Letter to the Editor

Comparison of clinical characteristics of the nasal manifestations of eosinophilic granulomatosis with polyangiitis (EGPA) and eosinophilic chronic rhinosinusitis (ECRS)

Dear Editor,

Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare autoimmune small-vessel vasculitis.1,2 EGPA involves multiple organs, including the pulmonary, renal, nervous, and vascular systems.3 Among them, the nasal cavity, including the paranasal sinuses, is one of the most frequently affected organs and often proceeds other manifestations.

We previously reported the nasal manifestations of EGPA closely resemble ECRS,4 one phenotype of chronic rhinosinusitis with nasal polyps (CRSwNP), characterized by severe eosinophil infiltration into the nasal mucosa and high a recurrence rate after surgery.5 In addition, both of EGPA and ECRS are often accompanied by bronchial asthma and peripheral eosinophilia.1,2,5,6 Although the two eosinophilic-inflammatory conditions share common clinical characteristics, the prognoses are completely different. While ECRS does not directly threaten life or necessarily require prompt therapy, EGPA is a possibly life-threatening disease that requires appropriate and prompt systemic therapy. In fact, it was reported 12% of patients with EGPA died within 1 year without adequate diagnosis and treatment.7 The prevalence ratio also differs, with the number of patients with ECRS being much greater than that of those with EGPA. In daily practice, therefore, it is often difficult but very important to identify EGPA, a rare but possibly fatal disease, from among the many patients with ECRS.

To examine the differences in the clinical characteristics between EGPA and ECRS, we retrospectively reviewed patients diagnosed with EGPA or ECRS at the Department of Otolaryngology, Hokkaido University Hospital. The diagnosis of EGPA and ECRS were made on the basis of the criteria set by the American College of Rheumatology (1990)10 and the JESREC criteria,5 respectively. All analyses were performed using the JMP® 11 (SAS Institute Inc., Cary, NC, USA). P values < 0.05 were considered statistically significant. Details of subjects, diagnosis, and statistical analysis are found in the Supplementary Methods.

First, we compared peripheral eosinophilia between the 18 EGPA patients with sinusitis and 20 ECRS patients (Table 1). At the initial visit, there were no patients who received biologics and two patients with EGPA took systemic steroid therapies for bronchial asthma. Two patients with EGPA had been diagnosed as eosinophilic pneumonia before their initial visit to our institute and one patient with EGPA had as eosinophilic myocarditis. There was significant difference in peripheral eosinophilia between the patients with EGPA and those with ECRS (EGPA 34.06 ± 20.97% vs. ECRS 10.04 ± 5.44%, p < 0.001). A ROC curve for peripheral eosinophilia showed the AUC for distinguishing EGPA from ECRS was as high as 0.84 (Fig. 1). The ROC curve also showed the optimal cut-off value for peripheral eosinophilia was 21%. The sensitivity, specificity, PPV, and NPV for the cut-off value were 72.2%, 100.0%, 100.0%, and 80.0%, respectively.

Next, we examined patients with EGPA in terms of the nasal findings typical of ECRS such as nasal polyps and ethmoid-dominant inflammation.1 Although the nasal manifestations of EGPA closely resembled those of ECRS as previously reported,4 several significant differences were found. First, patients with EGPA had significantly less ethmoid-dominant inflammation than patients with ECRS (p = 0.026). There was no significant difference in peripheral eosinophilia between EGPA patients with and without ethmoid-dominant inflammation (ethmoid-dominant 36.31 ± 21.31% vs. not ethmoid-dominant 26.20 ± 17.63%, p = 0.41). Although most of patients with EGPA had nasal polyps as well as ECRS patients did, patients with EGPA also had significantly less risk of nasal polyps (p = 0.002). There was no significant difference in peripheral eosinophilia between EGPA patients with nasal polyps and those without nasal polyps (with nasal polyps 31.71 ± 18.38% vs. without nasal polyps 35.55 ± 23.21, p = 0.72).

We also examined whether the nasal manifestations of EGPA met the criteria for ECRS according to JESREC score, where CRS patients with a score greater than or equal to 11 points are classified as having ECRS. The score of the 18 patients with EGPA was 14.83 ± 2.26 and did not differ significantly from the score of patients with ECRS in this study (15.05 ± 2.26). Among the 18 patients with EGPA, 15 patients (83.3%) “met” the criteria for a diagnosis of ECRS.

Our results suggested peripheral eosinophilia could be useful in distinguishing the nasal manifestations of EGPA from ECRS. Peripheral eosinophilia is often examined as part of routine screening for a diagnosis of ECRS and there is no need for an additional examination. ROC analysis also showed the optimal cut-off value for peripheral eosinophilia was 21%. Tokunaga et al. reported the peripheral eosinophils for 672 patients with ECRS was 7.13 ± 5.54%.7 This figure means only 0.57% of patients with ECRS have peripheral eosinophilia of more than 21%. It is, therefore, reasonable to consider the possibility of EGPA in patients with peripheral eosinophilia over 21%, followed by screening for EGPA by examining ANCA and chest X-ray and/or CT. Biopsies also should be considered from possibly involved organs. Even if the cases were not diagnosed as EGPA, the cases with eosinophilia over 21% should be closely followed up as the symptoms developed long time after the initial visit, in some cases.
In addition to peripheral eosinophilia, our result also showed that although the majority of EGPA patients have nasal polyps and ethmoid-dominant inflammation as ECRS patients do, some patients with EGPA “lack” the nasal findings typical to ECRS. Considered that all ECRS patients had nasal polyps and ethmoid-dominant inflammation, the “lack” of the typical nasal findings of ECRS in a patient with peripheral eosinophilia could provide a simple but useful clue to the diagnosis of EGPA.

On the other hand, our results imply JESREC score does not aid in the differential diagnosis of EGPA and ECRS. The scores in EGPA patients in this study were as high as those in the ECRS patients. This means the possibility of EGPA could not be ruled out just because the score was high enough to suggest a diagnosis of ECRS.

There are some limitations to this study. First, the number of patients reviewed was relatively small due to the rarity of the disease. Second, patients with ECRS were not matched to patients with EGPA from EGPA (n = 20) P value

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EGPA (n = 18)</th>
<th>ECRS (n = 20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral eosinophilia (%)</td>
<td>34.06 ± 20.97</td>
<td>10.04 ± 5.44</td>
<td>&lt;0.001</td>
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<tr>
<td>Ethmoid-dominant inflammation</td>
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<td>20</td>
<td>0.026</td>
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<td>Nasal polyps</td>
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<td>20</td>
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<tr>
<td>Bilateral lesions</td>
<td>17</td>
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<td>0.285</td>
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<tr>
<td>Bronchial asthma</td>
<td>16</td>
<td>15</td>
<td>0.270</td>
</tr>
<tr>
<td>Aspirin intolerance</td>
<td>0</td>
<td>4</td>
<td>0.045</td>
</tr>
<tr>
<td>JESREC score &gt;11</td>
<td>14.83 ± 2.43</td>
<td>15.05 ± 2.26</td>
<td>0.778</td>
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<tr>
<td>Severity</td>
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<tr>
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<td>0</td>
<td>2</td>
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<tr>
<td>Moderate</td>
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<td>4</td>
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<tr>
<td>Severe</td>
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<td>14</td>
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In conclusion, our results suggested several important clinical points: Peripheral eosinophila could be useful in distinguishing EGPA from ECRS. The “lack” of the nasal findings typical to ECRS in patients with high peripheral eosinophil count is a simple but useful first clue to suspect EGPA. The possibility of EGPA could not be ruled out just because the JESREC score was greater than 11 points. Last but not least, in consideration of EGPA as a potentially fatal disease without early diagnosis and appropriate therapy, care should always be taken when ruling out this systemic disease from patients with ECRS in daily practice.

Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.alit.2020.05.009.

Conflict of interest
The authors have no conflict of interest to declare.

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References

Received 24 December 2019
Received in revised form 23 April 2020
Accepted 13 May 2020
Available online 4 July 2020