

# Mood disorder with psychotic symptoms and overlooked skin lesions: the strange case of Mrs. O

## *Disturbo dell'umore con sintomi psicotici e lesioni cutanee trascurate: lo strano caso della signora O*

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**SUMMARY.** Here we report the case of Mrs. O., a 57 years-old woman presenting with mood disorder with psychotic symptoms developing strange skin lesions, ultimately leading to the suspected diagnosis of varicella-zoster encephalitis. The later appearance of a post-infectious acute inflammatory demyelinating polyradiculoneuropathy further confirmed the suspect. This case stresses the importance for not discarding a priori neurological diagnoses when facing with psychiatric patients, especially when atypical details are present.

**KEY WORDS:** encephalitis, varicella-zoster virus, differential diagnosis, psychiatric onset.

**RIASSUNTO.** Riportiamo qui il caso della signora O., una paziente di 57 anni giunta alla nostra attenzione per un disturbo dell'umore associato a sintomi psicotici e strane lesioni cutanee, la cui interpretazione ha poi portato a formulare il sospetto diagnostico di encefalite da virus varicella-zoster. La successiva comparsa di una poliradicolonevrite demielinizante infiammatoria acuta post-infettiva ha ulteriormente rafforzato tale sospetto. Questo caso sottolinea l'importanza di non scartare a priori diagnosi neurologiche quando si affrontano pazienti psichiatrici e specialmente nel caso in cui siano presenti dettagli di atipicità.

**PAROLE CHIAVE:** encefalite, virus varicella-zoster, diagnosi differenziale, esordio psichiatrico.

### CASE REPORT

Mrs. O. is a 57-year-old woman holding a university degree and mother of two sons; she works as manager's secretary and her past medical history is unremarkable for either psychiatric or any other type of disease. She came to the ER accompanied by her husband because of few days of a sudden and severe depressive symptomatology including thoughts of death and refusal of food and beverages; the family connected this behavior to a very important emotional stress period caused by work-related problems and by a conflicting relationship with her daughter. Her thoughts appeared sometimes delusional centered on ruin ideas and other depressive themes. Moreover, sometimes

she presented very short episodes of confusion during which she displayed depersonalization, identification of herself with her mother, recalling specific biographic details and showing short moments of spatial and temporal disorientation. These latter moments presented unexpectedly, giving the impression of a discontinuous process, within a general frame of mood dysfunction with good enough orientation competences, both in time and space. She was hospitalized in the psychiatric ward and underwent to blood routine tests, neurological examination and a brain MR scan, without showing any significant abnormality. Notably, she presented a maculopapular rash following a T5-T6 dermatomal distribution on the right side of the trunk, later becoming vesicular and that was compatible with

herpes zoster. Dysesthesias were present all along in about the same territory. The patient was treated with valacyclovir and vesicles eventually became hemorrhagic and crusted over after seven days. Fluvoxamine was started and haloperidol was given as well, at the maximum dose of 4 mg/day, before tapering off in ten days. Mrs. O.'s psychical symptoms slowly but steadily improved, although a complete insight regarding the event that led her to hospitalization was still missing. Thirteen days later, she was feeling much better and was, therefore, sent home with the indication to follow-up, keeping fluvoxamine at the dose of 100 mg b.i.d.

A week later Mrs. O. was brought again to the ER by her family since she presented a mixed episode also in this case with psychotic symptoms, as she tried to obtain from her bank an important amount of money that she believed was due to her by the Italian Minister of Treasury as compensation for a work tort. In this case her thoughts were characterized by persecution ideas; her mood cycled within the same day from depression to mania without any insight of disease. Fluvoxamine was stopped and Mrs. O. was started on haloperidol up to 8 mg/die, gradually tapered off. An attempt of associating carbamazepine 150 mg b.i.d. was initially made, although the drug was subsequently discontinued. During this second period of hospitalization, Mrs. O. presented persistent mild fever, and more evident brief moments of spatio-temporal disorientation were noted accompanied by psychomotor slowing. The impression of an underlying process was further confirmed and a neurological consultation was asked again. A brain MR scan showed now two frontal white matter lacunae, while the EEG showed generalized electric dysfunction with a slowed rhythm in the delta-theta range in absence of epileptiform abnormalities. A lumbar puncture (LP) was then performed, documenting: 100 cells/ $\mu$ l (mainly mononuclear cells), proteins 57 mg/100 ml (normal values: 15-45), glucose within normal values. CSF cultures were negative and samples were sent for PCR research on viral antigens: Epstein-Barr virus, cytomegalovirus, enteroviruses, herpes simplex virus type 1 and 2, and varicella-zoster virus (VZV). Suspecting viral encephalitis, the patient was admitted in the neurological department and started on IV acyclovir 10 mg/kg t.i.d., demonstrating an initial improvement on psychiatric symptoms. The follow-up brain MR scan (one month since onset of the first psychotic episode) was normal and the LP documented: 9 cells/ $\mu$ l, proteins 63 mg/100 ml, and normal glucose. The patient started physiotherapy but distal lower limb paresthesias subacutely appeared, followed by increasingly worsening ascending limb areflexic hypostenia. A suspect of acute inflammatory de-

myelinating polyradiculoneuropathy (AIDP) was formulated. A further LP did not show a clear pattern of albumino-cytological dissociation (16 cells/ $\mu$ l, proteins 65 mg/100 ml, normal glucose) and oligoclonal bands were present in the CSF but not in the corresponding plasma sample. The EMG was compatible with an axonal involvement. The patient received a course of IV Ig and was started on gabapentin. Due to the plasma increase of the neoplastic marker CA19.9, a total-body [ $^{18}$ F]FDG PET scan was performed searching for malignancies, documenting a focal area of increased capitation at the transverse colon level subsequently demonstrated to be an adenoma at the colonoscopy followed by biopsy. PET hypocaptation was shown at the cortical level within the frontal lobes. Subsequent controls demonstrated the normalization of the CA19.9 levels. At that moment, psychopathological conditions of Mrs. O. were characterized by partial regression of the mixed mood disorder with psychotic symptoms, but paranoid delusions, focused on her job and family were still present, along with poor critic, depression (that sometimes switched in euphoric mood) and detachment from the usual environmental context. The LP control showed: 10 mononuclear cells/ $\mu$ l, proteins 46 mg/100 ml, normal glucose, positive oligoclonal bands). CSF PCR viral tests came back completely negative. The ENG follow-up documented a picture of axonal dysfunction with minor variations with respect to the previous exam. Glove-and-stocking paresthesias ameliorated increasing gabapentin dose and fluvoxamine was reintroduced. Thirty days later Mrs. O.'s strength deficits were improving steadily and she was transferred to the rehabilitation wards for continuing physiotherapy. The psychiatric symptoms had now completely receded.

## DISCUSSION

Viral encephalitides often present with psychiatric symptoms including psychosis and mania (1,2); only rarely the presenting picture might represent a challenge in the differential diagnosis since prominent focal neurological deficits and unusual clusters of psychiatric symptoms are common. Age represents also an important clue, since psychotic breaks in older adults might warrant further searches for an underlying "organic" brain disease. In these cases, the subsequent neuroimaging often solves the conundrum since clearly demonstrates structural anomalies pointing out to the correct diagnosis of the mimic. This was not our case since the MR scan showed only minor and aspecific alterations. Nevertheless, middle age and the ab-

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sence of previous psychiatric manifestations argued for further search and both the EEG and, especially, the LP were compatible with the diagnosis of encephalitis. Surprisingly, viral search came back negative although the concurrent presence of a Herpes Zoster skin lesion suggests the possible involvement of VZV. LP timing and the initial valacyclovir course might have been crucial, in this case, in influencing PCR results (3). The absence of MR alterations is still compatible with VZV encephalitis, although discrete subcortical non-enhancing spherical lesions that eventually coalesce developing enhancement and spreading to the gray matter are commonly found (4). Moreover, MR abnormalities have also been observed in patients with herpes zoster presenting without clinically apparent CNS involvement (5). Accordingly with the hypothesis of a viral episode, the following AIDP is compatible with a post-infectious disimmune etiology, and Guillain-Barré syndromes post-VZV infection have already been reported (6). Moreover, also VZV involvement in isolated psychiatric cases has already been reported: McKenna and colleagues (7) described the case of a 38-year old woman with a history of panic disorder and dysthymia and with a previous single manic episode that developed prominent mental changes and manic symptoms. Six weeks before she had been treated for a herpes zoster ophthalmicus, and both the subsequent EEG and LP were compatible with the diagnosis of VZV encephalitis. Although the CSF cell count was only mildly elevated with respect to our case (20 cells/ $\mu$ l), the CT scan demonstrated a compatible lesion within the right temporo-parietal region. Notably, this patient presented with a positive history of manic disorder that raised the differential diagnostic issue of delusional mania. In contrast, our patient's history was negative for psychiatric disturbances, possibly prompting for a more suspicious approach to her mental status changes.

Usually, VZV encephalitis is more common when the trigeminal nerve is involved, often developing between one and eight weeks from the vesicular eruption. The CSF pattern comprises mild pleocytosis and sometimes increase of protein concentration (8). Also other herpesviridae are known to induce encephalitides and herpes simplex virus type 1 (HSV-1) is one of the most common causes involved in sporadic cases. Although usually abrupt, the resulting picture often includes altered mentation that sometimes might represent the prominent symptom at presentation in absence of focal neurological signs (9).

Remarkably, encephalitides due to non infectious causes might also present as diagnostic challenges for the psychiatrist. For example, Parrat et al. (10) report-

ed a 21-year old woman admitted for an acute psychotic mania, subsequently complicated by seizures and dyskinesias, which was found positive for antibodies against N-methyl-D-aspartate (NMDA) NR1-NR2 receptors, consistently with anti-NMDA-receptor encephalitis, often in a paraneoplastic context. No tumour was found in this case. Analogously, cases of systemic lupus erythematosus (11), ADEM (12), or even Wilson's disease (13), among other conditions, have been reported presenting as isolated psychiatric disorders. Typically, the following laboratory and/or other tests point out to the correct diagnosis and most psychiatrists are already alerted when facing with mental changes in an older patient, especially with a negative history of psychiatric disorders (14).

Furthermore, from a clinical and semeiological point of view, this case might show the importance of those brief moments of confusion observed during both the first and, more clearly, the second hospitalization. In fact, as reported in other clinical conditions, such as epilepsy (15,16), the presence of brief moments of spatio-temporal confusion with amnesia can sometimes be crucial for the differential diagnosis, as they are less common in pure psychic conditions where orientation and memory functions are usually maintained. In fact, in the case of Mrs. O., the impression of an underlying neurological disorder was specifically raised only after carefully noticing and discussing the fast cycling features of these intermittent moments of disorientation, since the patient few minutes later returned back every time to a state of standard orientation in time and space.

Nevertheless, our patient clearly claims the attention of the psychiatrist toward cases of isolated depression and/or mania with psychotic symptoms that can be initially overlooked and tagged as "non-organic", delaying the necessary therapies and diagnostic tests. On the other hand, a point of interest of this case consists in the fact that a careful neurological examination and the consultation with a neurologist were performed immediately, but were both not informative, with the presence of neurological signs only later on. This might suggest that special attentions might be always justified in atypical psychiatric presentations, since it can be difficult to diagnose them, at least at the onset, as neurological, for example due to the expression of an encephalitic process.

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