Short Communication

An Autopsy Case of Disseminated Strongyloidiasis Combined with Cytomegalovirus Infection

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SUMMARY: We report a rare autopsy case of disseminated strongyloidiasis combined with cytomegalovirus co-infection involving a 68-year-old man, who was originally from Okinawa Prefecture in southern Japan, where strongyloidiasis occurs sporadically among the elderly. This patient was admitted with a diagnosis of drug eruption and hypeeosinophilic syndrome. He was administered steroid therapy, but suffered complications of fever, respiratory distress, and pulmonary hemorrhaging. The autopsy findings showed disseminated strongyloidiasis in the alveolar spaces and the intestine and cytomegalovirus inclusion body foci in the lungs.

Strongyloides stercoralis is widely distributed in tropical and subtropical areas (1). However, although strongyloidiasis is rare in mainland Japan, it has been reported in 3.4% of the population of Okinawa Prefecture (2). Most individuals infected with intestinal strongyloidiasis are asymptomatic or suffer only mild gastrointestinal symptoms. Occasionally, however, fatal cases involving massive systemic migration by the larval stage of the parasite have been reported in immunocompromised hosts (3). Herein we present an autopsy case of disseminated strongyloidiasis combined with cytomegalovirus (CMV) foci. To the best of our knowledge, this is only the fourth such report.

A 68-year-old man, originally from Okinawa Prefecture in southwest Japan, was admitted to the Department of Cardiology at our hospital because of congestive heart failure (CHF), mitral valve regurgitation, and significant eosinophilia (1,925/mm³) with a normal leukocyte count (7,700/mm³) one month prior to his current admission. He was prescribed allopurinol and furosemide for hyperuricemia and CHF respectively.

One month after being discharged, he complained of systemic skin eruptions and marked eosinophilia. He was admitted and diagnosed with drug eruption and underwent oral steroid therapy at the Department of Dermatology (prednisolone, 60 mg/day). The following abnormal laboratory data were found on admission: leukocytes, 15,700/mm³; eosinophils, 10,911/mm³; aspartate aminotransferase (AST), 52 U/ml; lactate dehydrogenase (LDH), 422 IU/l; alkaline phosphatase (ALP), 892 IU/l; blood urea nitrogen (BUN), 48.1 mg/dl; and creatinine (Cr), 2.04 mg/dl. Although his level of consciousness declined, necessitating intubation, and he was administered steroid pulse therapy for acute respiratory distress syndrome. He died on the 43th day after admission. Only autopsy of the thoracic and abdominal organs was permitted. His family gave their informed consent for this study.

The autopsy specimens were fixed in 10% formalin and embedded in paraffin. Tissue sections (thickness, 4 μm) were stained with hematoxylin and eosin (HE). Immunohistochemical studies were performed using anti-CMV antibody (monoclonal mouse, code M0854, clones DDG9/CCH2; Dako, Glostrup, Denmark). The secondary biotin- and streptavidin-conjugated antibodies in the kit were reacted for 20 min each. Finally, visualization was performed using 3,3'-diaminobenzidine (Roche, Basel, Switzerland), and counterstaining was performed with hematoxylin.

The patient’s voluminous lungs weighed 1,110 g (left) and 1,050 g (right), and extensive hemorrhaging was detected in all lobes. Microscopically, the lungs showed marked hemorrhaging in the alveolar spaces and focal hyaline membrane; the detection of scattered mononuclear cells indicated acute interstitial pneumonia. Filariform S. stercoralis larvae were observed in the alveolar spaces (Fig. 1A). The gastrointestinal tract showed diffuse erosion and submucosal hemorrhaging, and abundant larval proliferation was observed in the stomach and duodenum (Fig. 1B), jejunum, ileum, and colon. Adult female S. stercoralis covered with a thick cuticle, measuring up to 1–2 mm in length, and possessing an esophagus, intestine, and paired ovaries were observed in the above sections. Filariform S. stercoralis larvae had migrated to the submucosal, muscle, and subserosal tissue, as well as the lymphatic channels (Fig. 1C). These larvae were obtained from a postmortem intestinal mucosal specimen fixed by formalin (Fig. 2A), where the characteristic notched end of the larval tail was observed (Fig. 2B). A small number of typical CMV viral inclusion bodies were also observed in the alveolar epithelium (Fig. 2C). Viral inclusion bodies were identified by anti-CMV antibody in the immunohistochemistry study (Fig. 2D). A small number of CMV inclusion bodies were also observed in the cecum and liver. No obvious eosinophilic infiltration was noted in other organs.

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Fig. 1. (A) Microscopic appearance of the lungs with pulmonary hemorrhage. The *S. stercoralis* larva in the alveolar spaces (arrow, ×200). HE staining. Sections of the intestine: (B) filariform *S. stercoralis* in the duodenal lumen (×200) and (C) lymphatic penetration in the cecum by *S. stercoralis* (×200). HE staining.

Fig. 2. (A) The filariform *S. stercoralis* larva obtained from postmortem intestinal mucosal specimen fixed by formalin (×200). (B) The unique notched end of larval tail was seen (×400). Microscopic appearance of the lungs: (C) cytomegalovirus (CMV) inclusion body: an intranuclear inclusion body surrounded by a halo and granular cytoplasm (×400) in the alveolar space. HE staining. (D) Immunohistochemical staining for CMV showing a positive reaction (×400).
S. stercoralis is uniquely capable of penetrating both soil and human host tissue (1). Indeed, under appropriate soil conditions, free-living adult worms can produce rhabditiform larvae which, after undergoing several molts, become filariform larvae that are capable of infecting humans. The parasites enter the lymphatic system and blood vessels through the skin and are then carried through the right heart to the lungs, where they penetrate the alveolar spaces. The worms are expelled through the larynx and then swallowed. The adult females burrow into the mucosal folds of the duodenum, where they lay eggs. These eggs subsequently develop into rhabditiform larvae. As these rhabditiform larvae transverse the intestinal tract, some of them metamorphosize into the infective filariform larvae. These may then penetrate the gut or perianal skin, thereby completing the internal migration into the infective filariform larvae. These may then penetrate the gut or perianal skin, thereby completing the internal cycle. This process is known as autoinfection. Disseminated strongyloidiasis is frequently fatal, with a mortality rate of up to 60% (4). This case is noteworthy for two reasons. First, strongyloidiasis is frequently fatal, with a mortality rate of up to 60% (4). This case is noteworthy for two reasons. First, strongyloidiasis combined with CMV infection has only been reported in three previous cases (6–8). In the first case report, the strongyloidiasis combined with CMV was detected in a biopsy specimen of the stomach and proven by immunohistochemical analysis. The second case report only described the CMV and did not provide histological images. The third case was an autopsy study of the lungs in which HE staining was performed but immunohistochemical analysis was not.

These cases of strongyloidiasis combined with CMV may have coincided with infections requiring steroids. Our case involved a detailed systemic autopsy examination, and we proved the presence of CMV using an immunohistochemical study. CMV inclusion bodies are usually identified by HE staining, whereas immunohistochemical techniques are useful for detecting the approximate locations of viral inclusion bodies (9).

The other reason why our study is significant is that one of the most significant causes of death in strongyloidiasis is marked intra-alveolar hemorrhaging. Kinjo et al. reported four cases of disseminated strongyloidiasis involving extensive intra-alveolar hemorrhaging, including two acute cases that received steroids (10). These cases demonstrated no inflammatory infiltration, abscesses, or granuloma in the lungs, thereby suggesting that the vascular damage that follows infection is mediated by an immunologic mechanism (5,10).

In addition, we examined our patient’s serum, which was sampled from his postmortem blood, for human T-lymphotropic virus 1 (HTLV-1) antibody and found it to be positive. Hirata and Uchima reported a cohort study of strongyloidiasis in which they estimated that the risk of developing strongyloidiasis is twice as high among HTLV-1 infected people than among healthy controls (11).

Finally, this case also involved asymptomatic hypereosinophilia and drug eruption. In the majority of cases involving hypereosinophilia, the diagnosis will ultimately be allergy and parasitosis. Other less frequent causes of hypereosinophilia include chronic eosinophilic leukemia, Hodgkin’s lymphoma, cutaneous T-cell leukemia, systemic vasculitis, connective tissue diseases, infectious diseases such as scabies, allergic bronchopulmonary aspergillosis, or endocrine diseases such as adrenal insufficiency. According to recently issued guidelines, unexplained peripheral eosinophilia is indicated for screening for asymptomatic strongyloidiasis, especially in immunosuppressed patients who have resided in, or travelled to, areas where strongyloidiasis is endemic (12). S. stercoralis infection should be considered in immigrants and travelers with eosinophilia or compatible symptoms coming from endemic areas (13).

On his last admission, our patient was found to be suffering from an allergic reaction (skin eruption) to allopurinol, which is frequently used in the treatment of hyperuricemia. On admission, a dermatologist and pathologist diagnosed his skin eruption by skin biopsy, the results of which were consistent with drug eruption, and no evidence of strongyloidiasis skin migration was found. We believe that the premortem diagnosis of drug eruption was appropriate, but it is difficult to rule out disseminated strongyloidiasis from occult strongyloidiasis because of the absence of abdominal symptoms. It is suggested that the disseminated strongyloidiasis was induced by the steroid therapy. Autopsy was necessary to diagnose strongyloidiasis combined with hypereosinophilia and intra-alveolar hemorrhaging in this case, which is probably the first case of strongyloidiasis combined with CMV infection to be diagnosed by a systemic autopsy examination involving immunohistochemistry.

Conflict of interest None to declare.

REFERENCES