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Pathology/Biology Section - 2015

H11 A Case of Lethal Idiopathic Plasmacytic Lymphadenopathy With Polyclonal Hypergammaglobulinemia: A Medical Challenge for the Forensic Pathologist

Giancarlo Di Vella, MD, PhD*, University of Torino, Dept Public Health Sciences, Sezione di Medicina Legale, Corso Galileo Galilei 22, Torino 10126, ITALY; Oronzo Schiraldi, University of Bari, Sez Med Legale Policlinico, Bari 70100, ITALY; Lucia Tattoli, PhD, Sezione di Medicina Legale, University of Bari, Bari, ITALY; and Biagio Solarino, PhD, Università degli Studi di Bari, Sezione di Medicina Legale, P.zza Giulio Cesare, 11, Bari 70125, ITALY

After attending this presentation, attendees will understand that the pathophysiology of Idiopathic Plasmacytic Lymphadenopathy (IPL) is not elucidated sufficiently and further clinical, histological, and immunological studies will be required in the forensic field, especially when medical malpractice is suspected.

This presentation will impact the forensic science community by reporting an uncommon case of lethal IPL with polyclonal hypergammaglobulinemia and renal failure in a young woman in which other differential diagnoses such as collagen, autoimmune, and infectious diseases were ruled out when she was still alive.

IPL was first described by Mori et al. in the early 1980s as a new disease entity resembling the plasma cell type of Castleman's Disease (CD). Both have multicentric lymphadenopathy, prominent polyclonal hypergammaglobulinemia, elevated erythrocyte sedimentation rate, elevated serum interleukin-6 (IL6) concentration, bone marrow plasmacytosis, and various abnormal laboratory data. Nevertheless, CD usually has an aggressive and fatal outcome associated with infectious complications or malignant tumors. IPL has a clonal B-lymphocyte proliferation producing high levels of immunoglobulin and/or their chains which affect the entire body. The clinical features are polymorphic because of the involvement of several organs (skin, and pulmonary, digestive, and renal systems). IPL can be asymptomatic for a long time but can exhibit an unexpected and rapidly fatal course. The treatment of IPL has not yet been established, but the efficacy of corticosteroid treatment, anti-cancer chemotherapy, and monoclonal antibodies has been indicated. Even though IPL is reported in literature, it is rarely recognized clinically and is often first diagnosed after the patient's death as a medical examiner's case for the forensic pathologist, who has to include it in the differential diagnosis of other diseases when medical malpractice is suspected.

This study reports the case of a 40-year-old woman admitted to the emergency room with acute renal failure and hypergammaglobulinemia. She had previously had frequent otitis, pharyngitis, and a poorly defined rheumatic disease. In the last month, she received antibiotics for bronchitis. Multiple myeloma was first suspected. The patient rapidly developed back pain, pericardial effusion, generalized pruritic rash of the face and trunk, splenomegaly (with no liver and lymph node enlargement), and finally coma (after six days). Bone marrow biopsy showed polyclonal plasmacytosis. Multiple myeloma was ruled out as well as infection, collagenopathy, and coagulopathy; therefore, a hypergammopathy due to a proliferative hematological malignancy was suspected. Despite medical efforts, the woman expired nine days after admission. A medicolegal autopsy was performed because of the lack of a diagnosis. The external examination of the body was negative. The autopsy showed brain swelling, pulmonary congestion, pleural adhesions, and hepato-splenomegaly. Histological examination of lymph nodes showed diffuse infiltrates of plasma cell and lymphocytes with features of erythrophagocytosis. Immunohistochemical staining confirmed plasma cells (CD138+) with a prevalence of kappa-positive cells, B (CD20+) cells, and T (CD3+) cells. Kidneys showed advanced glomerulosclerosis containing similar infiltrates. Toxicological analyses were negative. The final cause of death was multiple organ failure due to IPL with polyclonal hypergammaglobulinemia and advanced renal failure. The rapid worsening of the patient's condition did not allow the physicians to make the correct diagnosis. This case was particularly notable for the renal complications resulting from glomerulosclerosis and interstitial infiltration. The exact mechanisms of renal damage in IPL have an unknown etiology. It is supposed that an overproduction of IL6 induces proliferation of mesangial cells and interstitial infiltration of plasma cells. The process can be increased by paracrine or autocrine IL-6. No systematic evaluation of treatment regimens is available because much remains to be discovered about IPL. Possible medical liability associated with failure to diagnose and treat IPL deserves discussion.

IPL, Hypergammaglobulinemia, Autopsy