Rasmussen’s encephalitis (RE) is generally considered to be a disease of childhood, with the vast majority of cases occurring in children less than ten years of age. However, there are at least 29 cases of adult or adolescent onset Rasmussen’s in the literature (Table), with the oldest reported case to date occurring in a 54-year-old female. Despite a lack of strict diagnostic criteria, RE is generally accepted as the appropriate diagnosis in the setting of a chronic, progressive, focal encephalitis which is commonly accompanied by seizures (classically epilepsia partialis continua [EPC]), hemiparesis, and cognitive decline. Importantly, other causes of focal encephalitis such as active viral infection should be ruled out before a diagnosis of RE. There are several emerging reports of glutamate receptor autoantibodies as possible contributors to the pathogenesis of RE, although antibodies are also found in other epilepsy subtypes and are not specific to RE. We report the diagnosis and management of a 58-year-old previously healthy female, with clinical, radiological, and histopathological evidence of Rasmussen’s encephalitis, representing the oldest confirmed case to date.

CASE REPORT

The patient was referred to our center following her first generalized tonic-clonic seizure. History revealed that she had suffered three episodes of complex partial seizures over the previous three months, each characterized by numbness of the left face and arm with decreased
responsiveness and staring for 15-30 seconds. Physical examination was normal. Electroencephalogram (EEG) revealed periodic lateralized epileptiform discharges over the right region. Cerebrospinal fluid (CSF) analysis revealed 8 WBC/mm$^3$ and was negative for herpes simplex virus DNA by PCR. Serologic testing was negative for acute CMV, VZV, HSV, and EBV infection. An MRI showed T2 hyperintensity in the right temporoparietal region but no diffusion restriction on diffusion weighted imaging. The patient experienced no further episodes in hospital, and was discharged home on phenytoin and clopidogrel.

The patient returned two weeks later complaining of dysarthria, ongoing paresthesias and intermittent low amplitude twitching of the left face. Examination revealed mild dysarthria and subtle irregular

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**Table: Summary of adult cases of Rasmussen’s encephalitis**

<table>
<thead>
<tr>
<th>Author (Year, ref)</th>
<th>Number of Patients (ages/sex)</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gray et al. (1987; 8)</td>
<td>1 (29/F)</td>
<td>Anticonvulsants</td>
<td>Died 2 years after onset of seizures</td>
<td>Biopsy and autopsy consistent with RE</td>
</tr>
<tr>
<td>McLachlan et al (1993; 2)</td>
<td>3 (36, 24, 16)</td>
<td>Cortical resection</td>
<td>Improved seizure control</td>
<td>All 3 biopsies positive for CMV</td>
</tr>
<tr>
<td>Hart et al (1997; 5)</td>
<td>13: 4 pts age 21-40, 5 adolescents aged 13-16, 3 adults presenting as mass lesions</td>
<td>Anticonvulsants, surgery</td>
<td>Variable</td>
<td></td>
</tr>
<tr>
<td>Leach et al (1999; 7)</td>
<td>2 (39/M, 33/F)</td>
<td>Steroids followed by IVIG</td>
<td>Striking improvements in cognition, seizure control, and motor function</td>
<td>Patient 2 not biopsy confirmed</td>
</tr>
<tr>
<td>Vadlamudi (2000; 3)</td>
<td>1 (54/F)</td>
<td>Anticonvulsants, steroids, IVIG, Gancyclovir</td>
<td>Ongoing seizures, cognitive decline, progression of MRI changes</td>
<td>Gadolinium enhancing lesions, not otherwise described. CSF normal</td>
</tr>
<tr>
<td>Hennessy et al (2000; 9)</td>
<td>2 (22/F, 31/F)</td>
<td>Temporal lobectomy</td>
<td>Stable with infrequent seizures, no further cognitive decline</td>
<td>Biopsies consistent with RE</td>
</tr>
<tr>
<td>Villani et al (2001; 4)</td>
<td>1 (45/F)</td>
<td>IVIG</td>
<td>Resolution of EPC, 75% reduction in seizure frequency, improvement of neurologic deficits</td>
<td>Onset of EPC 13 years after onset of disease</td>
</tr>
<tr>
<td>Wennberg et al (2003; 1)</td>
<td>1 (24/F)</td>
<td>Anticonvulsants</td>
<td>Stable for 5 years, clinically and on serial MRI</td>
<td>Biopsy consistent with RE</td>
</tr>
<tr>
<td>Granata et al (2003; 6)</td>
<td>1 (45/F)</td>
<td>IVIG</td>
<td>Resolution of EPC, 75% reduction in seizure frequency, improvement of neurologic deficits</td>
<td>Only adult patient in series of 15. Children showed less improvement with IVIG</td>
</tr>
<tr>
<td>Lagrange et al (2003; 10)</td>
<td>1 (40/M)</td>
<td>Anticonvulsants, 2 temporal lobe resections</td>
<td>Mild improvement but ongoing daily seizures</td>
<td>Presented with narcolepsy</td>
</tr>
<tr>
<td>Takahashi et al (2005; 11)</td>
<td>3 (23/F, 25/F, 28/F)</td>
<td>N/A</td>
<td>N/A</td>
<td>2 patients positive for antibodies to GluR$_2$</td>
</tr>
</tbody>
</table>

EPC = Epilepsia Partialis Continua; F = Female; GluR$\_2$ = NMDA Glutamate receptor $\varepsilon 2$ subunit; IVIG = Intravenous Immunoglobulin; M = Male; RE = Rasmussen’s encephalitis
twitching of the left facial muscles including masseter, orbicularis oris and platysma, with sparing of the forehead. Repeat MRI revealed extension of the lesion in the right temporoparietal region. Gyriform T1 hyperintensity was identified with underlying T2 hyperintensity in the subcortical white matter (Figure 1). There was little associated mass effect and minimal regional sulcal effacement. Repeat CSF examination revealed an elevated WBC count of 23/mm³ with a predominance of lymphocytes. Antibodies to glutamate receptor R3 were not detected in the CSF. Repeat EEG showed ongoing periodic lateralized epileptiform discharges. An angiogram of the cerebral vessels was normal.

Over the next several weeks the patient developed continuous, irregular, large amplitude myoclonic movements of the left face at 5-10 Hz. Eventually the right face became involved, although to a lesser extent than the left. The patient also developed twitching of the tongue and palate, characterized by irregular large amplitude and high frequency jerks synchronous with those of the left face. Consciousness and cognition were not measurably impaired at this point. However, the patient lost the ability to speak and had significant incoordination of swallowing, but was able to communicate effectively by writing. Several anticonvulsant medications were administered with very limited response.

The patient then experienced insidious onset of deficits in cognition, attention, and visuospatial reasoning. The patient was unable to form simple mathematics, tended to perseverate, and lost the ability to communicate using handwriting. She was unable to ambulate or sit upright independently. Frequent episodes of unresponsiveness and staring developed. There was no evidence of neglect.

Biopsy of the right temporoparietal region revealed diffuse astrocytic gliosis (Figure 2) and microglial activation, with microglial and neurophagocytic nodules in the cortex (Figure 3), and occasional microglial nodules in subcortical white matter. Perivascular lymphocytic cuffing was present in the cortex, and to a lesser extent in the leptomeninges and subcortical white matter (Figure 4). Scattered intraparenchymal and leptomeningeal lymphocytes were also present. Perivascular and leptomeningeal lymphocytes consisted of CD3 immunopositive T cells and CD20 immunopositive B cells, while intraparenchymal lymphocytes were predominantly T cells. Intracellular viral inclusions were not identified, and immunohistochemistry was negative for CMV and HSV1 and 2, as was in-situ hybridization for EBV.

A diagnosis of Rasmussen’s encephalitis was made and a course of intravenous immunoglobulin was initiated. There was marked improvement over the next several weeks following just four days of

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**Figure 1**: (A) Axial T1 weighted MRI demonstrates hypointense signal in the right temporoparietal region with cortical gyriform hyperintense signal (arrow). (B) T2 weighted MRI demonstrates hyperintense signal in the corresponding region.

**Figure 2**: Diffuse astrocytic gliosis involving cortex (asterix) and subcortical white matter (cross). (Dako GFAP immunoperoxidase, DAB/hematoxylin; original magnification x 40)

**Figure 3**: Neuronophagic nodule in cortex (arrowheads). Arrow points to neuron. (H&E; original magnification x 400).

**Figure 4**: Perivascular lymphocytic cuff (large arrow) and scattered intraparenchymal (small arrows) and leptomeningeal (arrowheads) lymphocytes. (NeoMarkers CD3 immunoperoxidase, DAB/hematoxylin; original magnification x 100).
IVIG therapy, both with respect to cognition and seizure activity. The patient was again able to speak after several weeks of very limited communication by handwriting and gestures. Treatment was complicated by a deep venous thrombosis and anemia with a positive coomb’s test, and treatment was stopped after eight days (deletion). The patient continued to improve symptomatically and functionally for approximately 14 days, after which her condition was stable for an additional week. At this time, slow progression of deficits returned with increased weakness and jerking of the left hand and face as well as palate with loss of comprehensible speech. There was no improvement with a course of plasmapheresis. After placement of an inferior vena cava filter, IVIG was resumed with weekly 2-day courses, which resulted in moderate improvement in cognition, speech and seizure activity. At a one year follow-up visit, with ongoing treatment, the patient was living independently, ambulating unassisted, and seizure free with minimal cognitive impairment. She had, however, developed neglect and astereognosis of the left hand. At 18 months, the patient was demonstrating some clinical evidence of focal seizures affecting the left face although functionally and cognitively was stable. Neglect and astereognosis had resolved.

**DISCUSSION**

This patient represents the oldest confirmed case of Rasmussen’s encephalitis and adds to the growing body of evidence suggesting that the adult variant is more common than previously thought. Rasmussen’s encephalitis should therefore be included in the differential diagnosis for any patient with chronic, progressive, focal encephalitis, particularly when characterized by epilepsia partialis continua. This case also poses important questions with respect to management of this disease in adults. While hemispherectomy is the standard of care for this condition in children, this may not be as suitable for adults, in whom cerebral functional plasticity is more limited. In patients with refractory seizures who are poor candidates for surgical intervention, the benefits of IVIG have been clearly demonstrated,\(^5\)\(^6\)\(^7\) and are further supported by the dramatic improvements seen in our patient. We therefore propose that IVIG be employed as a first line agent in the treatment of adult onset RE.

**REFERENCES**