APMIS ACTA PATHOLOGICA, MICROBIOLOGICA ET IMMUNOLOGICA SCANDINAVICA

APMIS

DOI 10.1111/apm.12694

Letter to the Editor

Erdheim–Chester disease with unusual clinicopathological features complicated by DRESS syndrome, disseminated *Cytomegalovirus* infection and hemophagocytic lymphohistiocytosis

INTRODUCTION

Histiocytic disorders are a group of complex disorders characterized by abnormal functioning of the monocyte–macrophage system. The individual disease phenotype is related to the degree of excessive activation of non-neoplastic cells of the monocyte–macrophage lineage or neoplastic transformation (1). Thus, the clinical manifestation varies from benign self-limiting course to life-threatening disease. In some, the disease under question cannot be definitively categorized into either neoplastic or non-neoplastic. Erdheim–Chester disease (ECD) is an extremely rare form of non-Langerhans cell histiocytosis of unknown etiology (2). The gold standard for diagnosis is a histopathological examination of the affected site supplemented by ancillary studies in an appropriate clinical context (1). We describe a fatal case of ECD wherein the ante-mortem manifestations proved to be a red herring that was resolved only by autopsy.

CASE SUMMARY

A 24-year-old lady in puerperium was referred to our emergency services with a history of fever, rash and jaundice for 2 weeks. Before delivery, she was evaluated at another center for fever, and had received cefpodoxime which led to the development of a generalized blistering rash all over the body. The patient had preterm vaginal delivery 5 days after the development of blisters. At admission in our institute, she was febrile (103^0 F), icteric and had crusting over the skin blisters occupying more than 95% of the body surface area. Her pulse rate was 106/min and systolic blood pressure was 60 mm of Hg. Per-vaginal examination revealed uterus size of 16–18 weeks with blood clots in the uterine cavity. The adnexa were within normal limits. Ultrasonography (USG) and computed tomography (CT) of the abdomen showed hepatosplenomegaly. The cardiovascular, respiratory and central nervous system examinations were within normal limits. The initial suspicion was puerperal sepsis and drug-induced rash. Her blood cultures were negative. Serological tests for Hepatitis B and C virus, and HIV were negative. Investigations for malaria, typhoid and scrub typhus were also negative. Over the due course in the hospital, she developed generalized lymphadenopathy, anemia, thrombocytopenia with deranged coagulogram and eosinophilic leukocytosis (absolute eosinophil count 1.6 × 109/L). Drug reaction (or rash) with eosinophilia and systemic symptoms (DRESS) syndrome was strongly favored. Steroids were administered following which the patient's condition deteriorated further with the development of loose stools, metabolic acidosis, raised lactate levels (1510 U/L, normal range: 240–480), raised serum ferritin (838 pg/mL, normal range 25–240), hypokalemia, hypernatremia, progressive derangement of renal and liver function tests, disseminated intravascular coagulation (DIC), and multiorgan dysfunction syndrome (MODS). Despite best supportive efforts, the patient succumbed to her illness and an autopsy (excluding brain and spinal cord) was performed. The spleen (Fig. 1A), liver and kidneys were enlarged. Microscopic examination revealed sheets of foamy histiocytes and numerous Touton giant cells in the spleen (periarteriolar sheaths) (Fig. 1B–C), liver (portal tract and sinusoids) (Fig. 2A), kidneys (interstitium and around arteries) (Fig. 2B), small and large intestines (mucosa and muscularis propria) (Fig. 2C), lungs (septae and alveoli) (Fig. 3B), lymph nodes (sinuses) (Fig. 2D), bone marrow (Fig. 2E) and uterine cervix (stroma) (Fig. 2F). These cells were positive for CD68 and S100 immunostains (Fig. 1D, E), and negative for CD1a immunostain (Fig. 1F). The affected skin revealed keratinocyte necrosis, apoptosis and separation of epidermis from dermis along with dense mononuclear infiltrate in the superficial dermis (Fig. 3A). The dermatopathologic findings were consistent with erythema multiforme-like DRESS syndrome (3). In addition to the primary pathology, disseminated *Cytomegalovirus* (*CMV*) infection (Fig. 3B) and hemophagocytosis in bone marrow and liver were evident. BRAFV600E mutation study was performed using the DNA extracted from formalin-fixed, paraffin-embedded (FFPE) tissues of all organs with histopathological evidence of infiltration by amplification refractory mutation system polymerase chain reaction (ARMS-PCR) technique. The technique involved amplification of three products in a single reaction tube: a 200 bp common product serving as an amplification control, a 144 bp BRAFV600E specific product and a