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Short Communication

Eosinophilic Pneumonia Due to Visceral Larva Migrans Possibly Caused by *Ascaris suum*: a Case Report and Review of Recent Literatures

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SUMMARY: We report the case of a 62-year-old man who developed eosinophilic pneumonia due to visceral larva migrans (VLM) that was possibly caused by *Ascaris suum*. The patient, a resident of the middle Kyushu area who was fond of eating raw porcine liver, complained of dry cough without dyspnea. The chest radiography showed a migration of infiltrative shadow. Transbronchial lung biopsy of the right middle lobe revealed massive infiltration of eosinophils. The multi-dot enzyme-linked immunosorbent assay (ELISA) and microtiter plate ELISA showed positive results for *A. suum*; therefore, the patient was diagnosed with VLM caused by *A. suum*. The patient was administered albendazole (600 mg/day) for 28 days; he recovered successfully with no adverse effects except mild liver dysfunction. Several cases of VLM caused by *A. suum* have been reported in Japan, with a majority of the cases being reported in Kyushu. Careful history taking of the patient's area of residence and dietary habit is essential for the diagnosis of this parasitic disease with underestimated prevalence.

Visceral larva migrans (VLM) caused by *Ascaris suum* is a major parasitic infection that especially affects people living in southern Kyushu, Japan, which has a prominent livestock industry (1). *A. suum* infects pigs, and 30% of all the pigs in southern Kyushu are infected (2). Humans are usually infected when they eat the raw liver or meat of infected cattle or chicken or fresh vegetables grown in soil fertilized with porcine excrement contaminated with *A. suum* eggs. In humans, the larvae of *A. suum* migrate to various organs and cause a wide variety of nonspecific symptoms such as general malaise, cough, liver dysfunction, hypereosinophilia with hepatomegaly and/or pneumonia (3,4). Here, we report a case of eosinophilic pneumonia resulting from VLM that could have been possibly caused by *A. suum*, and present a review of the recent literature on VLM.

A 62-year-old man living in Shimabara, Nagasaki Prefecture, Kyushu, Japan, was referred and admitted to Izumikawa Hospital because he had dry cough and chest radiography had shown an infiltration shadow in both lungs. All in one cold and flu capsules prescribed in a previous clinic had not been effective. The patient complained of dry cough without dyspnea at the time of admission. He had no remarkable underlying diseases, although he possessed a unique dietary habit such as eating raw porcine, chicken, and cattle livers.

At the time of admission, the vital signs of the patient were as follows: body temperature, 36.8°C; heart rate, 72 beats/min (regular rhythm); respiratory rate, 16 breaths/min; and blood pressure, 110/60 mmHg. Auscultation revealed no abnormal pulmonary crackles or heart sounds. The patient showed no clinical signs of lymphadenopathy, hepatosplenomegaly, and pretibial edema.

Chest radiography showed an infiltrative shadow in both the middle and lower lung fields (Fig. 1A), and computed tomography (CT) showed consolidation with ground-glass opacity in both lung fields (Fig. 1B and 1C). The laboratory test results were as follows: leukocytes count, $9.5 \times 10^3/\mu L$; eosinophil count, $2{,}175/\mu L$ (22.9%); C-reactive protein (CRP) concentration, 0.4 mg/dL; and IgE level, 333.2 IU/mL. All other results were within the normal range. The results of the arterial blood gas (ABG) analysis at room air were as follows; pH, 7.404; PaO_2, 72.6 Torr; and $PaCO_2$, 40.8 Torr. Routine microbiological tests revealed no causative bacteria. Bronchoscopy was performed and the bronchoalveloar lavage (BAL) fluid was analyzed; the results of the cell count analysis were as follows: alveolar macrophages, 2%; eosinophils, 93%; lymphocytes, 3%; and basophils, 2%. No microorganisms, including fungi and mycobacteria, could be isolated from the BAL fluid in routine microbiological tests. Although the polymerase

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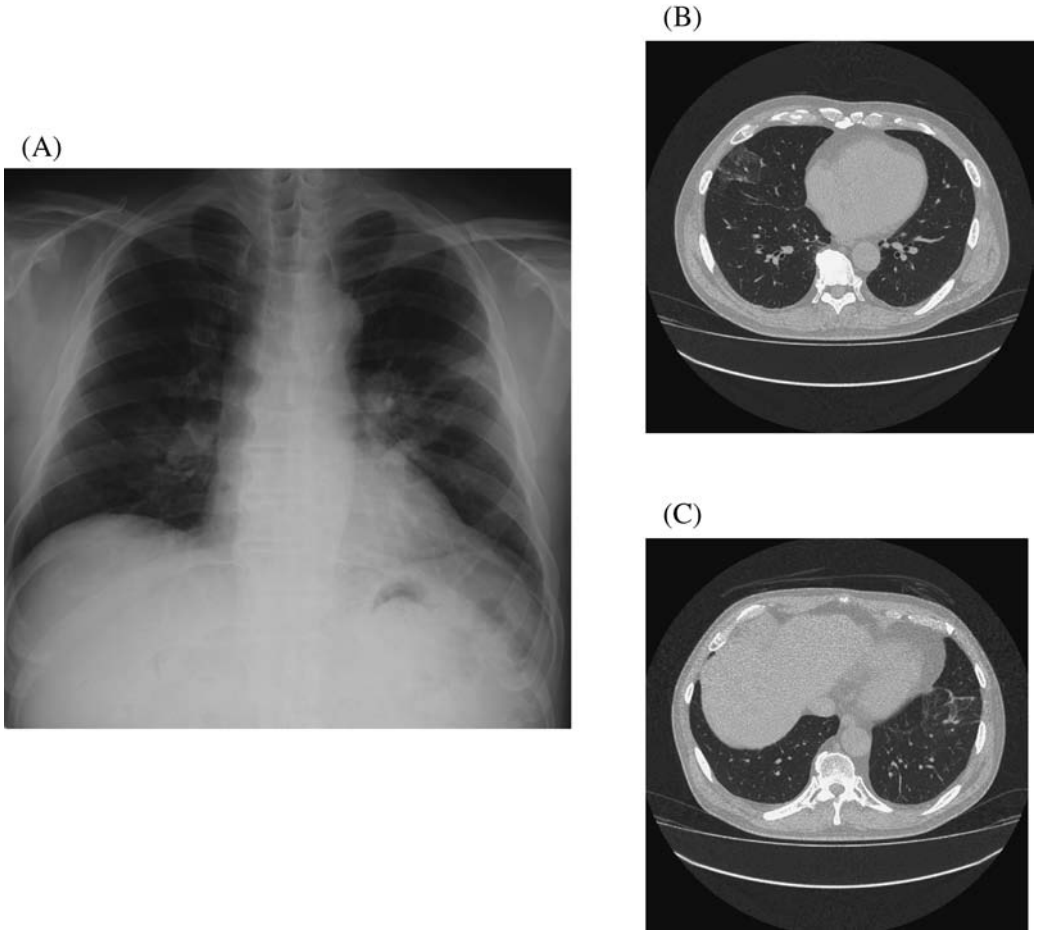

Fig. 1. Chest X-ray films on admission. (A) Chest X-ray film showing infiltrative shadow in both middle and lower lung fields. (B) and (C) CT scan images showing consolidation with ground-glass opacity at right upper lobe and left lower lobe.

chain reaction test for mycobacteria showed positive results for *Mycobacterium intracellulare*, an 8-week culture of the BAL fluid sample showed negative growth. Transbronchial lung biopsy of the right middle lobe (B_4) revealed massive infiltration of eosinophils in the parenchyma and that of alveolar macrophages in the alveoli. Eosinophilic pneumonia was diagnosed on the basis of the results of this pathological analysis (Fig. 2). Multi-dot enzyme-linked immunosorbent assay (multi-dot ELISA) was performed for detecting anti-parasitic antibodies in the patient's serum (5). A serum sample of the patient showed positive results for *Dirofilaria immitis, A. suum*, and *Gnathostoma doloresi* but negative results for *Toxocara canis* (the test was not performed for *T. cati*). A microtiter plate-ELISA for the semi-quantitative measurement of the antibodies for the three parasites (6) was performed, and the strongest reaction was observed for *A. suum* antibodies. Since the patient had a history of eating raw porcine liver, we diagnosed his condition as eosinophilic pneumonia due to VLM that was possibly caused by *A. suum*.

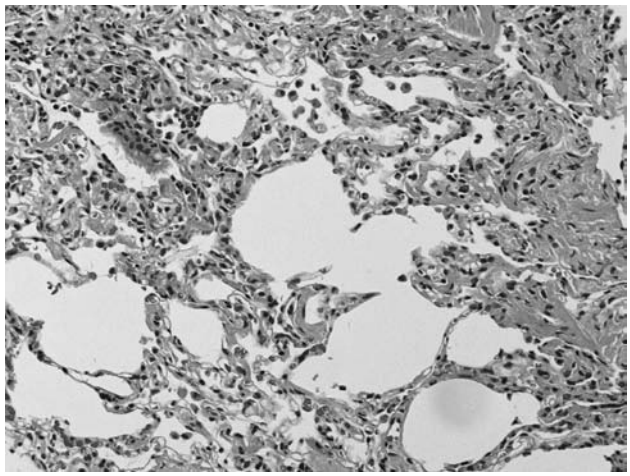

Fig. 2. Pathology of transbronchial lung biopsy from the right middle lobe (right B_4) demonstrates severe eosinophil infiltrations in lung parenchyma. HE stain, ×40.

The patient received no treatment during an observation period of 17 days after the diagnosis of VLM, and the clinical symptoms and signs such as cough and hypereosinophilia persisted. Chest radiography performed on day 17 after the admission showed that the infiltrative shadow in the right middle and lower lung fields had migrated, and CT showed new consolidation with ground-glass opacity in the right upper and lower lobes of the lungs (Fig. 3A, 3B, and 3C). The patient was administered albendazole (600 mg/day) for 28 days. The clinical symptoms resolved completely, and the eosinophil count decreased to 390/μL. The infiltra-

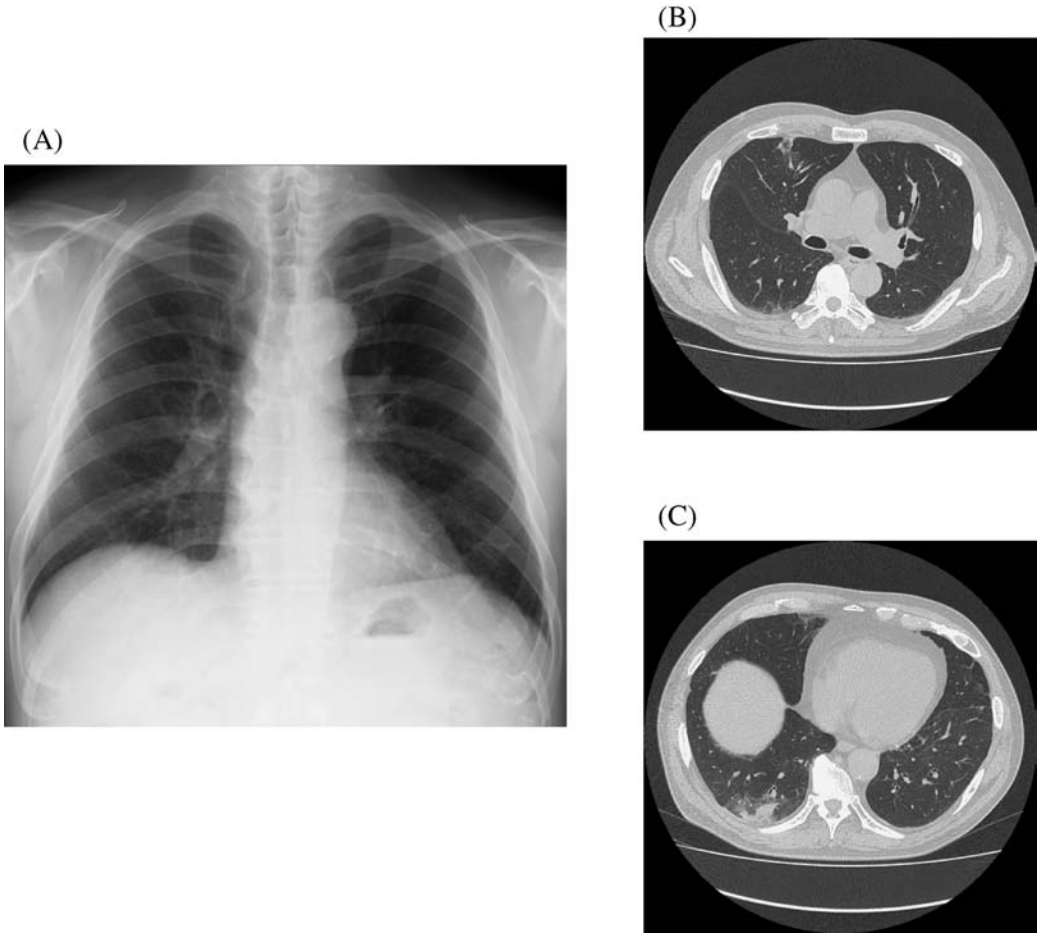

Fig. 3. Chest X-ray films before albendazole treatment (17 days after admission). (A) Chest X-ray film showing infiltrative shadow in right middle and lower lung fields and migrated from the time of admission. (B) and (C) CT scan images showing new consolidation with ground-glass opacity at right upper and lower lobes.

tive shadow disappeared completely in 28 days. No adverse effects except mild liver dysfunction were noted during the 28 days. No recurrence was observed after discharge.

VLM was first described by Beaver et al. in 1952 and is mainly caused by *T. canis* and *T. cati* (3,7). Humans become infected when they ingest *Toxocara* eggs. *A. suum* is also a known cause of VLM (8), especially in Kyushu, Japan, because the residents of this region eat the raw meat and liver of cattle, poultry, and horse or fresh vegetables cultivated using organic fertilizers (9).

VLM as a zoonosis has emerged as a clinical concern because of an increase in the number of dogs and cats kept as pets in Japan. People who have a habit of eating the raw meat of wild animals are at risk of infection with parasitic worms. The current trend of eating fresh vegetables as a part of a healthy lifestyle also increases the risk of infection with parasitic worms since fresh vegetables may be contaminated with them.

A definitive diagnosis of VLM is possible only if the larvae of *Toxocara* or *Ascaris* are found in the patient's body; however, detecting these larvae is quite difficult and not practical. To date, no suitable or applicable molecular methods are available for accurately detecting the genomic DNA of parasites. The multi-dot ELISA method (5), performed using the patient's serum sample, is a useful and convenient tool for diagnosing VLM. Although it is a simple method, cross-reactions among the parasite antigens have been observed. Therefore, a definite diagnosis of VLM cannot be made unless the larvae or DNA of the causative organism, such as *Toxocara* or *Ascaris*, is detected in the patient's body. Information such as the patients' area of residence and their dietary habits should be obtained and carefully evaluated by attending physicians.

An outbreak of VLM caused by *A. suum* in Japan was reported by Maruyama et al. (6) in 1996, with a total of 17 patients with pronounced eosinophilia and high antibody titers against the *A. suum* antigen. A review of recent literature on *A. suum* cases showed that at least 9 cases of VLM in Japan were reported in various journals after 1996 (Table 1). All the patients, except 2, were infected in the Kyushu island, and possible sources of infection were the raw meat of chicken, boar, deer, and cattle (5 patients); vegetables (2 patients); raw meat of poultry or horse, raw liver of cattle or vegetables cultivated using organic fertilizer (1 patient); and unknown (1 patient). Because the eggs of *A. suum* could not be detected in these possible sources, the apparent source and route of infection were not confirmed. Almost all the patients showed high levels of serum IgE and hypereosinophilia. Albendazole and ivermectin were administered and were effective in 7 patients and 1 patient, respectively. Only one patient was diagnosed

Table 1. Summary of cases of visceral larva migrans due to *Ascaris suum* in Japan

Study (ref. no.)	Year	Age (y)	Sex	Place	Case	Possible source of *A. suum*	Eosinophil (/μl)	Serum IgE (IU/ml)	Treatment
Matsushita et al. (12)	1997	70	Female	Miyazaki, Kyushu	Eosinophilic pneumonia, + intrahepatic lesion	Raw chicken	9,440	7,022	Albendazole
Takeyama et al. (13)	1997	56	Female	Kyushu	Eosinophilic colitis	N.A.	7,872	10,960	Predonisolone
Matsuyama et al. (14)	1998	46	Male	Kagoshima, Kyushu	Eosinophilic pneumonia	Fresh vegetables cultivated using pig manure	9,188	3,190	Ivermectin
Arimura et al. (15)	2001	26	Male	Miyazaki, Kyushu	Pulmonary nodule	Raw boar, deer meat	750	926	Albendazole
Arimura et al. (15)	2001	57	Male	Miyazaki, Kyushu	Pulmonary nodule	Raw chicken, turkey	342	832	Albendazole
Sakakibara at al. (16)	2002	32	Male	Aichi, Honsyu	Eosinophilic pneumonia, + intrahepatic lesion	Fresh vegetables cultivated using organic fertilizer, raw meat of cattle liver, poultry meat, horsemeat	10,773	20,284	Albendazole
Sakurai et al. (17)	2003	25	Female	Tokyo, Honsyu	Eosinophilic pneumonia	Raw liver of caw	7,290	98	Albendazole
Tokojima et al. (18)	2004	50	Male	Kagoshima, Kyushu	Eosinophilic pneumonia	Vegetables	445	1,208	Albendazole
Hirakawa et al. (19)	2009	64	Male	Kagoshima, Kyushu	Eosinophilic pneumonia	Raw chicken liver	4,223	279	Albendazole

All cases are diagnosed with multi-dot enzyme-linked immunosorbent assay.
Outcome of all cases are cured.
N.A., not available.

with eosinophilic colitis and was administered predonisolone but not albendazole.

In the present case, the follwoing clinical signs were consistent with those of VLM: (i) remarkable eosinophilia and high IgE levels, (ii) positive results in the multi-dot ELISA and the strongest reaction for the antibody for *A. suum*, in microtiter plate-ELISA, (iii) migration of the pulmonary infiltrates, and (iv) eosinophilic pneumonia, as diagnosed on the basis of the results of BAL fluid analysis and transbronchial lung biopsy. Although there is little evidence in favor of any treatment modality for VLM caused by *A. suum*, administration of albendazole or ivermectin for 2 to 3 weeks is recommended (10,11). The patient was administered albendazole (600 mg/day) for 28 days, and he showed no remarkable adverse effects except mild impairment of liver function (a common adverse effect of albendazole). Although most of the cases of VLM caued by *A. suum* are not fatal, VLM could sometimes become life threatening if a large number of *A. suum* eggs are ingested (8). It is important for clinicians to consider VLM caused by *A. suum* in case a patient presents hypereosinophilia, high IgE levels, and a migrating pneumonia shadow in addition to various nonspecific symptoms. Careful history taking of the patients' area of residence and dietary habit is essential for the diagnosis of this parasitic disease with underestimated prevalence. Furthermore, although VLM caused by *A. suum* is most prevalent in Kyushu, a couple of VLM cases have been reported in the Honshu region as well (Table 1). Owing to advances in mass-transportation of fresh vegetables and meat and improvement of the related logistics, cases of such originally localized parasitic infections are now being detected in other areas of Japan and even in other countries.

Conflict of interest None to declare.

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