous amphotericin B and flucytosine. However, the patient continued to deteriorate, developed multiorgan failure, and died 4 days after presentation.

After obtaining permission from the family, a postmortem examination was performed (Figures 1 and 2), revealing metastatic melanoma in the pulmonary vasculature, liver, gastric mucosa, mesentery, peritoneum, urinary bladder mucosa, prostate and vertebral bones. Furthermore, there was diffuse melanosis in multiple organs and melanin pigment casts within the renal tubules. There was no morphologic evidence of fungal infection and fungal cultures from the blood, cerebrospinal fluid and liver were negative.

Discussion

We present a case of metastatic melanoma with diffuse melanosis, which was misdiagnosed as disseminated sporotrichosis based on a strongly positive anti-S. schenckii antibody latex agglutination test. The mechanism of the false-positive test is...
unknown. We hypothesize that antimelanin autoantibodies might have been present in the patient serum and reacted with *S. schenckii* melanin on the latex particles.

Diffuse melanosis is a rare manifestation of metastatic melanoma. Patients with diffuse melanosis demonstrate extracellular melanin in free form or in melanosomes. Melanin deposits in various tissues and is engulfed by macrophages. Skin deposition results in a characteristic slate-gray hue and excretion in the urine may cause cast nephropathy and black urine (melanurea). The pathogenesis of diffuse melanosis is debated. Elevated levels of melanocyte peptide growth factors appear to play an important role in melanocyte proliferation and excessive melanin production.

The latex agglutination test used in our case (Immuno-Mycologics Inc, Oklahoma, USA) is based on the principle that *S. schenckii*-coated latex particles will agglutinate with specimens containing anti-*S. schenckii* antibodies. Although the sensitivity of the test varies, it has been considered highly specific. As mentioned above, microbiologic work-up and autopsy examination failed to demonstrate any fungal infection in our patient. *S. schenckii* is a pigmented fungus that is known to produce melanin, which can be detected on the surface of the conidia and yeast cells and has an important role in the invasiveness of the organism.

Antimelanin autoantibodies have been detected in patients with metastatic melanoma. It is possible that the false-positivity of the test was a result of cross-reactivity between human antimelanin antibodies and *S. schenckii* melanin. Although this remains hypothetical, we believe it is a plausible mechanism that warrants investigation.

**References**