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LETTER TO THE EDITORS

Differential long-term evolution after surgery or pharmacotherapy of Rasmussen encephalopathy in adult patients

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Dear Sir,

Rasmussen encephalitis (RE) is a severe encephalopathy marked by a chronic brain inflammation including microglial nodules, perivascular infiltrates, neuronal loss and gliosis [1], which typically affects one hemisphere. Although clinical onset is usually in the childhood, some cases begin in the adolescence or young adulthood. Clinically, it is characterized by drug-resistant seizures, often epilepsia partialis continua (EPC) and epileptic status, motor and sensorial impairments, cognitive impairments secondary to progressive brain dysfunction. Magnetic resonance shows progressive unilateral atrophy of the cortex, caudate nucleus and signal alteration of the white matter. Treatment is aimed at controlling the seizures and stopping clinical worsening. To date, the surgical exclusion of the affected hemisphere has been the only therapeutic option to achieve both objectives [2, 3]. Functional hemispherectomy of the affected hemisphere is unanimously recognized as the treatment of choice when the disease has already caused focal signs (e.g., hemiparesis, hemianopsia, aphasia) [4]. In the adult patients, especially when the dominant hemisphere is involved, this option may be not feasible and the therapy is mostly pharmacological; limited cortical resection for treatment of EPC has also been applied [5]. To our knowledge, the Literature reports studies investigating the progress of adult RE patients, mostly related to clinical and neuroradiological aspects; it has been found that adolescent and adult patients have a more protracted and milder course with a longer, relatively unspecific, prodromal phase with respect to children with RE [4]. Here, we describe the long-term history of two adult left-hemisphere (dominant) RE patients, treated with brain surgery and pharmacotherapy, respectively; focus is kept on the evolution of language impairment.

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At age 23, PR presented with seizures represented by auditory hallucinations (whistles in the right ear), right deviation of the oral rhyme and head, hypertonic right limbs and secondary generalization. At the first neuropsychological assessment, spontaneous speech was marked by severe dysartria, poor fluency, anomia, frequent phonemic paraphasias, rare semantic paraphasias and automatisms. The sentences included one to two words and repetitions of the parts of the sentences. PR only understood simple verbal instructions and, at the description of figures, she only produced single words accompanied by the movements of the left hand aiming to imitate the action or to explain the figure. Writing was severely compromised, showing transpositions, omissions and fusions of letters or parts of the sentences. Upon first evaluation, diagnosis was confirmed and intensive immunomodulant and immunosuppressive treatment (mitoxantrone- MTX) began [6]. At the 4 years' follow-up, the seizures were characterized by staring and right motor seizures, persistent facio-brachial EPC. Overall, the language had an initial positive evolution that stabilized over time (Fig. 1), in particular the perseverations had been reduced; praxis and executive functions remained impaired. PR walked with help and autonomously ate using her left hand. During physical and language rehabilitation, this picture was stable.

CP presented, at age 20, with involuntary movements of the tongue and face on the right, dysarthria and myoclonic jerks of the right upper limb. Six years after onset, she presented super-refractory status epilepticus and a cortectomy confined to the central lobe, preserving the frontal operculum, was performed (see Villani 2014 for details) with complete control of seizures. At the first neuropsychological evaluation, spontaneous speech was characterized by articulatory difficulties and numerous phonemic alterations (letter substitutions, additions or transpositions) and conduites d'approches. The sentences were very simple, with numerous word-finding pauses, in the absence of grammatical functions. The oral and written comprehension of words and short sentences was moderately compromised.

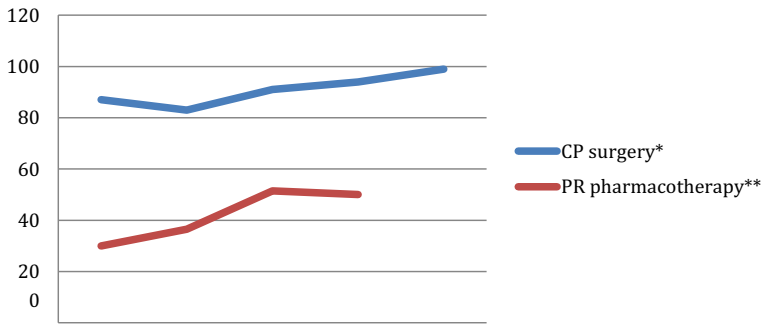

Fig. 1 Language trend after surgery or pharmacotherapy

*The language performance of this patient improved consistently after surgical cortical removal
** In this case, the language had an initial positive evolution that stabilized and remained unchanged over time

Spontaneous writing and writing under dictation were seriously compromised, as well as reading aloud. Three years later, she underwent the surgical excision of the left central cortex. Nine years after surgery, CP was seizure free. Oral language comprehended in part the grammatical rules, verbs conjugation and the automatisms were partially suppressed; praxis was improved. The picture was stable during post-surgical motor and language training.

These cases, presenting with very similar clinical pictures, show that tailored epilepsy surgery can be an effective tool in the treatment of RE. In particular, language may improve consistently after surgical cortical removal in the absence of side effects, in accordance with previous findings [7]. On the other hand, this study also showed that the language performance trend was improving after the treatment with MTX, although with a different profile and that it was effective in reducing seizure frequency [6].

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical standard statement The authors state that no approval by ethics committee is required for the issue of this letter, and that all applicable Italian laws have been observed.

References

1. Varadkar S, Bien CG, Kruse CA, Jensen FE, Bauer J, Pardo CA, Vincent A, Mathern GW, Cross JH (2014) Rasmussen's encephalitis: clinical features, pathobiology, and treatment advances. Lancet Neurol 13:195–205. https://doi.org/10.1016/S1474-4422(13)70260-6
2. Vining EP, Freeman JM, Pillas DJ, Uematsu S, Carson BS, Brandt J, Boatman D, Pulsifer MB, Zuckerberg A (1997) Why would you remove half a brain? The outcome of 58 children after hemispherectomy—the Johns Hopkins experience: 1968 to 1996. Pediatrics 100:163–171
3. Kossoff EH, Vining EP, Pillas DJ, Pyzik PL, Avellino AM, Carson BS, Freeman JM (2003) Hemispherectomy for intractable unihemispheric epilepsy etiology vs outcome. Neurology 61:887–890. https://doi.org/10.1212/01.WNL.0000090107.04681.5B
4. Bien CG, Schramm J (2009) Treatment of Rasmussen encephalitis half a century after its initial description: promising prospects and a dilemma. Epilepsy Res 86(2–3):101–112. https://doi.org/10.1016/j.eplepsyres.2009.06.001
5. Villani F, Didato G, Deleo F, Tringali G, Garbelli R, Granata T, Marras CE, Cordella R, Spreafico R (2014) Long-term outcome after limited cortical resections in two cases of adult-onset Rasmussen encephalitis. Epilepsia 55(5):e38–e43. https://doi.org/10.1111/epi.12596
6. Stabile A, Deleo F, Didato G, Pastori C, Antozzi C, de Curtis M, Villani F (2018) Adult-onset Rasmussen encephalitis treated with mitoxantrone. Eur J Neurol 25(12):e125–e126. https://doi.org/10.1111/ene.13795
7. Giovagnoli AR, Parente A, Didato G, Manfredi V, Deleo F, Tringali G, Villani F (2014) The course of language functions after temporal lobe epilepsy surgery: s prospective study. Eur J Neurol 23:1713–1721. https://doi.org/10.1111/ene.13113