competitor for host cell receptors, possibly interfering host immune response to the worms (Loukas and Maizels 2000; Loukas and Prociv 2001). As-CTL-1 might be able to bind to ligands for mammalian CTL, such as NK receptors and/or macrophage/dendritic cell receptors (Osorio and Reis e Sousa 2010; Sun and Lanier 2011). In the present study, As-CTL-1 showed high similarity to *Tc*-CTLs and specific expression in LL3 and cL4, both of which were exposed to attack by host immune responses. Considering these findings, *A. suum* larvae might interfere with host inflammation processes by As-CTL-1 to avoid protective immune responses in infected animals during tissue migration. Further study on functional aspects of this molecule will identify novel dimensions of the host–parasite relationship and the significance of tissue migration in ascarid infection.

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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 × $10^3/\mu L$; eosinophil count, 2,175/μL (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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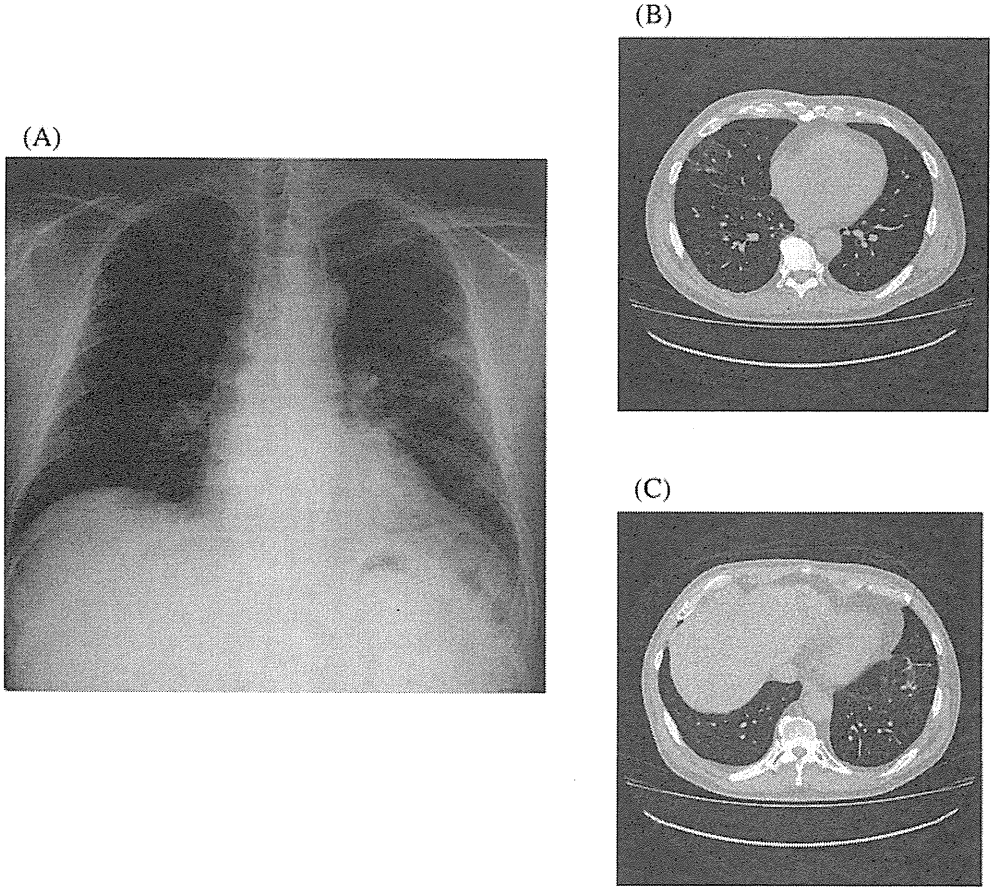

Fig. 1. Chest X-ray films on admission. (A) Chest X-ray film showing infiltrative shadow in both middle and lower lung fields. (B) and (C) CT scan images showing consolidation with ground-glass opacity at right upper lobe and left lower lobe.

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*.

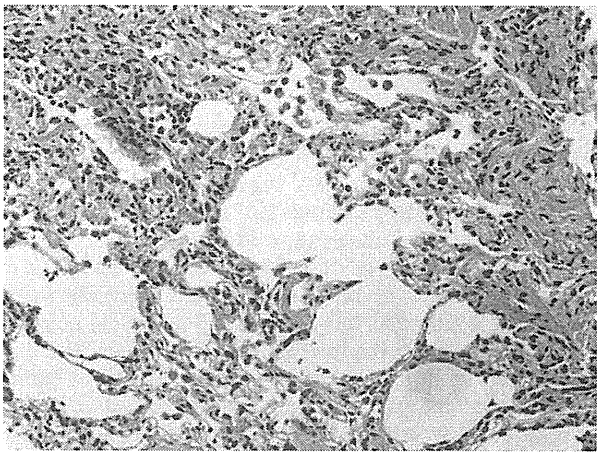

Fig. 2. Pathology of transbronchial lung biopsy from the right middle lobe (right B_4) demonstrates severe eosinophil infiltrations in lung parenchyma. HE stain, ×40.

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-

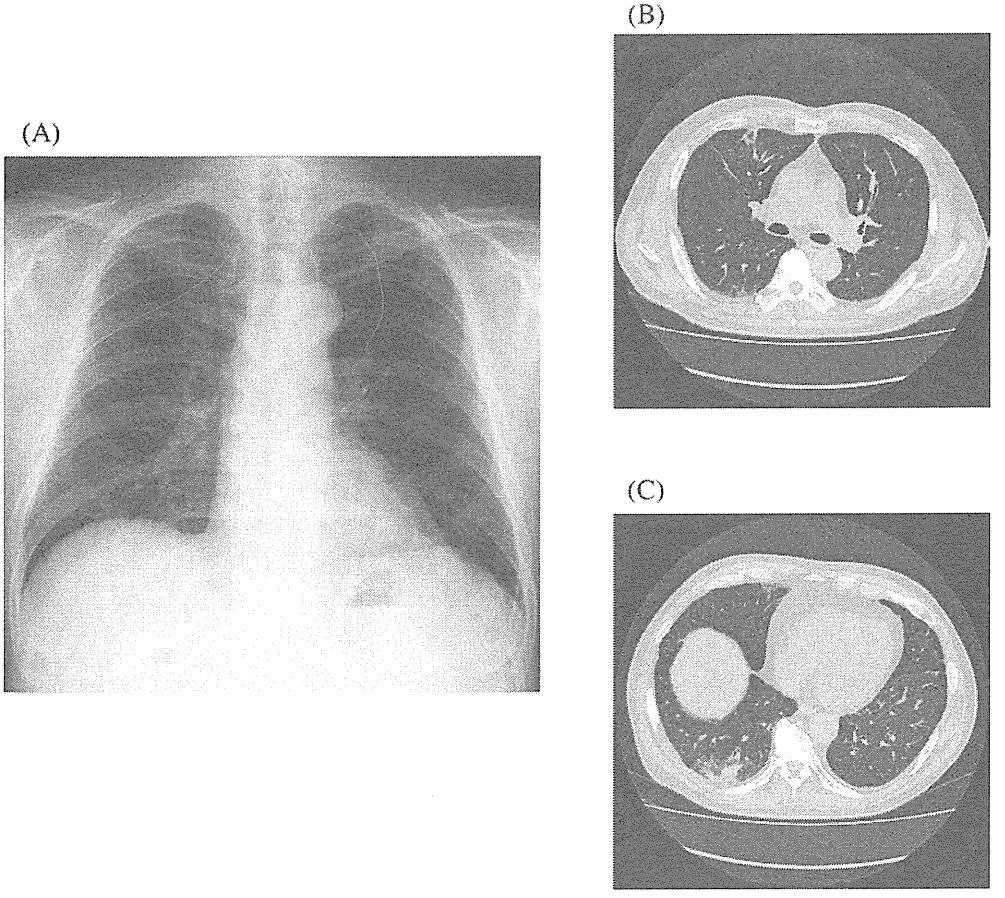

Fig. 3. Chest X-ray films before albendazole treatment (17 days after admission). (A) Chest X-ray film showing infiltrative shadow in right middle and lower lung fields and migrated from the time of admission. (B) and (C) CT scan images showing new consolidation with ground-glass opacity at right upper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

A patient who developed toe necrosis due to poor blood circulation after an interdigital tick bite

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KEYWORDS
Tick bite;
Toe necrosis;
Thrombogenic vasculopathy

Summary A 71-year-old female had worked on a farm in the mountains and noticed itching of the left 3rd toe. She visited a local hospital due to a color change to purple in this area. Attachment of a tick was observed between the left 2nd and 3rd toes, and it was extracted. However, due to persistent pain, she was referred to our department of cardiovascular medicine for close examination and treatment. Lower extremity angiography showed that vascular visualization was poor in the area supplied by the arteries distal to the tick bite site, but the other blood vessels of the toe were clearly visualized. Toe amputation was performed and pathological examination of a surgical specimen revealed that most blood vessels near the necrosis were occluded by thrombi. We speculated that tick bite reactions were associated with thrombogenic vasculopathy. This report shows a patient who developed toe necrosis due to poor blood circulation after an interdigital tick bite.

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Introduction

Tick bites are relatively frequently encountered in daily clinical practice. Most patients with tick bites develop dermatitis, but some develop Japanese spotted fever or Lyme disease via the bite. However, there have been no reports of peripheral necrosis due to poor blood circulation following tick bites. We report a patient who developed toe necrosis due to poor blood circulation after an interdigital tick bite.

Case report

A 71-year-old female had previously been healthy, and, although she had annually undergone a human dry dock, no abnormalities had been detected. She had worked on a farm in the mountains on June 7, 2009, noticed itching of the left 3rd toe on June 12, and visited a local hospital due to a color change to purple in this area on June 16. Attachment of a tick was observed between the left 2nd and 3rd toes. The tick was extracted, and minocycline was prescribed. However, due to persistent pain, she was referred to our department of cardiovascular medicine for close examination and treatment on June 23. She was obese, but had no history of smoking, hypertension, diabetes mellitus, or lipid abnormalities. The bilateral dorsalis pedis and posterior tibial arteries were palpable, and the skin temperature of the foot was normal. There was a decrease in the skin temperature, loss of sensation, and a color change to black distal to the middle phalanx of the left 3rd toe (Fig. 1A). The area between the 2nd and 3rd toes as the site of the tick bite showed erosion, but not redness or swelling (Fig. 1B). No eruptions were observed in the other areas. The thermography (Fig. 1C) showed an increase in the skin temperature in the left compared with the right foot. In the portion peripheral to the proximal interphalangeal joint of the left 3rd toe, the skin temperature showed a decrease in the area corresponding to that showing black necrosis. Lower extremity angiography (Fig. 1D) was performed with selective enhancement of the left external iliac artery. The area extending to the plantar artery and arch was clearly visualized, and no atherosclerotic changes were identified. Vascular visualization was poor in the area supplied by the arteries distal to the tick bite site, but the other blood vessels of the toe were clearly visualized. She was referred to the department of plastic surgery of our hospital on July 3, and toe amputation was considered to be indicated. On July 24, toe amputation was performed (Fig. 2A and B). Pathological examination of a surgical specimen revealed necrosis of the toe tip, and most blood vessels near the necrosis were occluded by thrombi. Between fat tissues, foam cells aggregated, and marked eosinophil infiltration was observed. There were no findings of angiitis (Fig. 2C and D). Her postoperative course was favorable. After walking became possible, she was discharged on August 4.

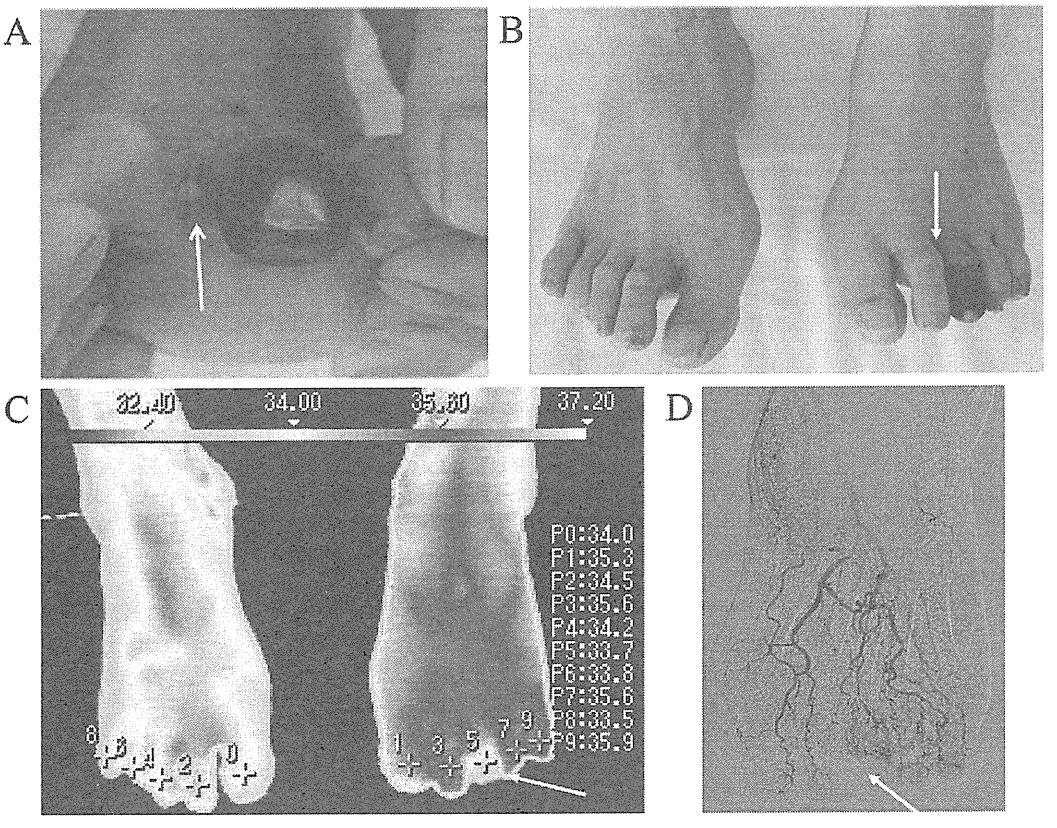

Figure 1 (A and B) Photo of the left toes (white arrow: tick bite site). (C) Thermography (white arrow: a decrease in the skin temperature was observed in the area corresponding to the site of black necrosis). (D) Lower extremity angiography (white arrow: blood flow interruption was confirmed in the area corresponding to the site of black necrosis).

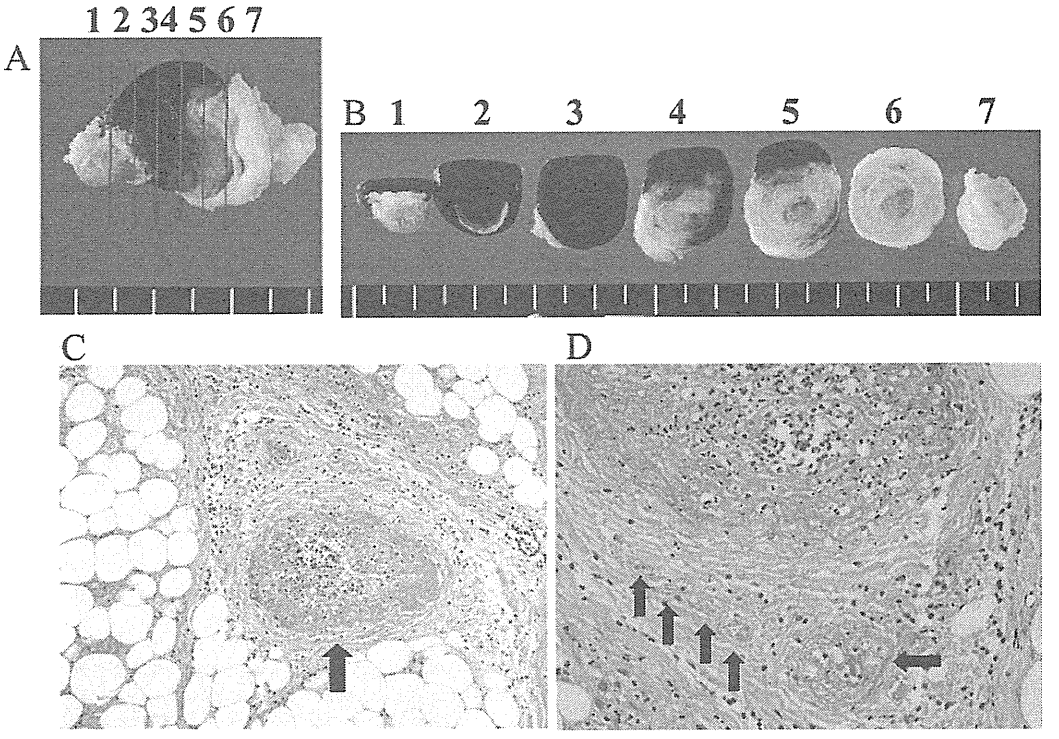

Figure 2 (A) Surgical specimen. (B) Cross-section of the surgical specimen. (C) Image of the pathological specimen (Cross-section 4, black arrow: blood vessels near the necrosis were occluded by thrombi. In the vascular lumens, granulomatous tissue formed, but reperfusion was observed in some parts. Hematoxylin-eosin staining). (D) Image of the pathological specimen (Cross-section 4, black arrows: microscopic vessels occluded by thrombus, hematoxylin-eosin staining).

Discussion

When this patient visited our department, about 2 weeks had passed since the tick bite. Since she had already been treated by a local doctor, and the tick had been extracted, we could not directly confirm the tick. However, in the southern part of Tokushima Prefecture where she lives, tick bites are often observed, and so the diagnosis of a tick bite made by the previous doctor may be accurate. There has been a report [1] of patients with tissue necrosis in a tick bite area, but no report of patients with necrosis distance from the bite site. Previous studies have shown blood coagulation responses as biological responses to ticks [2] and pathologically confirmed thrombi in about 66% of tick bite areas [3]. Histopathological examination in our patient showed the occlusion of many blood vessels by thrombi in the area near necrosis and the presence of necrosis peripheral to these thrombi. In general, tick bites lead to reactions such as the extravascular leakage of dermal erythrocytes, hardening of collagen fibers, epidermal necrosis, ulceration, dermal neutrophil infiltration, and thrombosis [3]. However, the saliva of ticks contains anti-hemostatic factors and immunosuppressive and anti-inflammatory components, which make tick removal difficult, facilitating long-term blood-feeding [4]. The intractability of areas bitten has been suggested to be associated with the formation of a foreign body granuloma due to remnant tick mouth parts, impairment of the wound healing process by fibrosis-promoting factors contained in the saliva, and ischemia in the wound area due to various types of local microvasculitis [5]. Since no pathological examination of the tick bite area was performed, detailed findings of this area such as the possible presence of thrombi could not be obtained. However, we speculated that thrombi induced by the tick bite caused peripheral embolism, and impaired peripheral blood circulation resulted in necrosis. We supposed that the involvement of angiitis was probably denied because the value of myeloperoxidase – antineutrophil cytoplasmic antibody was very small. Additionally, we denied the presence of shaggy aorta which was associated with blue toe syndrome by use of contrast-enhanced computed tomography. Coronary angiography was also performed in this patient, but showed no findings of stenosis. Lower extremity angiography also revealed no atherosclerotic findings anywhere except the occluded areas, most strongly suggesting the involvement of thromboembolism. Therefore, tick bites in areas with a few collateral circulation routes are associated with a risk of peripheral necrosis, and require caution. The thermography showed an increase in the foot skin temperature on the affected side. This may be an immune response or biological response such as vascular dilation in the central area due to impaired peripheral blood circulation, but the details were unclear. Dermatitis due to tick bites is often encountered in clinical practice. The most interesting point is the difference between patients with dermatitis not inducing serious conditions and those such as in the present patient who develop marked thrombotic circulatory impairment. Although an intractable case showing

local periarteritis nodosa after a tick bite to the thigh has been reported [6], peripheral necrosis was not induced in this case. We speculate that the degree of a host's immune tissue responses to ticks and the bite site are important factors associated with whether necrosis is induced. Tick bites in the peripheral areas of the four limbs, as in this patient, have the potential to induce necrosis because there are only a few collateral circulation routes, and so require caution. The characteristics of cases that show marked immunohistological responses at the tick bite site are unclear. A previous study showed that inflammatory reactions became marked, and severe inflammatory cell infiltration was histologically confirmed with an increase in the frequency of tick biting [7]. Our patient had no history of treatment for tick bites, but was a farmer, and so it is likely that she had a history of untreated asymptomatic tick bites. Concerning the association with background factors such as the residence, sex, and age, we have encountered no patient with tick bites leading to peripheral necrosis, and, therefore, could not perform statistical analysis. In the future, the accumulation of data on patients with similar necrosis may allow the clarification of more detailed mechanisms of peripheral necrosis.

We encountered a patient who developed toe necrosis due to poor blood circulation after a tick bite. We speculated that tick bite reactions were associated with thrombogenic vasculopathy. Tick bites in peripheral areas of the four extremities with only a few collateral circulation routes are associated with a risk of peripheral necrosis, and careful observation of the course is necessary.

Acknowledgments

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症例報告

好酸球増多を伴った糞線虫症の1例

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要　旨

症例は78歳女性．2008年6月乾性咳嗽と38℃の発熱があったため，当院を受診した．CRP値は上昇し，白血球増多と好酸球増多，胸部X線上左下肺野に網状の浸潤影をみとめ，CTでは小葉中心性の粒状影や浸潤影をみとめた．メロペネムを投与したが反応せず，プレドニゾロンの投与でも症状や胸部陰影の増悪や寛解を繰り返した．約2ヵ月後から再び好酸球の増多とIgE値の上昇をみとめた．上部消化管の内視鏡検査で十二指腸に小白粉性隆起をみとめ，病理学的に同部に寄生虫体の構造をみとめ，また糞便中にラブジチス型の幼虫が認められ，糞線虫に対する血清抗体価も上昇していた．糞線虫症と診断し，ivermectinを2週間隔で2回投与したところ，症状も所見も全く消失した．幼少時にフィリピンにて感染し，老齢化により症状が顕性化したものと考えた．

キーワード：糞線虫症，小白粉性隆起，イベルメクチン

はじめに

糞線虫（通常ヒトへの感染は*Strongyloides stecoralis*）は熱帯・亜熱帯に分布し，日本では沖縄地方に多くみられる寄生虫で，フィラリア型幼虫が経皮的に侵入して感染が成立するとされている[1)]．私達は九州・長崎において，その発症初期に慢性の好酸球性肺炎の徴候を示し，十二指腸内視鏡では小白粉性隆起を認め，血清中に糞線虫抗体の上昇と，且つ糞便中に糞線虫の虫体を認めた一例を経験したので，文献的考察を加えて報告する．

症　例

患者：78歳　女性．

既往歴，家族歴：特記すべきものはない．

生活歴：1933年フィリピン・ミンダナオ島で出生．1945年終戦で長崎県口之津に引き揚げ（13歳時），その後成人になってからは農業に従事．豚堆肥を用いた有機野菜を摂取．生肉，川魚，沢蟹は食べていない．ペットの飼育歴はなく，喫煙歴や旅行歴もない．

臨床経過：

第1回入院時：2008年5月中旬より乾性咳嗽が続き，前日より38℃台の発熱があった

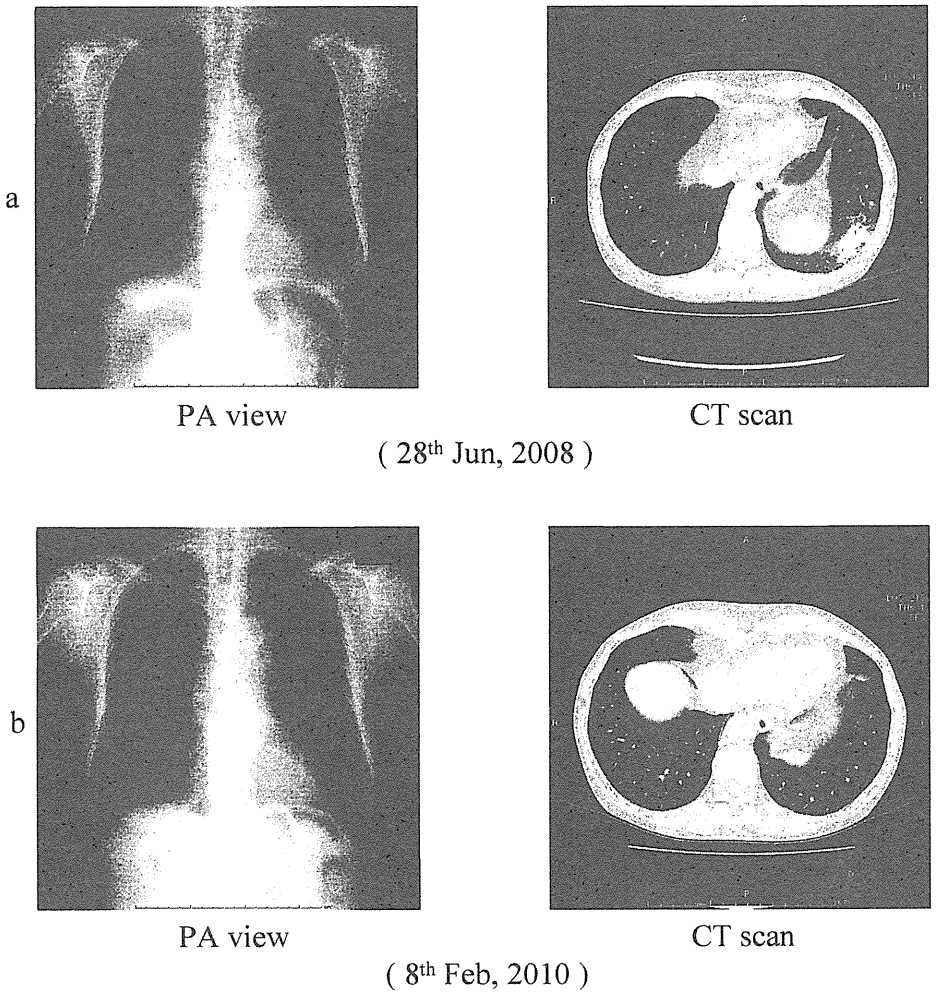

Fig. 1　Rontgenographic findings of chest

Dirofilaria immitis	+−	−	*Paragonimus westermani*
Toxocora canis	−	−	*P. miyazakii*
Ascaris suum	+−	+−	*Fasciola sp.*
Anisakis sp.	+−	−	*Clonorchis sinensis*
Gnathostoma doloresi	+−	−	*Spirometra erinacei*
Strongyloides sp.	++	−	*Cysticercus cellulosus*

Fig. 2　Multiple-dot ELISA of the patient's serum showing positive reaction against S. stercoralis.

ため，2008年6月下旬当院を受診，入院した．入院時，CRP値は上昇し，白血球増多と好中球増多，さらに好酸球増多(実数1436)をみとめ，胸部X線像では左下肺野に斑状の浸潤影をみとめ，CTでは小葉中心性の粒状影や淡い境界不明瞭な斑状の陰影を認めた(Fig 1a)．

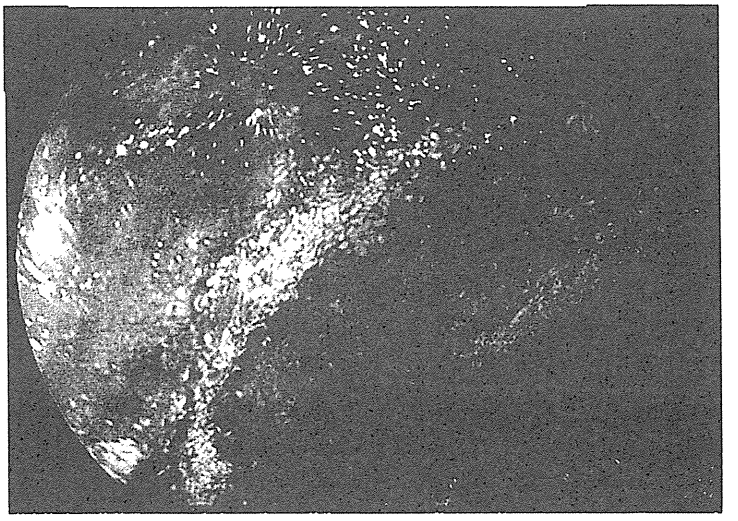

Fig. 3 Endoscopy findings in duodenum indicate a huge number of small white powder-like protrusions.

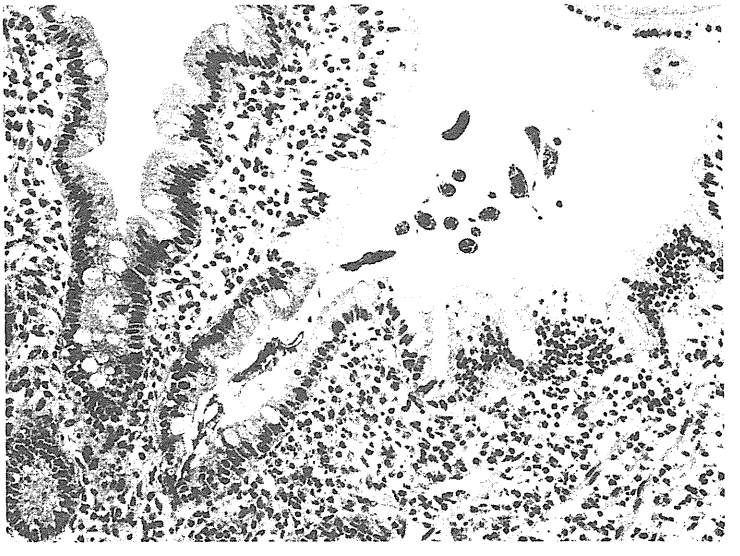

Fig. 4 In a duodenal biopsy specimen, eosinophilic inflammation of mucosa and parasites are recognized.

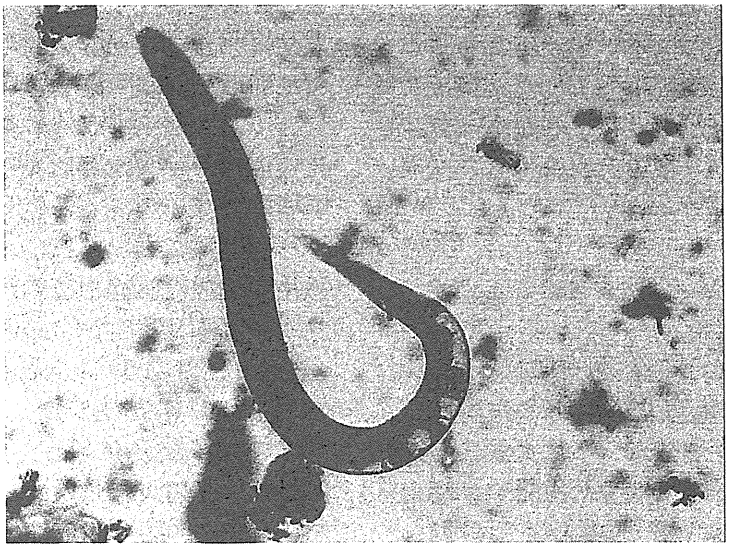

Fig. 5 Stool examination shows strongyloides larva.

細菌性肺炎の併発も考えてsulbactam/ampicillin(SBT/ABPC)で治療したが解熱せず，さらにmeropenem(MEPM)に変更したが，陰影は改善しなかった．好酸球性肺炎の診断のもとに，2008年7月上旬からpredonisolone 30mg/日より開始し，毎週5mgで漸減したが，症状も胸部の陰影も増悪や寛解を操り返した．さらに精査を進めようとしたが，同意が得られなかったので，外来で経過を観察することとした．その後も，慢性の咳嗽は持続したが，胸部の陰影は次第に消失した(Fig 1b)．2009年7月にPredonisoloneを中止したところ，同年9月頃から徐々に好酸球数の増加をみとめた．

第2回入院時：2010年2月上旬，咳嗽も続くため，精査のため第2回目の入院となった．入院時に貧血や黄疸はなく，口腔内は正常で，頚部や表在リンパ節は触知せず，心音は純，呼吸音も正常，腹部にも異常を認めなかった．検査では好酸球増多(実数1330)とIgEの上昇(1865，7 IU/ml)を認め，HTLV-1は陰性で，気管支肺胞洗浄液では，細胞数1130/μl，CD4/8 1.1，好中球42%，好酸球11%，リンパ球33%，肺胞マクロアージ14%であった．血清の寄生虫検査ではmultiple-dot ELISAにて糞線虫が陽性(Fig 2)で，十二指腸の内視鏡検査では小白粉性隆起(small white powder-like protrusion)を認め(Fig 3)，この部の生検では病理学的に十二指腸の腺窩に寄生虫(糞線虫に矛盾しない)と考えられる構造を認めた(Fig 4)．さらに糞便検査ではラブジチス型幼虫が確認された(Fig 5)．

糞線虫症と診断し，2010年3月上旬よりivermectin 6 mg(0.2mg/kg)/日を2週間隔で2回に分けて投与したところ，好酸球は減少し，咳嗽も消失，十二指腸内視鏡検査でも表層粘膜は正常となった．

考　　察

糞線虫のヒトにおける感染形式は，土の中のフィラリア型(F型)幼虫がヒトの皮膚から侵入し，リンパ系から肺，さらに気管・食道などを移動し，最終的には十二指腸や小腸上部に寄生する．そこで雌の成虫となり産卵し，孵化したラブジチス型幼虫は便と共に体外に排出されるが，一部の幼虫は排出される前に腸管内でフィラリア型幼虫に発育し，腸粘膜や肛門周囲の皮膚から再び体内に入ることがある．これを自家感染といい，糞線虫が長期に亘り持続感染する原因となっている[2]．

本患者においては，長期に亘って好酸球増多が認められ，肺の浸潤影と共に，気管支肺胞洗浄液中にも好酸球増多が認められた．糞線虫症による肺病変として，斉藤は虫体の直接的な機械的肺障害(direct destruction of vessels)すなわち肺内に寄生したラブジチス型幼虫が肺内毛細血管から遊出して血管の破綻をきたすものと，生体反応によるallergic reaction，および二次的な細菌感染によるaccompanied lesionの3つの型に分けている[3]．本症例では肺の組織学的所見が得られていないので明らかでないが，抗菌薬の効果が得られなかったことからaccompanied lesionは考え難く，前二者のいずれかであろうと考えられた．

消化器症状は本症にみられる一般的な症状で，腹痛・腹鳴，腹満感，軟便など，その程度は多様とされる．このような症例では，十二指腸や小腸上部の粘膜にカタル性ないしは浮腫性変化が強く認められ(small white powder-like protrusion)，潰瘍形成を伴うこともあるとされている[2]．糞線虫症の病理解剖学的検討を行った所見としては，十二指腸から回腸にかけて高度の浮腫状肥厚があり，組織的に粘膜に多数の虫や卵を認めたとしている[4]．私達の症例では，消化器症状は認められなかったが，これを裏付ける内視鏡所見と生検における病理所見を得ることができた．

とくに基礎疾患がない場合には，軽度の消化器症状や呼吸器症状を示す程度で，臨床上問題は少ないとされる．しかし，免疫能が低下した状態においては，本病原体による過剰感染や播種性糞線虫症の病態となることがあり，その誘因として，human T-lymphotropic virus 1(HTLV-1)，human immunodeficiency virus(HIV)感染のほか，免疫抑制剤やステロイドの投与などが考えられている[5),6]．本症例では，HTLV-1陰性で，とくに免疫不全を思わせる病態は考えられなかった．

本症の治療薬剤について，Zahaらはmebendazoleは高頻度の肝機能障害があり，albendazoleと共に，その駆虫効果は十分でなかったが，ivermectinは強い駆虫効果が認められ，毒性も少なかったことから，本症の駆虫における最も有用な薬剤として推奨している[1]．本症例においても，ivermectin 6 mg/日の2週間隔2回の投与によって，好酸球数の低下と共に諸症状の改善をみとめた．

最後に本症例の感染であるが，おそらく幼少時のミンダナオ島での生活で起こったと考えるのが妥当であろう．その後，誘因は明らかでないが，高齢化などの何らかの免疫能の低下がおこり，症状や所見が明らかになったものと推察された．しかし，長年農業に従事してきたことや，有機野菜を摂取してきたことなど，長崎県口之津での感染も全く否定はできない．日本においては最近になって，沖縄以外に宮崎[7]や福岡[8]，さらに長崎においても本症の報告がみられるようになってきた[9),10),11]．いずれにしろ，好酸球増多を伴って呼吸器系や消化器系の症状を示す感染性疾患においては，糞線虫症も念頭に入れるべきと思われた．

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A case of strongyloidiasis with eosinophilia

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A seventy-eight year old female patient was admitted complaining of dry cough and fever on June 2008. Leukocytosis, eosinophilia and elevated CRP value were recognized. Chest radiogram showed scattered reticular accompanied by a few infiltrative shadows in the left lower lung field. Thoracic CT scan also revealed centrilobular miliary and infiltrative shadows in the same lung field. Administration of meropenem and predonisolone were not completely effective, and relapse and remission of symptoms and laboratory data were seen. Elevation of IgE level and eosinophilia were seen two months later. Small white powder-like protrusion was indicated at the surface of duodenum which was confirmed to be a parasite structure pathologically. Rhabdiform larvae of *strongyloides stercoralis* was also present in the stool. Additional multiple-dot immunoserological test of serum was positive for *Strongyloides stercoralis*. A diagnosis of strongyloidiasis was confirmed, and ivermectin 6mg per day was given twice for two weeks. The symptoms totally disappeared and the level of eosinophilia normalized.

Key words: strongyloidiasis, small white powder-like protrusion, ivermectin

(Authors) (pp. 129-133)

4．小児にみられる吸虫症

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KEY WORDS
好酸球増多
胸部異常陰影
肝異常陰影
便虫卵検査
抗寄生虫抗体スクリーニング検査


Haruhiko Maruyama

はじめに

日本国内では吸虫症は成人の病気であり，小児における発生はごく限られている。とはいえ可能性が全くないわけではないので，鑑別診断から完全に脱落させてしまってはいけない。とくに，末梢血好酸球増多があったり熱帯～亜熱帯地域での居住歴があれば，吸虫症も念頭においた対応をすべきである。幸い吸虫は寄生虫の中では比較的穏健で，よほどの大量感染や長年月にわたる繰り返し感染でない限り，適切に治療すれば生命の危険を生じたり重篤な障害を残すことはない。駆虫薬にもよく反応するので，正しく診断することができれば問題は解決する。本稿では，吸虫類と吸虫感染症の特徴について述べ，どのような検査法が有効で，治療や予防はどうするのかという点などについて解説したい。

Ⅰ．吸虫と吸虫症の特徴

吸虫はれっきとした動物分類群の名称で，左右相称動物の中では比較的単純な体のつくりをした「扁形動物」という動物に属する。成虫は口吸盤と腹吸盤というふたつの吸盤を持つことから吸虫という。同じ扁形動物には，自由生活種であるプラナリアや，代表的な腸管寄生虫である条虫（サナダムシ），魚類の体表やエラに寄生するイカリムシやフタゴムシの仲間がいる。吸虫は消化管を持つが盲端で肛門がない。胸腔や腹腔のような体腔もなく，消化管や生殖器，排泄系は柔組織に埋まっている。

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表1　主な人体寄生吸虫

寄生虫名	寄生部位	主症状	検査所見	診断
横川吸虫	小腸	腹痛・下痢		便虫卵検査
肝吸虫	胆道系	腹痛・下痢・食思不振	肝機能障害，肝内胆管の拡張，好酸球増多	便虫卵検査，抗体検査
ウェステルマン肺吸虫 宮崎肺吸虫	肺，胸腔	咳・血痰	胸部異常陰影，好酸球増多	抗体検査（血清・胸水） 喀痰・胸水の虫卵検査
肝蛭	肝実質，胆管	腹痛・下痢・食思不振	肝機能障害，肝異常陰影，好酸球増多	抗体検査 十二指腸液虫卵検査
日本住血吸虫 マンソン住血吸虫	肝臓，小腸，大腸	腹痛・下痢・食思不振	肝機能障害，肝異常陰影，好酸球増多，血便	抗体検査，便虫卵検査
ビルハルツ住血吸虫	膀胱	排尿時痛，血尿	血尿	尿沈渣虫卵検査

吸虫類の名称は，成虫の寄生部位（肺吸虫や肝吸虫など）や人名（宮崎肺吸虫や横川吸虫など），あるいは形態にちなんで付けられている。種数は多くさまざまに分類されるが，臨床上問題になる種類はそれほど多くない。住血吸虫類とその他の吸虫類（肺吸虫，横川吸虫，肝吸虫，肝蛭など）とに分けて把握しておくのが便利である。

吸虫は，成虫が脊椎動物の消化管や肺，肝胆道系などに寄生して有性生殖によって次世代を生み出す。住血吸虫類を除いて雌雄同体である。人体寄生の吸虫では，成虫の大きさは，小さなもので体長1 mm程度（横川吸虫），大きなもので5～6 cm（肝蛭かんてつ）である。後に述べるように，幼虫時代には中間宿主の淡水産や陸産の巻貝に寄生し，無性増殖によって個体数を増やす。多くの吸虫は第二中間宿主も必要とする。

われわれヒトは吸虫にとっては終宿主なので，種によって決まった臓器に寄生し産卵する。吸虫症の症状と検査法は，成虫がどこにいるかでほぼ決定される（表1）。つまり，横川吸虫のように消化管の管腔内に寄生しているものでは便検査による虫卵の検出がもっとも適切な検査法であり，肺吸虫や肝蛭のように臓器の深いところに寄生している種類では抗体検査が主要な検査法になる。吸虫類でヒトだけが終宿主になり得るのはごく一部の種で，ほとんどの吸虫症は人獣共通感染症である。

吸虫は駆虫薬による治療によく反応し，肝蛭以外の吸虫にはプラジカンテル，肝蛭にはトリクラベンダゾールが著効を示す[1]。用法用量を表2にまとめた[2]。ただしトリクラベンダゾールは国内未承認薬であり，肝蛭症と診断がついた場合には「国内未承認薬の使用も含めた熱帯病・寄生虫症の最適な診療体制の確立」研究班（略称：熱帯病治療薬研究班，班長：木村幹男）までご相談いただきたい（連絡先は本稿末尾に掲載）。

Ⅱ．吸虫の生活環と感染経路（図1）

吸虫の生活環は感染経路と密接に関係する。ヒトへの感染は，住血吸虫類は経皮的

表2　主な吸虫症治療薬

	薬剤名	用量および用法	注意事項
横川吸虫症	プラジカンテル	50mg/kg，分3，1～2日間	プラジカンテルはリファンピシンと併用禁忌 住血吸虫症に対しては保険適用外
肝吸虫症		20～40mg/kg，分2，3日間	
肺吸虫症		75mg/kg，分3，3日間	
住血吸虫症		40mg/kg，分2，2日間	
肝蛭症	トリクラベンダゾール	10mg/kg，単回	国内未承認薬

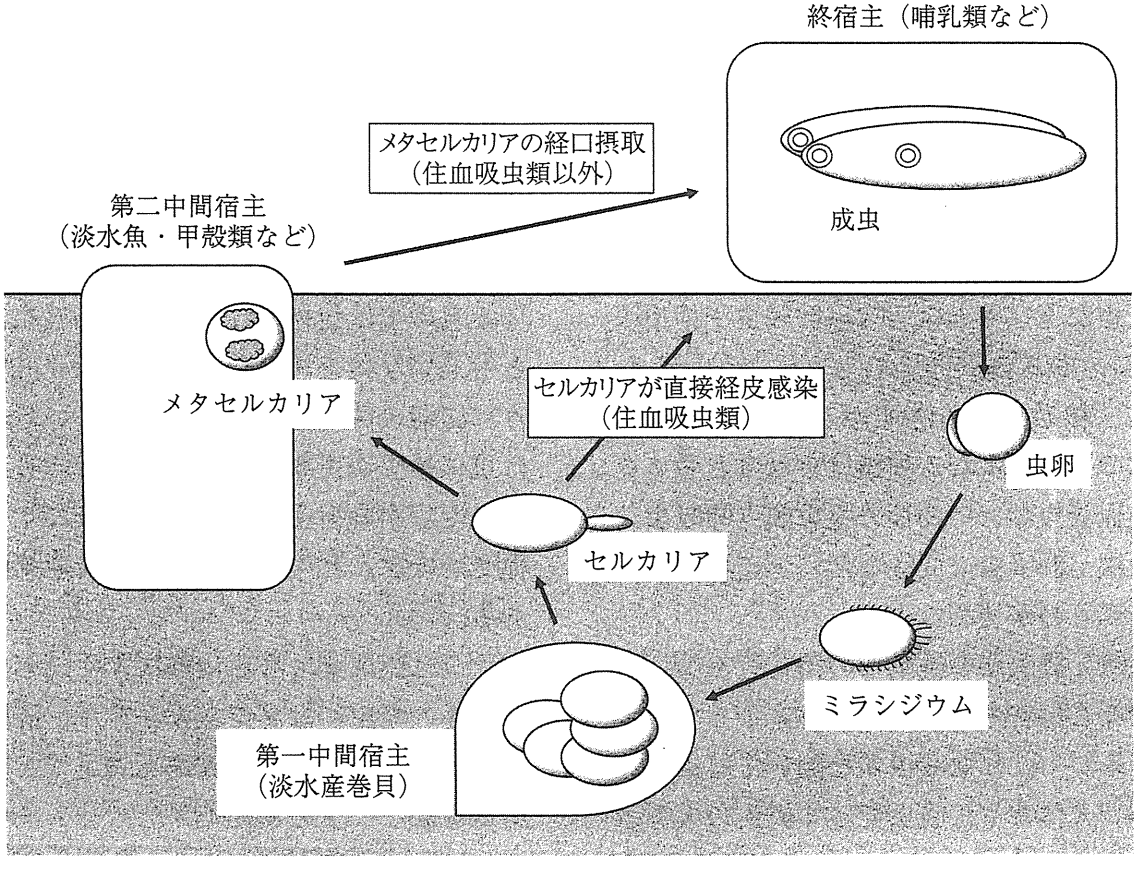

図1　吸虫の生活環
野生状態では，マンソン住血吸虫とビルハルツ住血吸虫を除いて，ヒトに感染する吸虫の終宿主はヒト以外の陸上の哺乳類である．したがって病気自体を根絶することは困難であり，予防が重要になる．

に，それ以外の吸虫類は経口的に行われる。

吸虫の成虫は終宿主の体内で産卵して糞便や尿などとともに虫卵が外界に排出される。虫卵の中には体表に繊毛をもった幼虫が形成されており，これをミラシジウムという。虫卵が河川や湖沼などの淡水に入ると孵化し，ミラシジウムが泳ぎ出して第一中間宿主の巻貝に侵入する。種によっては，ミラシジウムは孵化せずに虫卵ごと第一中間宿主の巻貝に食べられ，貝へ経口的に侵入する。

どの貝が中間宿主として利用可能かは吸虫の種によって決まっているので，特定の吸虫

表3　主な人体寄生吸虫の中間宿主と感染源

	第一中間宿主	第二中間宿主（感染源）	備考
横川吸虫	カワニナ	アユ・シラウオなど	無症状例が多い
肝吸虫	マメタニシ	コイ科淡水魚	激減したが絶滅はしていない
ウェステルマン肺吸虫	カワニナ	サワガニ・モクズガニ	待機宿主のイノシシも感染源
宮崎肺吸虫	ホラアナミジンニナ	サワガニ	
肝蛭	ヒメモノアラガイ	水草・野草・稲ワラ	感染は偶発的 終宿主のウシレバーの生食により肝臓に到達したばかりの虫体を摂取して感染したと考えられる症例がある
日本住血吸虫	ミヤイリガイ	水（経皮感染）	中国・フィリピンに分布
マンソン住血吸虫	*Biomphalaria*	水（経皮感染）	アフリカ・中南米に分布
ビルハルツ住血吸虫	*Bulinus*	水（経皮感染）	東西アフリカに分布

の分布は中間宿主貝の分布に依存する。例えば，かつて国内で多数の患者がみられた吸虫症に肝吸虫症がある。肝吸虫にはコイ科の淡水魚を生食して感染するが，今ではめずらしい病気になった。その原因として食生活が変化したこともあるが，肝吸虫の第一中間宿主であるマメタニシの個体数が激減した影響も大きい。貝がいなくなったせいで肝吸虫の世代が維持できなくなったのである。マメタニシは環境省の貝類レッドリストに絶滅危惧Ⅱ類（絶滅の危険が増大している種）として記載されているが，このリストには，ほかにもカワニナやホラアナミジンニナなど，人体寄生性の吸虫の中間宿主になる貝の名を見ることができる[3)]。

貝に侵入したミラシジウムは無性的に増殖する。この段階ではスポロシストやレディアと呼ばれる形態を取るが，最終的には貝の中で多数のセルカリアという幼虫が生じ，これが水中に泳ぎ出る。住血吸虫以外の吸虫では，セルカリアは魚類，甲殻類，植物などの第二中間宿主に接着または侵入してメタセルカリアという感染型になり，終宿主に第二中間宿主とともに食べられて生活環が完結する。よって多くの吸虫感染症は食品由来である。吸虫と第二中間宿主の関係も決まっているので，どのような食品を生食すればどんな吸虫に感染するのかがわかる（表3）。メタセルカリアは加熱すれば死滅するので，淡水産の魚介類を口にするときにしっかりと煮るなり焼くなりすれば，ほとんどの吸虫病は予防できる。

一方，住血吸虫類では第二中間宿主を必要とせず，水中のセルカリアが直接終宿主に経皮的に感染する。食品由来ではなく，その他の吸虫類とは予防法が根本的に異なる。かつてわが国にも，筑後川流域や甲府盆地などいくつかの地域では日本住血吸虫症が風土病として存在していた。これらの地域では水田や河川に中間宿主であるミヤイリガイ（宮入貝）が生息しており，住民は農作業などに際して多数のセルカリアの感染を受けていた。有効な対策が打てない時代が長く続き大変悲惨な病気であったが，20世紀初頭に感染経路が解明された後はミヤイリガイの撲滅が病気根絶の近道とされた。殺貝剤が散布され，ミ