Paraneoplasticextralimbic Encephalitis Associated with Thymoma: A Case Report

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Here we report a rare case of extralimbic encephalitis associated with thymoma. A 66-year-old woman was admitted to our hospital with cramping in her right leg and inability to walk. Magnetic resonance imaging of the brain showed multifocal high intensity signals on T2 flare images in the cerebral cortex, and chest computed tomography showed a 5-cm anterior mediastinal mass, which was considered to be a thymoma. We speculated that she had paraneoplastic encephalitis associated with thymoma. She underwent a thymectomy and was diagnosed with type B1 thymoma. On postoperative day 6, her neurological symptoms began to improve. On postoperative day 31, she was discharged without complications. Limbic encephalitis is a paraneoplastic neurological syndrome associated with thymoma, but extralimbic encephalitis has been described in the literature very rarely. We report the case of extralimbic encephalitis associated with thymoma along with a literature review.

key words: thymoma, paraneoplastic neurological syndromes, extralimbic encephalitis

Introduction

Paraneoplastic neurological syndromes (PNS) are defined as remote effects of cancer that are not caused by the tumor or its metastasis or by infection, ischemia or metabolic disruptions.1,2) Thymoma is the most common tumor of the anterior mediastinum. Forty percent of patients with thymoma have one or more PNS, and myasthenia gravis accounts for approximately 20%–25% of these PNS. Limbic encephalitis is a rare PNS associated with thymoma (about 30 cases reported to date), whereas extralimbic encephalitis (ELE) has been described in the literature very rarely.3–10)

Case Report

A rare case of ELE associated with thymoma is presented along with a literature review.

A 66-year-old woman was admitted to our hospital, with a 10-day history of cramping in her right leg and inability to walk. Magnetic resonance imaging (MRI) of the brain showed multifocal high intensity signals on T2 flare images in the cerebral cortex, and chest computed tomography showed a 5-cm anterior mediastinal mass, which was considered to be a thymoma (Fig. 1a). A total body computed tomography (CT) scan was performed, and the chest CT showed a 5-cm anterior mediastinal mass, which was considered to be a thymoma (Fig. 1b). In serological tests, the results of routine biochemistry and blood count tests were normal. The results for serum anti-acetylcholine receptor antibodies, anticardiolipin immunoglobulin G, ANCA, lupus anticoagulant and some cancer indicators (CEA, Ca-19.9, AFP and SCC) were negative but those for ANA (x160), anti-dsDNA (35 IU/ml) antibody and Ca-125 (53.0 U/ml) were positive. Therefore, we speculated that she had paraneoplastic encephalitis associated with a mediastinal tumor. She
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underwent a thymectomy through a median sternotomy and was diagnosed with type B1 thymoma (WHO). The thymoma showed extra capsular invasion of fatty tissue (Masaoka stage II).

On postoperative day 6, her neurological symptoms began to improve. On postoperative day 31, she was discharged without complications. She was followed up in the outpatient clinic at 1-month intervals. Two months later, due to the onset of the sigmoid colon perforation, she underwent Hartmann operation at our hospital. She was discharged from the hospital after 1 month. Brain lesions on MRI taken 3 months after thymectomy had disappeared (Fig. 2). Thereafter, she was treated on an outpatient basis, but the numbness in the lower extremities appeared around 7 months after the initial operation. Her symptoms caused no problems for activities of everyday life but continued to be monitored strictly.

Discussion

PNS are very rare diseases that are mainly associated with small cell lung cancer, testicular cancer, bladder cancer and breast cancer.11) PNS may be defined as disorders of the nervous system that occur as a result of malignancy but are not caused by direct tumor growth, metastases or metabolic or infectious complications.1,2) Thymoma is the most common neoplasm of the anterior mediastinum, and it is known as a tumor type that can cause PNS. Thymoma occurs often with paraneoplastic myasthenia gravis; however, it is rarely associated with encephalitis accompanying brain lesions that are usually confined to the limbic system. Approximately 30 cases of limbic encephalitis associated with thymoma have been reported,3) whereas only nine cases of ELE have been reported, including our case.3–10) The patients in these nine cases included four men and five women, with a median age of 43 years. Seven patients showed seizure as the primary symptom. All cases were treated by thymectomy. Two cases developed ELE during thymoma recurrence of thymectomy surgery (Okita and Hammond reported cases).6,7) In five cases, including our case, neurological symptoms improved after treatment (Table 1). In almost all cases that experienced postoperative favorable progress, with proven histological type, neurological symptoms improved during the early postoperative period. Several studies have reported PNS occurring

Fig. 1  (a) Preoperative brain magnetic resonance imaging (MRI) showed multifocal hyperintense lesion on T2 flare images in the cerebral cortex. (b) Preoperative chest computed tomography (CT) showed a 5 cm anterior mediastinal mass which was considered to be a thymoma.

Fig. 2  Follow-up brain magnetic resonance imaging (MRI) showed that the brain lesions had disappeared.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Age/Sex</th>
<th>Symptoms</th>
<th>Histology</th>
<th>Thymectomy</th>
<th>Symptomatic improvement after surgery</th>
<th>Elapsed time until symptoms are improved</th>
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<tbody>
<tr>
<td>Rickman</td>
<td>2000</td>
<td>55/M</td>
<td>Seizure Confusion Memory loss</td>
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<td>done</td>
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<td>–</td>
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<tr>
<td>Ances</td>
<td>2005</td>
<td>38/M</td>
<td>Confusion Memory loss</td>
<td>–</td>
<td>done</td>
<td>Unknown</td>
<td>–</td>
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<tr>
<td>Okita</td>
<td>2007</td>
<td>33/F</td>
<td>Seizure Confusion Memory loss</td>
<td>Type B2</td>
<td>done (7 years ago)</td>
<td>No change</td>
<td>–</td>
</tr>
<tr>
<td>Hammoud</td>
<td>2009</td>
<td>43/F</td>
<td>Seizure Confusion Aphasia</td>
<td>Type B2</td>
<td>done (4 years ago)</td>
<td>No change</td>
<td>–</td>
</tr>
</tbody>
</table>
| Rizzardi  | 2009 | 55/F    | Seizure Aphasia                   | Type AB   | done       | Improved                            | POD7, her symptoms completely disappeared.
| Werry     | 2009 | 33/M    | Seizure Memory loss               | Type B1   | done       | Improved                            | Two weeks after thymectomy, MRI showed that most of the former lesions had vanished while a multitude of new lesions had erupted in both temporal lobes.  
| Suh       | 2013 | 42/F    | Confusion Memory loss             | Type B1   | done       | Improved                            | POD10, the symptoms began to improve.  
| Aysal     | 2013 | 43/M    | Seizure                           | Type AB   | done       | Improved                            | After the thymectomy, his seizures completely disappeared. MRI showed most of the lesions had disappeared 49 days after the thymectomy.  
| Our case  | 2014 | 66/F    | Seizure                           | Type B1   | done       | Improved                            | POD6, the symptoms began to improve. Brain lesions had disappeared in the MRI that was taken for 3 months after thymectomy. |

MRI: magnetic resonance imaging
with a thymoma and revealed a variety of symptoms and disease types, with almost no specific findings for disorders of the central nervous system or in blood test findings, including auto-antibodies. By limiting the cases of thymoma to those that exhibited ELE, we may be able to evaluate a limited group, with similar disease types. It is also possible to consider only those who have a good response to surgical treatment within this specific group. PNS are group of diseases associated with autoantibodies, but no autoantibodies have been found commonly in patients who exhibited ELE. However, because not all autoantibodies have been reported, there is a possibility in the future that autoantibodies as specific markers will be identified in ELE associated with thymoma. In addition, the patient in the present case recovered without any conditions that limit activities of daily life, but neurological symptoms, such as numbness, still remain. Thus, strict observation is necessary due to the possibility of a thymoma recurrence; two cases have been reported in which neurological symptoms recurred following recurrence of the thymoma. An extended thymectomy or adjuvant radiation therapy could have been used to prevent relapse in this case. We still do not know the main cause of this disease, but the reported cases indicate that surgical treatment for ELE associated with thymoma during the early phase may be effective.

Conclusion

ELE associated with thymoma is a rare condition. Although the main cause of this disease remains unknown, neurological symptoms in these cases have been improved after thymectomy at an early stage. Thus, the reported cases suggest that surgical treatment for ELE associated with thymoma during the early phase may be effective, although there is a possibility that the observed improvements in symptoms is a temporary effect.

Acknowledgments

The authors would like to thank Enago (www.enago.com) for the English language review.

Disclosure Statement

Masato Aragaki and co-authors have no conflicts of interest to declare.

References