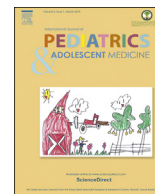


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Case report

Central nervous system manifestation of lupus erythematosus resembling brain abscess

Dimitrios Panagopoulos*, Marios Themistocleous

Neurosurgical Department of Pediatric Hospital of Athens, 'Agia Sophia', Thivon & Papadiamantopoulou St, Goudi, Athens, Attica, 11527, Greece

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ABSTRACT

Manifestations of central nervous system involvement are one of the leading causes of morbidity and mortality in patients suffering from systemic lupus erythematosus. It frequently involves the central nervous system and sometimes need to be differentiated from lesions of infectious etiology, thus representing a major diagnostic dilemma. We present the case of a male adolescent with a known history of idiopathic thrombocytopenic purpura who presented with a seizure ictus and a space-occupying lesion, which posed significant diagnostic challenges to specify its characteristics.

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1. Introduction

Neuropsychiatric manifestations in systemic lupus erythematosus (SLE) are currently recognized to be of broad spectrum and frequently encountered in clinical practice. In clinical terms, it may present as a diffuse disease (e.g., psychosis or depression) or focal disease (e.g., stroke or transverse myelitis) [1,2].

Nervous system involvement in SLE is referred to as neuropsychiatric SLE (NPSLE) [2] and occurs in 10–80% of patients [3].

Most lesions encountered in the CNS are related to ischemic injury in the territory of small-diameter vessels [4], thus suggesting a thromboischemic pathogenesis mechanism instead of an autoantibody-mediated inflammation as it is commonly encountered in SLE.

There is growing evidence indicating that patients with childhood-onset SLE (cSLE) have a more aggressive disease course than their adult counterparts (aSLE), in terms of involving organs such as the CNS [5]. In lupus, a higher prevalence of thrombocytopenia was detected in cSLE than in the adult patient population. The point is that this feature was correlated with a more severe and active disease course.

MRI abnormalities most commonly encountered in these

patients are small subcortical hyperintense lesions and infarcts, predominately seen in the NPSLE subpopulation of patients [6].

2. Materials and methods

The referred patient is a 15-year-old boy who was admitted to the emergency department after an ictus of grand mal epileptic seizure. The patient medical history revealed that he was suffering from chronic idiopathic thrombocytopenic purpura (ITP), which was under treatment with corticosteroids and gamma globulin.

His age at presentation was 6 years, and the initial manifestation was a sudden onset of bruising and a petechial rash. The onset of ITP was preceded by an upper respiratory tract infection, with an interval of approximately 2 weeks. Minor epistaxis was also observed. Platelet counts at presentation were $15 \times 10^9/L$. The blood smear showed a marked decrease in platelets, with some platelets being large (megathrombocytes). A bone marrow aspirate was performed, which revealed increased numbers of megakaryocytes, many of which were immature. An additional finding was an increase in the number of bone marrow eosinophil precursors. Clinically significant lymphadenopathy and a marked hepatosplenomegaly were not observed; however, shotty, cervical adenopathy was reported on the initial clinical examination and the spleen tip was not palpable.

The initial CT scan revealed a relatively hyperdense lesion located in the left parietal lobe, at the gray matter–white matter junction, with extensive surrounding edema, thus resembling a fingerprint configuration (Fig. 1).

* Corresponding author.

E-mail addresses: dimpanayop@gmail.com (D. Panagopoulos), mthemistocleous@gmail.com (M. Themistocleous).

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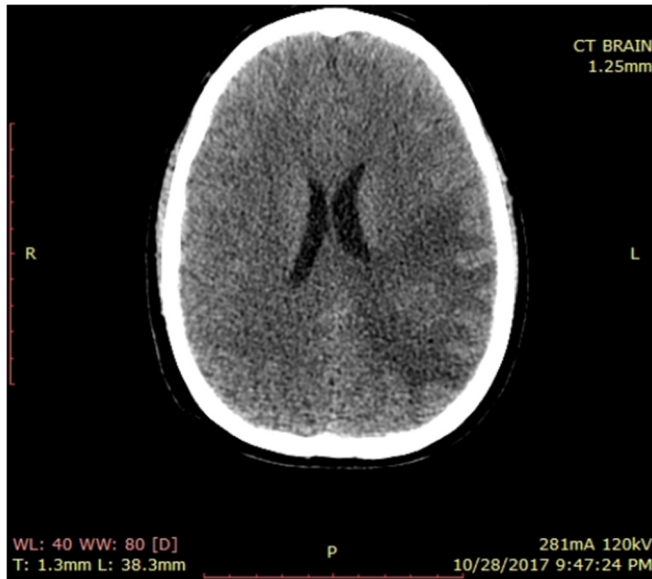


Fig. 1. CT scan, demonstrating the relatively hyperdense lesion with dense surrounding edema.

On the basis of the results of the CT scan, an MRI scan was immediately performed. It verified the presence of a lesion located in the left parietal lobe with a maximum diameter of 1.8 cm. It was surrounded by a significant amount of edema, extended toward the splenium of the corpus callosum and the occipital horn of the ipsilateral lateral ventricle, which was mildly compressed. After intravenous contrast administration, dense contrast uptake at the periphery of the lesion was documented, as well as a central enhancement area with linear characteristics. Furthermore, a lesion was also depicted at the junctional area between the left frontal and parietal lobe in the vicinity of cortex and subcortical white matter, with dense contrast enhancement.

Additional areas of abnormal signal characteristics were encountered on the right temporal lobe (cortex and subcortical white matter), and in the vicinity of the fourth ventricle, the aforementioned lesions did not demonstrate contrast uptake (Fig. 2A–C).

On the basis of these findings, the differential diagnosis included abscess formation and an inflammation process of undetermined etiology. The initial therapeutic regimen included cefotaxime, metronidazole, phenytoin, and dexamethasone because the definitive diagnosis was obscured and we had to encounter both clinical scenarios. We were aware of the fact that dexamethasone was contraindicated in case abscess was the definitive diagnosis. However, the extent of edema justified its use, at least for a short period of time. Furthermore, the possibility that the space-occupying lesion was of an inflammatory etiology mandated the use of corticosteroids.

The MRI scan was repeated 10 days after the admission of the patient, and MR spectroscopy was also performed for further diagnostic evaluation.

We observed that, at the repeat examination, the maximum diameter of the lesion was 1.2 cm and that edema surrounding the lesion was slightly reduced. In comparison with the previous MRI scan, edematous areas that were noted at the posterior-inferior region of the left temporal lobe, in the vicinity of the pole of the right temporal lobe, was diminished in size. Areas of abnormally low signal are encountered in the left frontal lobe and to the left middle cerebellar peduncle.

The lesion with the largest diameter continues to demonstrate abnormal contrast uptake, mainly in the periphery, although a centrally located area with linear contrast enhancement was mentioned the overall enhancement pattern remained unchanged, when compared with the previous imaging. Diffusion sequences reveal a peripheral rim with mild restriction of diffusion, whereas the central portion of the lesion did not reveal similar findings, and there was no increased blood supply to the lesion (Fig. 3A–C).

MR spectroscopy detected a mild increase in the concentration of choline, severe decrease in the N-acetyl aspartate level in the region of the lesion and the surrounding edema, and peaks of concentration for lactate lipids and esters, which were indicative of a necrotic lesion. There were no specific peaks of amino acids detected, which could indicate the possibility of infection, although their peaks may appear to be overlapped with those of the aforementioned ones (Fig. 4A–C).

The conclusion was that the most possible pathologic entities that should be included in the differential diagnosis were the following:

- Multiple abscesses, given that they recede due to intravenous broad-spectrum antibiotic coverage, suitable for gram-positive and -negative organisms. The limitation was that the morphological characteristics of the lesions were not consistent with this diagnosis, even if it refers to a lesion being at the late cerebritis stage.
- An inflammatory lesion of another etiology, as granulomatous or fungal, could not be excluded.

Because of this diagnostic dilemma, the next diagnostic step was to perform a biopsy of the lesion, under neuronavigation guidance. The limitations for this management strategy were the low platelet count of the patient due to ITP (consistently less than 30,000/ml) and the scenario that the underlying lesion was an incompletely encapsulated intracerebral abscess. In that case, the possibility of dissemination of the infection along the trunk of the needle could not be excluded and its clinical significance should not be overemphasized.

On the basis of that evidence, the patient underwent a full laboratory work-up for autoimmune disorders and infection from atypical organisms, including PCR of CSF samples. The microbiological work-up result was negative. However, the patient fulfilled four of the 11 criteria for the diagnosis of SLE, as they were developed by the American College of Rheumatologists.

More specifically, the patient fulfilled the following criteria:

- Neurological disorders, as seizures were noted.
- Blood disorders, as the patient had persistent anemia and thrombocytopenia.
- Immunologic disorders, in the form of anti-DNA positivity and positivity for antiphospholipid antibodies (values were in the pathologic range).
- Values of abnormal antinuclear antibodies (ANA) were measured.

Specifically, anti-double-stranded DNA (anti-ds DNA) of the IgG class was measured, and their value was 100 IU/ml. Measurement was based on the first international standard for anti-ds DNA (according to the Wo/80 of the World Health Organization).

Anti-DNA titer was 1:160 and anti-ANA titer was 1:320, respectively. Our investigation was also centered against antiphospholipid antibodies, specifically lupus anticoagulant and anticardiolipin antibodies. In the first instance, the results from the tests were considered positive, as they are above the local cutoff value (the cutoff value was the 99th percentile). Regarding

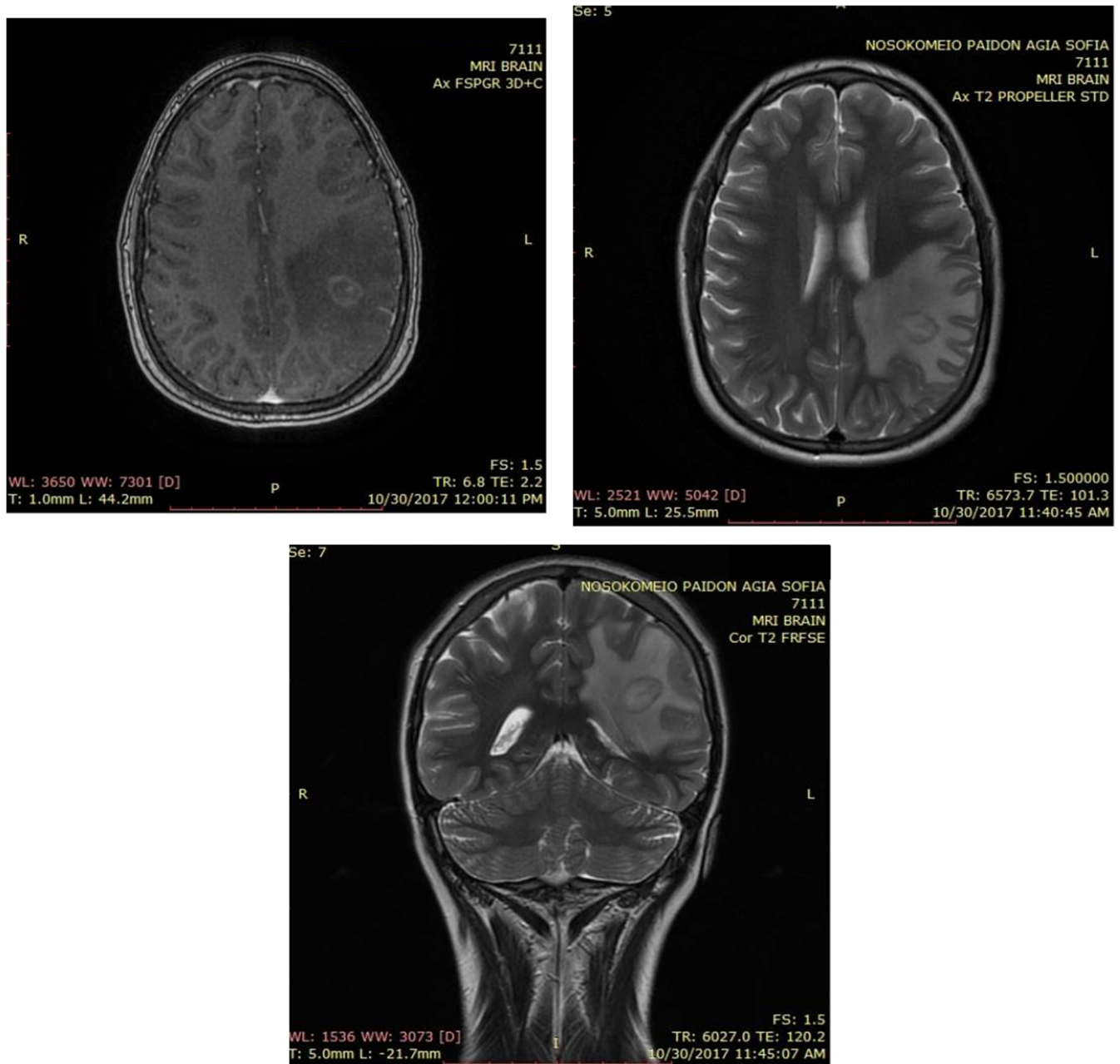


Fig. 2. A. MRI scan, axial slice with contrast administration, depicting the lesion with its underlying edema. B. MRI scan, axial T2 sequence, depicting better extent of edema. C. MRI scan, coronal T2 sequence, depicting similar findings as those obtained previously.

anticardiolipin antibodies, enzyme-linked immunoassay (ELISA) was the test used in our patient. The values were 50 immunoglobulin G (IgG) phospholipid units (GPL), and 45 immunoglobulin M (IgM) phospholipid units (MPL) and were considered as positive.

Additionally, the patient was constantly receiving the same therapeutic regimen, and we decided to re-evaluate the patient with a new MRI scan. Approximately four weeks after the previous imaging, a new MRI was executed to monitor the progression of the lesion and its response to therapy. It revealed that a lesion, whose maximum dimensions were 12 × 9 mm, was recognized at the left parieto-temporal region, which demonstrated a peripheral ring of contrast enhancement. It was surrounded by an area of vasogenic edema, which was reduced when compared with the first imaging. Some areas with pathologic signal

intensity, which were recognized in the previous examination, were not evident at that imaging.

The conclusion was that no significant difference in the dimensions of the main lesion was mentioned, except for the moderate restriction of the perilesional edema (Fig. 5A–C). Additionally, an MRA was executed to examine the possibility of a vasculitis of autoimmune etiology. This scenario could not be supported because the MRA did not reveal any pathologic findings (3D T1 Black Blood sequence did not reveal contrast uptake at the arterial wall).

On the basis of that evidence, antibiotics were discontinued, as more than six weeks of therapy were completed and the dimensions of the main lesion were not significantly altered. Instead, the main difference was related to the amount of perilesional

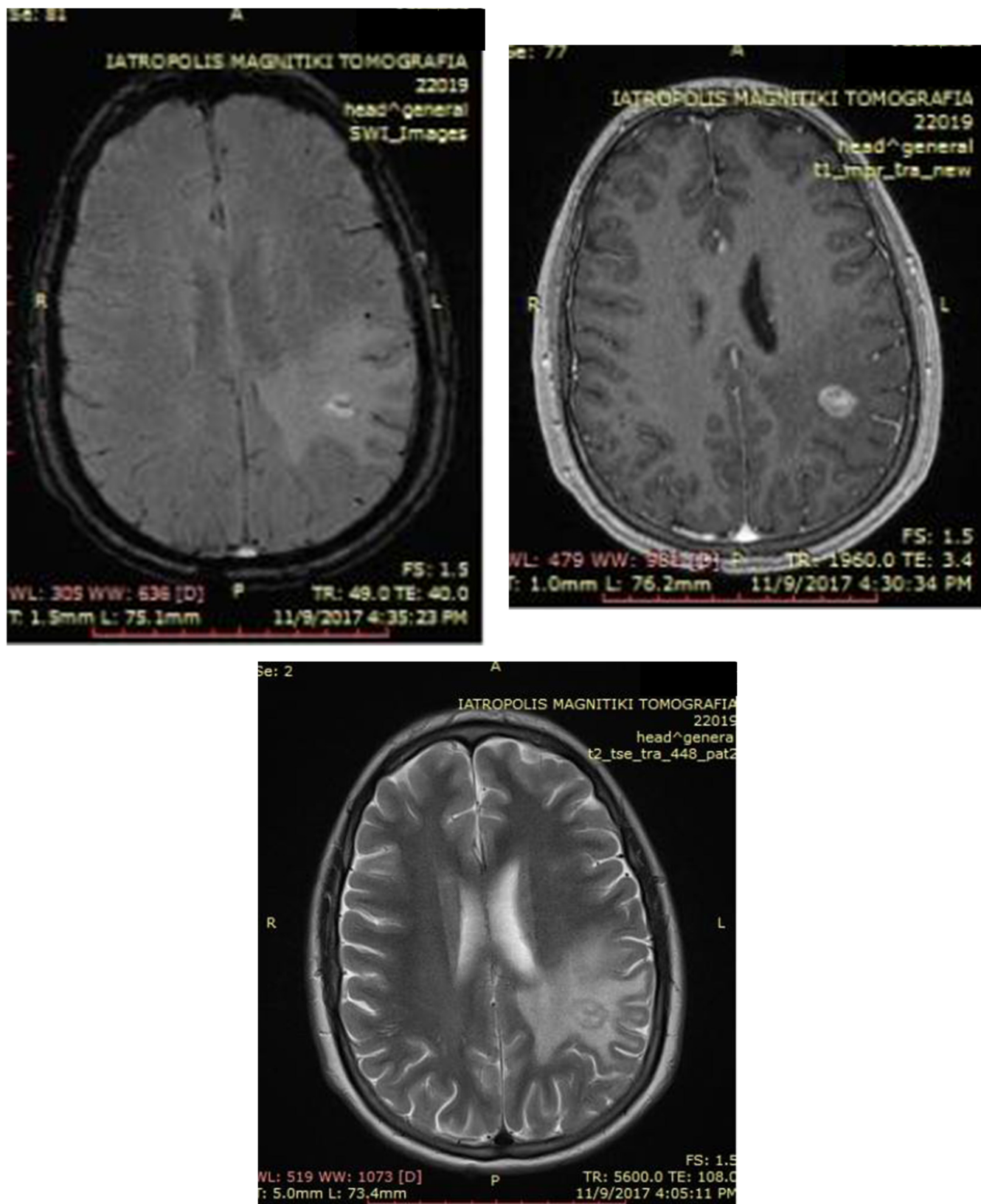


Fig. 3. A. MRI scan, axial susceptibility weighted imaging. B. MRI scan, axial multiplanar reconstruction imaging. C. MRI scan, axial T2 turbo spin echo imaging.

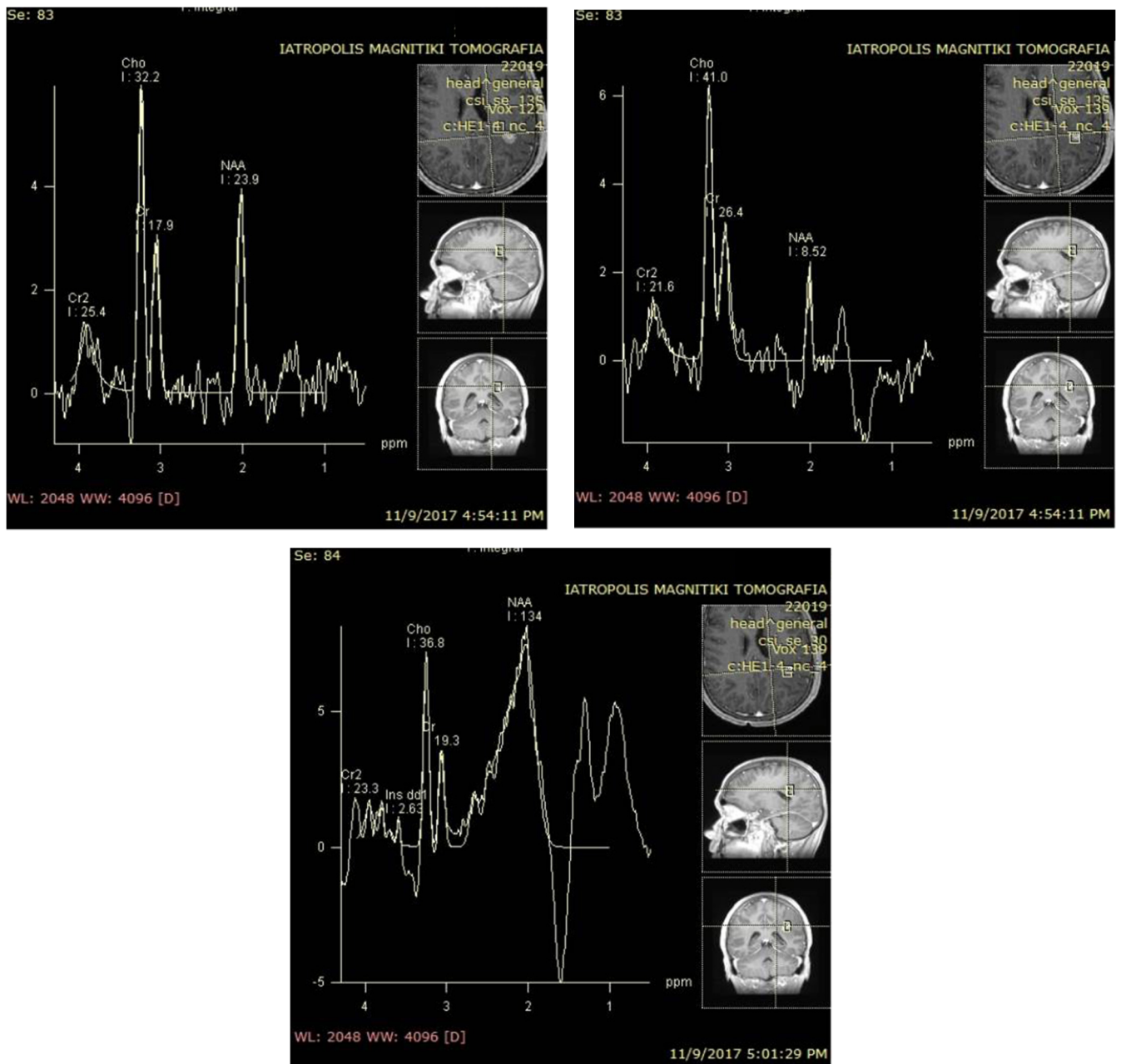


Fig. 4. A. MRS, demonstrating NAA peak. B. MRS, demonstrating creatine and choline peaks. C. MRS, demonstrating NAA and choline peaks at the margins of the lesion.

edema, and this should be attributed to the use of corticosteroids.

The dose of corticosteroids was adjusted depending on the diagnosis of SLE that was now established based on laboratory results, and the patient was discharged from hospital and re-evaluated at regular intervals.

2.1. Theory

In cases where significant diagnostic dilemmas occur in patients with known or suspected NPSLE, different modern imaging modalities, morphological and functional, can be used for evaluation and have become an invaluable tool in differential diagnosis. Although a clinical and neurological examination of the nervous system combined with psychological assessment continue to be the cornerstones of NPSLE diagnosis, modern imaging techniques can be useful in proving an accurate diagnosis.

3. Results

A repeat MRI scan was performed after two months, with the patient under constant corticosteroid therapy. It revealed that the main lesion has significantly reduced in size, along with the surrounding edema, while the other imaging characteristics of the lesion remained unchanged; the smaller, satellite-like lesions had mainly disappeared (Fig. 6A–C).

A final MRI scan was repeated at a six-month interval since the previous imaging, thus documenting that the offending lesions have essentially disappeared, with only a minimum remnant left, concerning the main lesion (Fig. 7A–C).

4. Discussion

Regarding the classification criteria of American College of

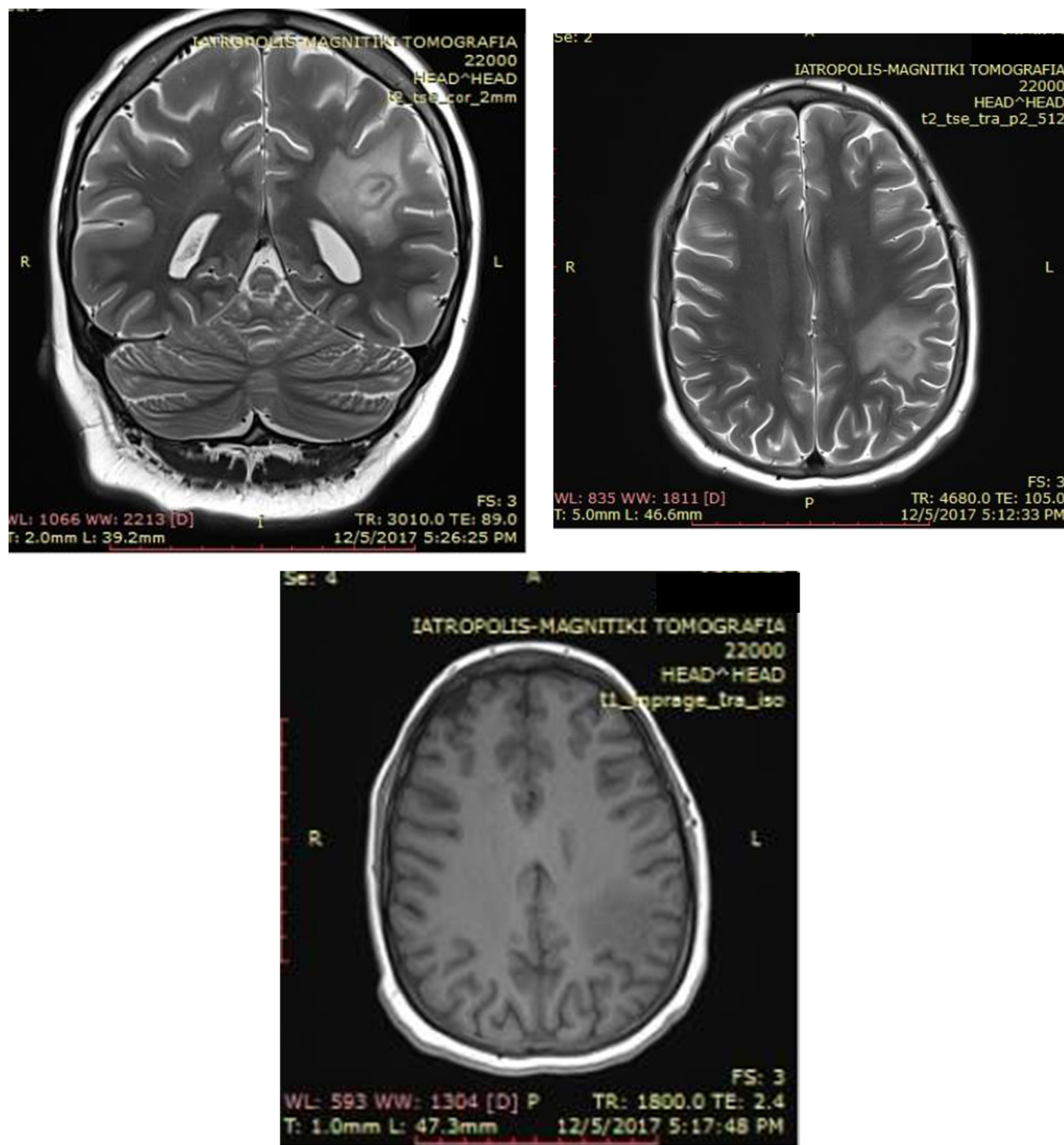


Fig. 5. A. MRI scan, coronal T2 turbo spin echo, depicting decrease in the amount of edema. B. MRI scan, axial T2 turbo spin echo, revealing similar findings. C. MRI scan, T1 axial multiplanar reconstruction sequence.

Rheumatology (ACR) for SLE, the most recently revised ones formally included only seizures and psychosis. Although it is not widely considered to be fully inclusive of all the possible neuropsychiatric manifestations that may be encountered in SLE, it is generally considered to represent a big step forward in the field regarding our attempt to standardize the classification for neuropsychiatric SLE [1]. Our case fulfills these criteria, and our patient can be clinically considered under the term of NPSLE.

Histopathological specimens derived from lesions of patients

suffering from NPSLE showed significantly more microinfarction, macroinfarction, vasculitis, and microthrombi than those from patients with SLE. These may explain the MRI findings of central necrosis in the largest diameter lesion, which complicated the differential diagnosis with abscess formation.

In lupus, a higher frequency of thrombocytopenia is reported in cSLE than in adult population [7], an observation that is in concordance with our data. ITP at cSLE has distinct features compared to that at aSLE, with a more severe presentation

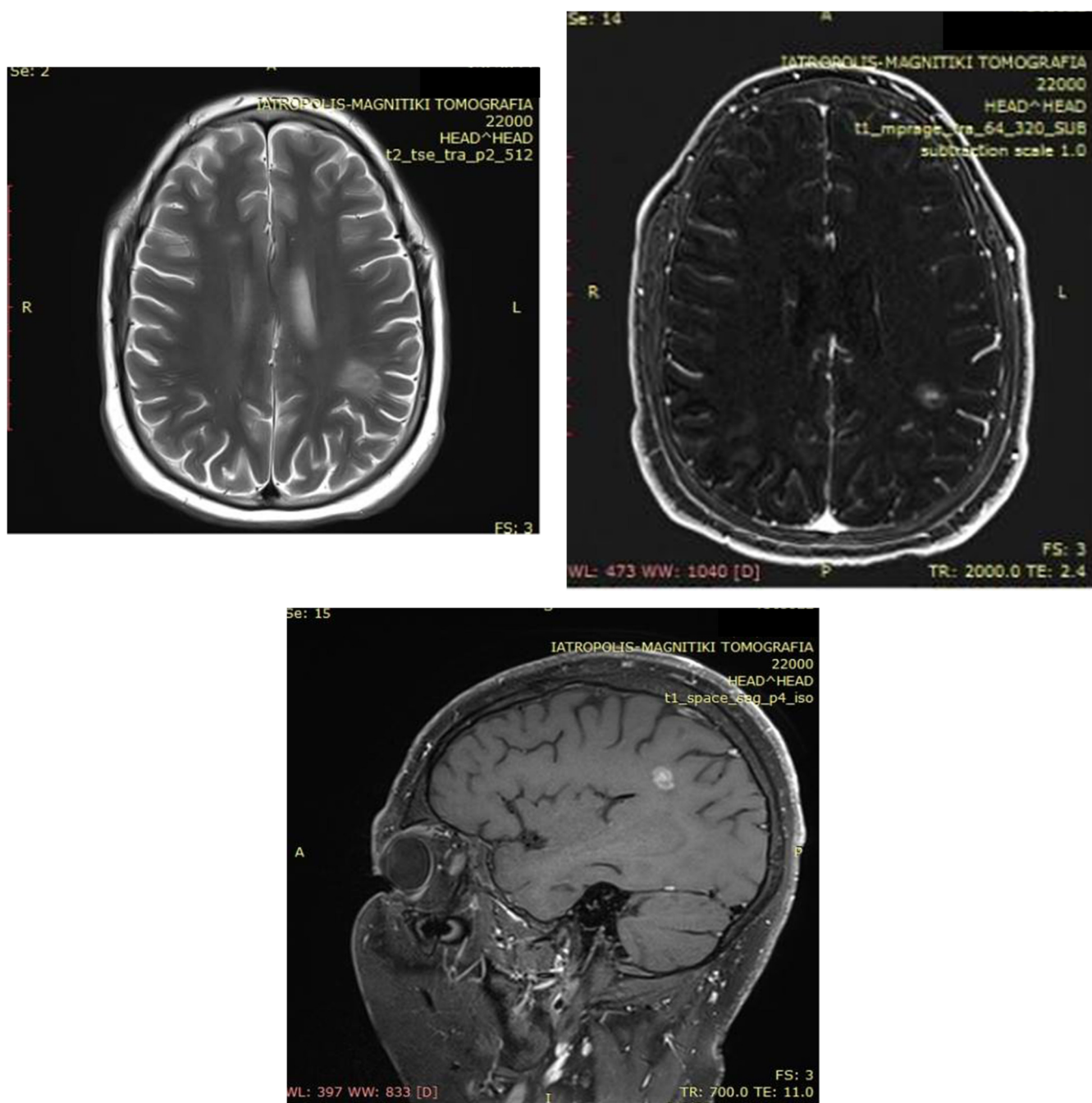


Fig. 6. A. MRI scan, axial T2 turbo spin echo, revealing significant reduction in the size of the lesion. B. MRI scan, T1 axial multiplanar reconstruction sequence, similar findings as those described above. C. MRI scan, T1 sagittal sequence, showing the relative position of the lesion in the anteroposterior dimension.

characterized by, in addition to other manifestations, CNS involvement and hemorrhagic complications [7]. The fact that the first and unique CNS manifestation of CNS involvement of our patient was a grand mal ictus, which underscores these observations.

Magnetic resonance imaging is considered the gold standard for NPSLE imaging [6], with large pathological signals (≥ 10 mm) occurring only in patients with NPSLE.

The most common molecules measured with the aid of MRS in the brain tissue are N-acetyl aspartate, choline, creatine, and myoinositol. MRS profiles have been studied and shown to be changed in patients with NPSLE, although these changes are far more from being specific and pathognomonic.

NAA is reduced in CNS lesions of patients with SLE, but it can also be marked in the normal-appearing brain. However, NAA changes are more profound in patients with NPSLE and can be permanent, which implies neuronal death or transitory damage to the cells [8,9].

Choline levels were shown to be elevated in patients with NPSLE, and its levels correlated with disease activity [10]. To date, MRS is not considered a diagnostic tool in NPSLE diagnosis but should be part of the diagnostic evaluation and follow-up, as it can help characterize the type of injury and its biochemical consistency. This was evident with our case, where MRS was an invaluable tool in our differential diagnostic effort.

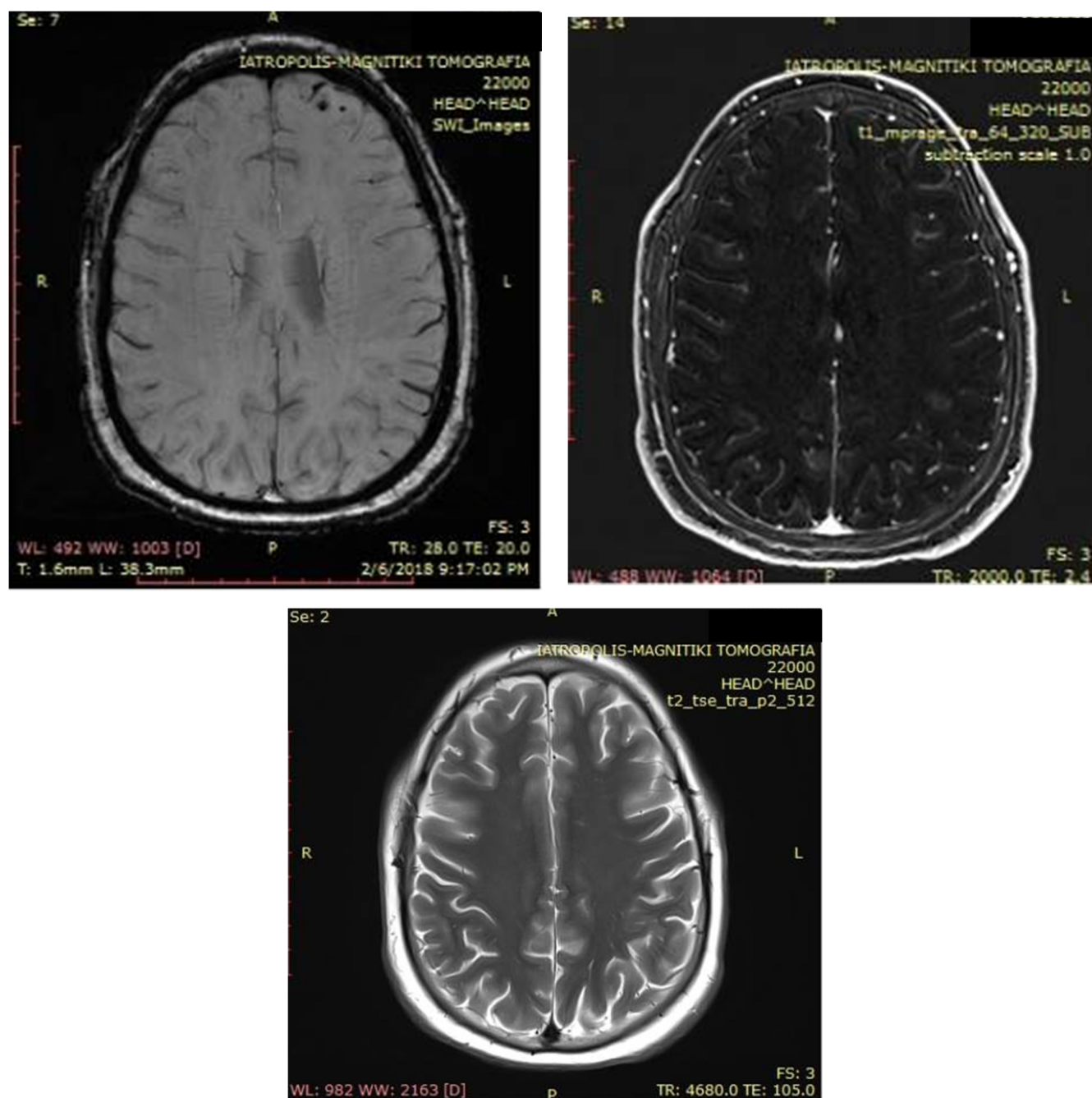


Fig. 7. A. Final MRI scan, Susceptibility weighted imaging, depicting the lesion to be almost disappeared. B. Final MRI scan, T1 axial multiplanar reconstruction, imaging only a very restricted region of edema. C. Final MRI scan, axial T2 turbo spin echo, depicting similar results as those in the previous sequence.

5. Conclusions

A broad spectrum of current imaging modalities is available for clinicians who are treating patients with SLE, mainly MRI and MRS. Although immunological blood tests and CSF analysis, as well as electroencephalography, along with the physical examination remain the mainstay of the diagnostic algorithm, there are some exceptional cases that necessitate the combined use of the aforementioned diagnostic tools. It is known that the most common MRI abnormalities in patients with SLE are small subcortical hyperintense lesions and infarcts, and they can be caused by the disease itself (primary NPSLE) or are due to disease complications or secondary to treatment [6].

However, in cases that are undiagnosed and are presented at an emergency basis, as is our case, a complete radiologic and laboratory work-up should be performed, although it may be inefficient to resolve our diagnostic dilemmas. In such cases, definitive diagnosis could be possibly obtained only after tissue sampling is performed and histopathologic evidence is available, although it was not technically safe in our patient due to aforementioned reasons.

Conflict of interest

No conflict of interest.

Declarations of interest statement

None.

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