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What Are the Clinical Features and Etiology of Eosinophilic Liver Infiltration?

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Background/Aims: Although eosinophilic liver infiltration (ELI) is not rare, few data exist regarding its clinical characteristics and etiology. Therefore, we evaluated these aspects to better understand the clinical implications of this lesion type, which is reasonably common in Korea. **Methods:** Patients suspected of having ELI, based on abdominal computed tomography results obtained between January 2010 and September 2017, were enrolled in this retrospective study. The presumptive etiologies of ELI were categorized as parasite infections, hypereosinophilic syndrome (HES), eosinophilic granulomatosis with polyangiitis (EGPA), malignancies, and unidentified. Clinical courses and treatment responses were also evaluated. **Results:** The mean age of the enrolled patients (male, 237/328) was 62 years. Most patients (63%) were diagnosed incidentally and had peripheral eosinophilia (90%). Only 38% of the enrolled patients (n=126) underwent further evaluations to elucidate the etiology of the suspected ELI; 82 (25%) had parasite infections, 31 (9%) had HES, five (2%) had EGPA, and five (2%) had drug reactions in conjunction with eosinophilia and systemic symptoms. Almost half of the other enrolled patients had cancer. Radiologic resolution was achieved in 191 patients (61%; median time to radiologic resolution, 185 days). Resolution of peripheral eosinophilia was achieved in 220 patients (79%). In most cases, the course of ELI was benign. **Conclusions:** This large ELI study is unique in that the incidence rate, underlying diseases, and clinical courses were comprehensively evaluated. Clinicians should investigate the etiology of ELI, as several of the underlying diseases require intervention rather than observation. **(Gut Liver 2019;13:183-190)**

Key Words: Eosinophilic infiltration; Etiology; Hypereosinophilic syndrome; Liver; Parasite

INTRODUCTION

Eosinophilic liver infiltration (ELI) can be observed on computed tomography (CT), and represents a common, focal, eosinophil-related inflammation, with or without necrosis.[1] The lesions appear on CT scans as multiple, hypoattenuated, small, round lesions that have blurred margins and are mainly discerned during the portal phase.[2] As a result of imaging advances, ELI is frequently found in clinical practice.[1,3] Although the lesions are often found because of clinical symptoms, they are sometimes incidentally detected during routine imaging checkups in patients with cancer or during regular checkups in healthy persons.[4]

ELI is associated with several common conditions that include peripheral eosinophilia,[2] such as parasitic infections, allergic diseases, and drug hypersensitivities.[5] Although associated with peripheral eosinophilia, a previous case report suggested that ELI is not always accompanied by peripheral eosinophilia.[6] Therefore, the strength of the relationship between peripheral eosinophilia and suspected ELI remains unclear.

In daily practice, we frequently encounter patients demonstrating CT findings suggestive of ELI. Until recently, ELI has tended to be regarded as having a benign course, resulting in its only being noted in imaging studies or being completely ignored.[1] However, various tests should be performed to evaluate the etiology of peripheral eosinophilia and ELI.

Parasitic infections, proven using serum samples and enzyme-linked immunosorbent assays (ELISAs), continue to be prevalent in Korea.[7,8] Paranasal sinus (PNS) imaging, total immunoglobulin E (IgE), and allergen-specific IgE assessments can be used to evaluate a patient's atopic and allergic disease status.[9] Furthermore, anti-neutrophil cytoplasmic autoantibody (ANCA) and antinuclear antibody (ANA) levels can be used in the diagnosis of connective tissue disease.[10,11] Chest X-rays, vitamin B_{12}

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and tryptase levels, and liver and bone marrow biopsies can be used to evaluate hypereosinophilic syndrome (HES) and other organ involvement due to eosinophilia.[12] Additionally, atypical lymphocytes in a peripheral blood smear (PBS) can provide important clues regarding the diagnosis of drug reactions with eosinophilia and systemic symptoms (DRESS) syndrome.[13]

Previous studies have mainly focused on the radiologic findings and clinical features associated with ELI.[1,2,14] However, there are limited comprehensive data regarding the etiologies and treatment of patients with suspected ELI.[1,2] Therefore, we evaluated these aspects of patients with suspected ELI.

MATERIALS AND METHODS

1. Patients

We retrospectively enrolled patients demonstrating suspected ELI on their abdominal CT scans, taken between January 2010 and September 2017, from the electronic medical records at Chonnam National University Hospital, South Korea.

2. Ethical considerations

The present study was conducted in accordance with the ethical guidelines of the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board of Chonnam National University Hospital (IRB No. CNUH-2017-290). The informed consent was waived.

3. Study design

A complete review of the medical records was conducted. This study involved convenience sampling, and all consecutive cases were included, without a formal sample size analysis.

The following data were collected: sex, age, medical history (drug history and allergies), food ingestion history (eating raw liver or meat of cows or other animals, raw blood of animals like deer, raw freshwater fish, and raw Chinese mitten crab), PNS images, chest X-rays, other organ involvement, laboratory findings (including leukocyte count, total eosinophil count, and eosinophil percentage), PBS results, vitamin B_{12} level, ANCA and ANA levels, and intake of antiparasitic medications. In addition, the follow-up imaging modalities, intervals, and lesion resolution status were reviewed. The medical review was conducted by two physicians.

Patients were classified into the following groups, based on the suspected cause of the ELIs: parasite, HES, eosinophilic granulomatosis with polyangiitis (EGPA), neoplasm, DRESS syndrome, and unidentified.

4. Definitions

Eosinophilia is defined as eosinophil count in the peripheral blood exceeding 500 cells/mL.[15] Eosinophilia has been categorized into three groups according to total eosinophil count: mild, 500 to 1,500 cells/mL; moderate, 1,500 to 5,000 cells/mL; severe, >5,000 cells/mL.[16]

Patients with serology test results positive for *Paragonimus westermani*, *Clonorchis sinensis*, or *Toxocara canis* or a positive stool examination were classified into the parasite group. The neoplasm group comprised patients with biopsy-diagnosed cancer. Patients were classified into the HES group if they fulfilled the following criteria, using the approach of Chusid *et al.*:[17] presence of peripheral blood eosinophilia, with an absolute eosinophil count of >1,500 cells/mL for >6 months; no other evident cause of eosinophilia, including allergic diseases or parasitic infections; or the presence of signs or symptoms of organ involvement by the eosinophilic infiltrate. The EGPA group comprised patients satisfying ≥4 of the following 6 American College of Rheumatology (1990) criteria:[18] asthma, eosinophilia (>10% of the total whole blood cell count), neuropathy, nonfixed pulmonary infiltration, PNS abnormalities, and extravascular eosinophils. The DRESS syndrome group comprised patients who fulfilled the RegiSCAR criteria for DRESS syndrome.[13] The RegiSCAR criteria include the presence of at least three of the following seven characteristics: skin eruptions, fever (>38°C), lymphadenopathy involving at least two sites, involvement of at least one internal organ, lymphocytosis ($>4\times10^3/\mu L$) or lymphocytopenia ($<1.5\times10^3/\mu L$), blood eosinophilia (>10% or 700/μL), and thrombocytopenia ($<120\times10^3/\mu L$). Patients who did not meet any of the above criteria were allocated to the unidentified group.

During the evaluation of the clinical course of the suspected ELI, based on CT results, we defined radiologic resolution as the disappearance of results on follow-up imaging.

5. Statistical analysis

Statistical analyses were performed using SPSS version 20.0 (IBM Corp., Chicago, IL, USA). Continous data are presented as median (range), and categorical data are shown as absolute and relative frequencies. Group differences were evaluated using the Kruskal-Wallis test followed by the Dunn test for continuous variables and Fisher exact or chi-square tests for categorical variables. $p\leq0.05$ was considered statistically significant.

RESULTS

1. Baseline patient characteristics

A total of 79,739 patients underwent abdominal CT scans during the study enrollment period, including 328 (0.41%) cases with suspected ELI, based on CT findings. The initial CT scans were conducted in 27 departments, mainly within the Division of Gastroenterology and the Departments of Internal Medicine and General Surgery. Table 1 shows the baseline characteristics of enrolled patients. The median age of the enrolled patients was 62 years (range, 19 to 95 years), including 237 (72%) men (Fig. 1A). A total of 288 patients (90%) had peripheral eosinophilia, with a median peripheral eosinophil count of 1,033/μL (range, 0

Table 1. Baseline Characteristics According to Underlying Disease

Characteristic	Parasite (n=82)	HES (n=31)	EGPA (n=5)	DRESS syndrome (n=5)	Neoplasm (n=2)	Unidentified (n=203)	p-value
Age, yr*	60 (19–82)	67 (48–88)	63 (32–81)	52 (48–56)	52 (42–62)	63 (20–95)	0.084
Elderly†	34 (42)	18 (58)	2 (40)	0	0	95 (47)	0.348
Male sex	63 (77)	24 (78)	3 (60)	2 (40)	1 (50)	142 (70)	0.581
WBC, cells/μL	8,400 (4,700–17,700)	9,700 (5,800–24,600)	11,900 (6,200–30,900)	11,300 (5,300–24,300)	6,150 (6,100–6,200)	7,000 (620–29,100)	<0.0001
Leukocytosis	8 (10)	10 (32)	2 (40)	3 (60)	0	12 (6)	<0.0001
TEC, cells/mL	1,545 (0–11,400)	2,930 (850–15,360)	1,800 (1,000–21,870)	1,800 (320–3,500)	295 (230–360)	727 (0–7,160)	<0.0001
Eosinophilia	81 (99)	31 (100)	5 (100)	5 (100)	1 (50)	168 (83)	<0.0001
Cancer history	16 (20)	3 (10)	0	0	2 (100)	93 (46)	<0.0001
Raw food ingestion	56 (68)	20 (65)	2 (40)	0	0	13 (6)	<0.0001
Radiologic resolution‡	59 (72)	15 (48)	2 (40)	1 (20)	0	114 (56)	0.007

Data are presented as number (%) or median (range).
HES, hypereosinophilic syndrome; EGPA, eosinophilic granulomatosis with polyangiitis; DRESS, drug reactions with eosinophilia and systemic symptoms; WBC, white blood cell; TEC, total eosinophil count.
*Mean (range); †Elderly was defined as age greater than 65 years; ‡Radiologic follow-up was performed for 227 of the study populations.

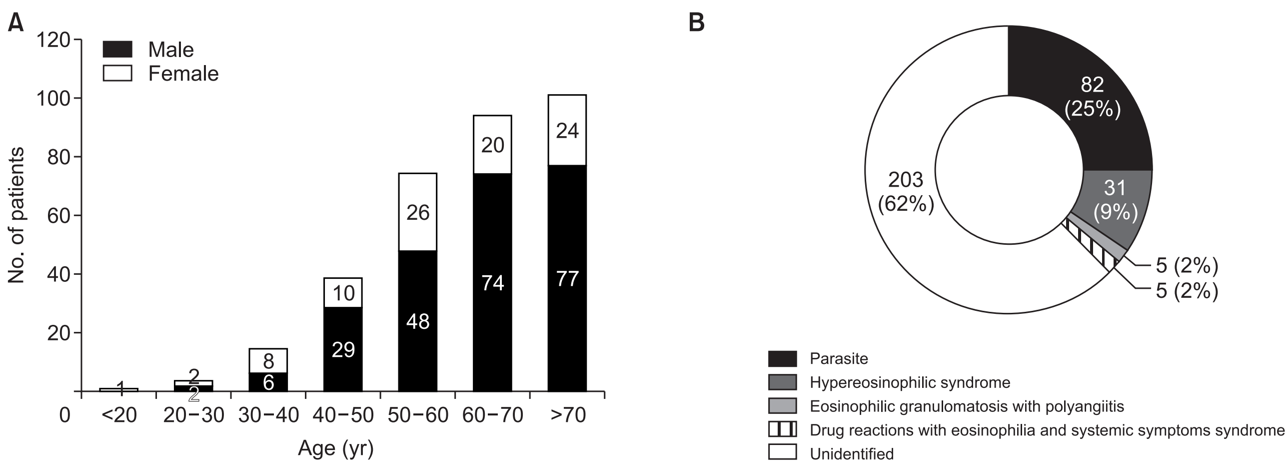

Fig. 1. (A) Distribution of gender and age in enrolled patients. (B) Presumptive causes of eosinophilic liver infiltration in this study.

to 21,870/μL). The whole blood cell and total eosinophil counts differed significantly among the six etiologic groups. In the neoplasm and unidentified groups, the mean total eosinophil counts were significantly lower than those in the other groups ($p<0.001$).

Thirty-one patients (9%) fulfilled the HES criteria, with more than half of these patients showing an involvement of >2 organs (data not shown). Other than the liver, the next most commonly involved organ was the lung.

Five patients (1.5%) fulfilled the EGPA criteria and five (1.5%) fulfilled the DRESS syndrome criteria. Among patients with DRESS syndrome, the culprit drugs were identified as allopurinol (two patients, 40%), carbamazepine (two, 40%), and tuberculosis medications (one, 20%) (data not shown).

Patients in the unidentified group were further divided into two subgroups, based on the presence of cancer (data not shown). The identified malignancies in patients with cancer were stomach cancer (38, 41%), colorectal cancer (26, 28%), cholangiocarcinoma (seven, 8%), esophageal cancer (six, 7%), and other cancers including hepatocellular carcinoma, lymphoma, renal cell carcinoma, lung cancer, prostate cancer, cervix cancer, and breast cancer. A total of 110 patients (33.5%) in the unidentified etiology group did not have cancer. Within the unidentified group, a significantly higher proportion of patients with cancer had peripheral eosinophilia than did patients without cancer ($p=0.010$) (data not shown). However, in terms of leukocytosis, the patients with cancer did not differ from those without cancer.

A total of 10 patients (3%) with suspected ELI underwent liver biopsies (data not shown). Of those, only two patients had confirmed metastatic malignancies. Although the other eight patients did not have confirmed metastatic malignancies, they had diverse results, including mild inflammation in the portal areas (six patients), a cirrhotic nodule (one patient with underlying liver cirrhosis), and liver involvement of HES (one patient).

2. Testing patterns for patients with suspected ELI

Table 2 shows the diagnostic tests used to evaluate ELI in the enrolled patients. In most cases, clinicians conducted tests for whole blood cell and total eosinophil counts. However, further evaluations to elucidate the cause of the peripheral eosinophilia were infrequently conducted; only 126 patients underwent at least one additional test for this purpose. The specific tests and numbers of patients tested were as follows (Table 2): PBS (126 patients, 38%), IgE (108, 33%), allergen sensitization profile (35, 11%), simple chest X-ray (287, 88%), PNS imaging (47, 14%), vitamin B_{12} level (123, 38%), ELISA for *P. westermani*, *C. sinensis*, and *T. canis* (126, 38%; 130, 40%; 111, 34%, respectively), and stool examination (88, 27%). Bone marrow biopsies were performed in 27 patients (8%), with 30% demonstrating abnormal results. Abnormal chest X-ray or chest CT findings were observed in 70 patients (24%). Physicians collected raw food histories from only 100 patients (30%); of those, 12 (12%) did not undergo any examinations for parasitic infections.

3. Presumptive causes of the suspected eosinophil liver infiltration

The presumptive causes of the suspected ELI cases, based on clinical laboratory tests, other imaging, and medical histories are shown in Table 1 and Fig. 1B.

Within the parasite group, the identified parasites were *P. westermani* (four patients, 5%), *C. sinensis* (14, 17%), and *T. canis* (64, 78%); toxocariasis was the most common cause of parasitic infection. Three patients showed negative parasite antibody ELISA results in serum, but were diagnosed with a parasitic infection based on stool test results; all three had *C. sinensis* infections (data not shown). In a subgroup analysis, patients infected with *T. canis* tended to be older than those infected with the other two parasites. Additionally, patients infected with *T. canis* tended to have higher total eosinophil counts than did patients infected with the other parasites. However, neither of these results demonstrated statistical significance (Table 3).

4. ELI resolution and response to antiparasitic treatments

A total of 126 patients were treated with antiparasitic drugs, regardless of parasite examination results (Table 4); of these, 74 (59%) were determined to have parasite infections. The empiric parasitic treatment involved oral albendazole (400 mg, twice/day, for 1 week) and/or oral praziquantel (25 mg/kg, three

Table 2. Clinical Approach for the Evaluation of the Etiology of Eosinophilic Liver Infiltration (n=328)

Diagnostic test	No. of patients tested	Abnormal results	No. of patients with abnormal results
Whole blood cell count	324 (99)	Leukocytosis	35 (11)
Eosinophil count	324 (99)	Eosinophilia	291 (90)
PBS	126 (38)	Abnormal result of PBS	120 (94)
Total IgE	108 (33)	Elevation of total IgE	35 (11)
Allergen specific IgE	35 (11)	Sensitization of one or more allergen	13 (37)
Chest X-ray	287 (88)	Abnormal finding of chest X-ray	70 (24)
PNS X-ray	47 (14)	Abnormal finding of PNS X-ray	19 (40)
Vitamin B_{12}	123 (38)	Elevation of vitamin B_{12}	23 (19)
Bone marrow biopsy	27 (8)	Abnormal finding of bone marrow biopsy	7 (26)
ANCA	68 (21)	Abnormal result of ANCA	0
ANA	63 (19)	Abnormal result of ANA	5 (8)
Tryptase	65 (20)	Abnormal result of tryptase	1 (2)
Parasite test			
ELISA for *Paragonimus westermani*	126 (38)	Positive result	4 (3)
ELISA for *Clonorchis sinensis*	130 (40)	Positive result	14 (11)
ELISA for *Toxocara canis*	111 (34)	Positive result	64 (58)
Stool test for parasite	88 (27)	Positive result	5 (6)
History taking of raw foods	100 (30)	Ingestion of raw foods	91 (91)

Data are presented as number (%).
PBS, peripheral blood smear; IgE, immunoglobulin E; PNS, paranasal sinus series; ANCA, anti-neutrophil cytoplasmic autoantibody; ANA, antinuclear antibody; ELISA, enzyme-linked immunosorbent assay.

Table 3. Clinical Characteristics of Parasitic Infection by Presumptive Causes (n=82)

Characteristic	*Paragonimus westermani*	*Clonorchis sinensis*	*Toxocara canis*	p-value
No. of patients	4 (5)	14 (17)	64 (78)	
Male sex	2 (50)	10 (71)	51 (80)	0.261
Age, yr*	56 (46–64)	59 (19–78)	64 (27–82)	0.301
WBC, cells/mL	9,650 (6,600–14,500)	9,550 (5,600–17,700)	7,850 (4,700–17,300)	0.126
TEC, cells/mL	3,180 (1,300–7,395)	1,731 (600–11,400)	1,400 (0–8,510)	0.055
Eosinophilia	4 (100)	14 (100)	63 (98)	1.000
Moderate eosinophilia	3 (75)	10 (71)	30 (47)	0.201
Radiologic resolution†	3 (75)	9 (100)	47 (92)	0.397
Time to radiologic resolution, day†	188 (98–387)	189 (52–521)	183 (14–1,506)	0.920
Eosinophil normalization‡	2 (67)	12 (92)	56 (93)	0.272
Time to eosinophil normalization, day†	195 (42–276)	93 (34–196)	118 (2–1,323)	0.617

Data are presented as number (%) or median (range).
WBC, white blood cell; TEC, total eosinophil count.
*Mean (range); †Radiologic follow-up was performed for 60 of the study populations; ‡Total eosinophil count follow-up was performed for 77 of the study populations.

Table 4. Clinical Course of Suspected Eosinophil Infiltration on Liver According to the Administration of Antiparasitic Treatment

	Untreated	Treated	p-value
No. of patients	202	126	
Radiologic resolution	114 (56)	77 (61)	0.284
Time to radiologic resolution, day	183 (14–1,346)	189 (14–1,506)	0.449

Data are presented as number (%) or median (range).

times/day, for 3 days).[1,19] Although, the parasite group showed a significantly higher radiologic resolution rate than did the other groups (p=0.007) (Table 1), there were no differences in the radiologic resolution and eosinophil normalization rates between patients empirically treated and not treated with antiparasitic drugs (56% vs 61%, p=0.284) (Table 4). Among patients achieving radiologic resolution, the median time to resolution did not differ significantly between patients empirically treated and not treated with antiparasitic drugs (p=0.449) (Table 4). Among the patients without any serum or stool evidence of parasitic infection, 50 (20%) received antiparasitic medication and 196 (80%) did not; there was no significant difference in the radiologic resolution rates (44% vs 56%) (data not shown).

5. Clinical course and follow-up modalities of ELI

Most patients (312 patients, 95%) revisited the hospital after being diagnosed with suspected ELI (Table 5). More than 70% of these patients underwent follow-up imaging, including abdominal CT (132 patients, 58%), abdominal ultrasonography (19, 8%), or magnetic resonance (MR) imaging (10, 4%); 66 patients (29%) received follow-up imaging involving more than two modalities, and most of them (53 patients, 80%) underwent MR imaging alone or combined CT and MR imaging for follow-up

Table 5. Clinical Course and Follow-up Modalities of ELI (n=328)

	No. of patients
Follow-up the clinic	312 (95)
Radiologic resolution	191 (61)
Remained the ELI	40 (13)
Time of radiologic resolution, day	185 (14–1,506)
Peripheral eosinophilia normalization	220 (67)
Remained the peripheral eosinophilia	26 (8)
Follow-up the imaging	227 (69)
Kind of follow up imaging modalities	
Abdominal computed tomography	132 (58)
Abdominal ultrasonography	19 (8)
Magnetic resonance imaging	10 (4)
More than 2 combined modalities use	66 (29)
Including magnetic resonance imaging	53 (80)

Data are presented as number (%) or median (range).
ELI, eosinophilic liver infiltration.

and further evaluation (Table 5). Among the 312 patients who revisited the hospital, radiologic resolution was achieved by 191 (61%), with a median time to resolution of 185 days (range, 14 to 1,506 days) (Table 5). The remaining 40 patients (13%) did not achieve radiologic resolution, but peripheral eosinophilia resolution was achieved in 21 of these patients (53%) (data not shown). The patients without radiologic resolution had a median follow-up duration of 174 days (range, 6 to 3,642 days) (data not shown).

Of the 312 patients returning to the hospital, peripheral eosinophilia was initially detected in laboratory samples from 278 patients. Among these individuals, 220 (79%) achieved complete resolution, including normalized peripheral eosinophil counts; 26 (9%) did not achieve normalized peripheral eosinophil counts; and 32 (12%) did not undergo subsequent testing for peripheral eosinophilia.

DISCUSSION

This large, retrospective study is unique in that the incidence rate, underlying disease, and clinical course of ELI were comprehensively evaluated in the patients. In the present study, the incidence rate of clinically-diagnosed eosinophilic liver lesions was 0.41%, and most patients had no specific symptoms; this is similar to a previous study,[1] which reported an incidence rate of 0.68%. Only 38% of the enrolled patients underwent further evaluations to elucidate the etiology of the suspected ELI, and the most common cause was determined to be parasitic infection. The rate of radiologic resolution was 61%, and the rate of peripheral eosinophilia resolution was 79%. In most cases, the lesions followed a benign course. Furthermore, there was no difference in the radiologic resolution and eosinophil normalization rates between patients empirically treated and not treated with antiparasitic drugs.

The imaging and clinical features associated with ELI have been reported by many Korean researchers.[1,2,14,20,21] Most recent studies have mainly focused on the radiologic findings and clinical features associated with ELI.[1,2,14] In contrast, the present study focused on the diagnostic approach used to determine the etiology of suspected lesions.

Consistent with other studies,[1,2] 63.1% of patients with radiologically suspected ELI did not have any specific symptoms. Further, only 38% of the patients underwent at least one test to identify the cause. Most often, physicians did not take raw food and/or drug histories to determine the likelihood of parasitic infections, which are frequent in Korea. In general, the most common causes of ELI are parasitic infections and medications; the lesions are also associated with malignant tumors.[22] However, in the present study, parasitic infections and HES were identified as likely causes more frequently than expected, whereas medication-related ELI was identified less frequently than expected. HES and parasitic infections do not naturally resolve without intervention. Therefore, clinicians should perform appropriate tests and take complete histories to determine the etiology of presumptive ELI.

In Korea, toxocariasis is the most common cause of peripheral blood eosinophilia and eosinophilic infiltrations in various organs.[12,23] This is consistent with our finding that *T. canis* was the most common parasite identified in patients with ELI in the present study. As in a previous study,[24] more than half of the patients (41 patients, 64%) with parasitic infections did not present with clinical symptoms such as cough, dyspnea, chest discomfort, or pruritus in the present study.

Most of the patients (288, 89%) in this study showed peripheral eosinophilia, which was not further evaluated. Regardless, approximately 10% of patients with suspected ELI were finally diagnosed with HES. This is consistent with a previous report that revealed that liver involvement is a relatively common manifestation in patients with HES.[25] As this disease is a myeloproliferative disorder with persistent eosinophilia and multiple organ damage,[26] it can be life-threatening; in 1989, the 5-year survival rate was 80%.[27] Fortunately, HES survival rates appear to have been improving, possibly because of new medication options and quicker diagnoses.[28] In the present study, all patients diagnosed with HES received treatment, and mortality was not observed. Since the early diagnosis of HES is very important in reducing patient mortality, we suggest that incidental ELI, with more than moderate peripheral eosinophilia (>1,500 cells/mL), may be an indicator of HES. Thus, when a patient demonstrates these two conditions (ELI CT finding and moderate eosinophilia), physicians should consider the possibility of HES. In addition, patients with suspected eosinophilic infiltration on abdominal CT images should undergo whole blood and total eosinophil count determinations, at a minimum.

Liver involvement in patients with EGPA has been rarely reported.[29-31] Nevertheless, EGPA was diagnosed in 1.5% of the patients in the present study. Although EGPA is rare, patients with ELI and a history of asthma should be questioned to determine if they fulfill the EGPA criteria.[29]

Liver impairment is the most common visceral manifestation of DRESS syndrome, but in most cases, it is only discovered through abnormal laboratory results. The most important treatment for medication-induced DRESS syndrome is discontinuation of the medication, as soon as possible. Thus, physicians should determine the recent medication history in patients with ELI.[32]

Toxocariasis has been suggested to be the most important cause of ELI.[23,33,34] As a result, one previous study suggested that empiric antiparasitic medication therapy produces more rapid radiologic resolution in patients with ELI of unidentified etiology than any other treatment.[1] In Korea, a common cultural practice involves the eating of raw food, which might increase the prevalence of ELI, compared with other countries. Therefore, empirically administering anti-parasite medications to patients with suspected ELI would be appropriate in Korea. However, in this large present study, we did not observe any differences in the resolution rates between patients empirically treated or not treated with anti-parasite medications. Therefore, more studies on the effects of this treatment approach will be needed.

In our study, many patients had coexisting malignancy, but very few patients needed biopsy to distinguish ELI from metastatic malignancy and primary malignancy lesion. The reason was that some patients underwent MR imaging after abdominal CT scan. According to previous reports, MR imaging was helpful in differentiating them from the features of focal liver metastasis.[2,35] Malignancy has some unique features on MR imaging. For example, malignancy showed a prominent washout of contrast material in the lesions with delayed capsular enhancement, but most of the ELIs did not show a prominent washout on the dynamic delayed phase.[22] MR imaging is considered a good modality for distinguishing ELI from malignancy.

Follow-up imaging showed that cases of suspected ELI pursue rather benign courses. However, ELI, like other medical conditions, needs identification of the cause and appropriate treatment. Furthermore, in the case of patients with remaining hepatic lesions during follow-up imaging, physicians should try to actively look for the etiology of ELI such as HES, drug allergy, parasite infestation, and malignancy. In cases of malignancy, the results of our study suggest that the physician may suspect hidden gastrointestinal cancer.

The present study has several limitations. First, its retrospective design is associated with known risks of bias and data limitations; thus, the duration of cases of suspected ELI could not be accurately determined. Second, the study was conducted in a tertiary hospital in Korea, and patients were preferentially enrolled if they specifically required abdominal CT scans; thus, the findings may not reflect the actual incidence of focal eosinophilic infiltrations, which are usually asymptomatic.

In conclusion, to the best of our knowledge, the present study is the largest comprehensive study to evaluate the incidence, etiology, and clinical course of suspected ELI. Although ELI is usually a benign condition commonly caused by parasitic infections, HES and malignancies are the more common causes. Therefore, physicians should undertake evaluations to establish the cause of focal hepatic eosinophil infiltrations observed in patients.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Author contributions: D.W.S. and D.J.S. drafted the manuscript. D.J.S., E.C., S.K.C., and S.S.S. were involved in the data acquisition. D.W.S. and C.H.J. analyzed and interpreted the data, designed the research, and reviewed the manuscript.

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