UNIVERSITÉ MOHAMMED VI DES SCIENCES ET DE LA SANTÉ
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الجمعية المغربية لأمراض الدم
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Malignant Varicella Complicated by Meningoencephalitis in a Multiple Myeloma Patient : A Therapeutic and diagnostic Dilemma

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Introduction

Malignant varicella is a rare but severe complication in immunocompromised patients undergoing chemotherapy for hematologic malignancies. Varicella-zoster virus (VZV) meningoencephalitis represents a serious neurological manifestation, often life-threatening.

THERAPEUTIC DILEMMA :

Acyclovir = gold standard treatment for VZV infections

ESRD patients: risk of dose-dependent neurotoxicity

Challenge: balancing efficacy vs. safety in vulnerable population

Case report

We report the case of a 67-year-old man with newly diagnosed multiple myeloma (May 2025), discovered during investigation of end-stage renal disease (ESRD) requiring chronic hemodialysis. The patient had no significant prior medical history beyond his recently diagnosed hematological malignancy and renal failure. He was initiated on VCD chemotherapy regimen (Bortezomib 1.3 mg/m^2 IV days 1, 8, 15, 22; Cyclophosphamide 300 mg/m^2 PO days 1, 8, 15, ; Dexamethasone 40 mg PO days 1-4, 9-12, 17-20) along with prophylactic acyclovir 400 mg once daily, adjusted for renal function.

The first cycle was completed uneventfully. However, on day 8 of the second chemotherapy cycle, the patient developed an acute febrile illness (temperature 38.9°C) accompanied by a progressive cutaneous eruption evolving over three days.

Clinical Examination

Physical examination revealed a disseminated vesiculobullous eruption with polymorphic lesions at various stages of evolution. The rash consisted of vesicular, purpuric, and sometimes necrotic lesions scattered over the trunk and limbs, notably sparing the face, with mild involvement of the scalp. Several lesions showed hemorrhagic crusting. The distribution and morphology were highly suggestive of disseminated varicella-zoster virus (VZV) infection in the setting of severe immunosuppression. No mucosal involvement was noted.

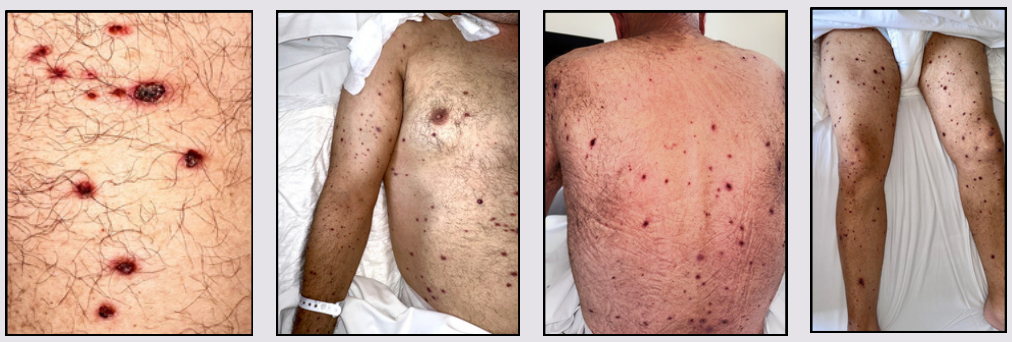

Figure 1.**Disseminated Malignant Varicella** *Polymorphic cutaneous lesions (vesicular, purpuric, necrotic) at various evolutionary stages, predominantly affecting trunk and limbs*

Laboratory findings showed marked inflammation (CRP 318 mg/L, procalcitonin 14.43 ng/mL), hyperleukocytosis (14,330/mm3 with 88.1% neutrophils), thrombocytopenia (87,000/mm3), and severe renal impairment (creatinine 113.6 mg/L). Empiric treatment was initiated with renal-adjusted acyclovir (Cicloviral® 750 mg/day) along with antibiotic therapy (ciprofloxacin and ceftriaxone). VCD cycle 2 was interrupted.

By day 4, neurological deterioration occurred, including incoherent speech, psychomotor agitation, tremors, myoclonus, and focal seizures with tonic deviation of the head. **Electroencephalogram (EEG)** revealed findings consistent with **non-convulsive status epilepticus,** characterized by: Continuous or near-continuous generalized epileptiform discharges, rhythmic delta activity with superimposed sharp waves, and bilateral temporal predominance with independent multifocal spikes.

MRI revealed findings highly suggestive of VZV-associated cerebral vasculopathy with multifocal areas of acute and subacute infarction involving both cortical gray matter and subcortical white matter , predominant involvement of the frontal and temporal lobes bilaterally, with additional scattered lesions in the parietal regions, and lesions demonstrated restricted diffusion on diffusion-weighted imaging (DWI) with corresponding low apparent diffusion coefficient (ADC) values, consistent with acute cytotoxic edema and ischemic injury.

Lumbar puncture showed elevated cerebrospinal fluid (CSF) protein (1.89 g/L) without pleocytosis, and VZV was detected by PCR.

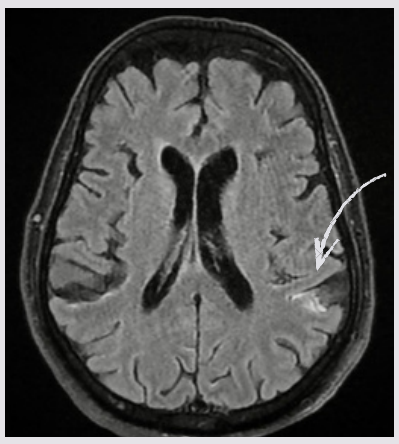

Figure 2. **Axial view of brain MRI in FLAIR sequence** *showing cortico-subcortical hyperintensities in the left parietal region.*

The combination of markedly elevated protein without pleocytosis (albuminocytologic dissociation) along with positive VZV PCR is diagnostic of VZV encephalitis/meningoencephalitis. The absence of pleocytosis is characteristic in severely immunocompromised patients who cannot mount an adequate inflammatory CSF response.

The patient was admitted to intensive care where he received antiepileptic treatment (phenobarbital and levetiracetam), along with adjustment of antiviral therapy. Dexamethasone 4 mg IV every 6 hours for cerebral edema and inflammatory vasculopathy and monitoring for secondary bacterial infections.

Discussion

- Clinical Dilemma

VZV encephalitis risk persists in immunocompromised patients despite antiviral coverage

Standard acyclovir 400 mg/day prophylaxis was insufficient in this high-risk patient (active chemotherapy, multiple myeloma, renal failure). Guidelines suggest higher doses (800 mg twice daily) or valacyclovir for high-risk patients.

- Diagnostic challenge

VZV encephalitis vs. acyclovir-induced neurotoxicity in ESRD. Similar cases reported in literature highlighting this dual diagnostic dilemma (1)

MRI is superior to CT for detecting VZV vasculopathy and encephalitis

VZV can cause cerebral vasculitis mimicking stroke, requiring prolonged antiviral therapy

Lack of CSF pleocytosis does not exclude encephalitis in immunocompromised patients

EEG monitoring is essential for altered mental status even without obvious seizures

- Critical Differential Diagnosis

Acyclovir neurotoxicity: must be considered in all ESRD patients on treatment

Overlapping clinical presentations complicate diagnosis. Both conditions can cause altered consciousness and neurological symptoms

- Diagnostic Approach

Gold standard: VZV PCR on CSF for definitive diagnosis (2)

Molecular diagnostics guide appropriate management strategy

MRI findings support but may be non-specific

- Key Management Principles

Close neurological monitoring mandatory in high- risk patients

Dose adjustment essential in renal failure Hemodialysis timing coordination critical Multidisciplinary approach improves outcomes

Conclusion

Malignant varicella can evolve into life-threatening meningoencephalitis in patients with hematologic malignancies and chronic renal insufficiency. Prompt recognition, renal-dose adjusted antiviral therapy, and rigorous neurological surveillance are crucial to improving patient outcomes in this vulnerable population. This case required coordination between hematology, nephrology, infectious disease, neurology, and critical care teams.

References

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