Neurological manifestations of primary Varicella infection

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Case presentation

- **An 43 year-old man with a one-week history of gradually worsening headaches presented to the emergency department.**
- **Approximately 24 h later, he progressed to hallucinations and progressive obtundation, and two episodes of generalized tonic–clonic seizures.**

- **DH: neg**
- **History of alcohol use: neg**
- **Social history : High risk behavior**

Case Presentation
PH/EX

Upon admission, BP=136/79,PR=90, RR=18,T=38°C

Skin examination: Notably, no vesicular rash or cutaneous lesions were present

His neck was mildly stiff, but without clear meningeal signs (negative Kernig's and Brudzinski's signs).

Neurological examination revealed a non-verbal, obtunded and mildly agitated patient, who was unable to follow commands. Cranial nerves were intact.

Case Presentation
PH/EX

The patient moved all extremities equally. Sensation, coordination, and gait could not be tested because of the patient's obtundation. Reflexes were 1+. Plantar reflexes were upgoing.

Genitourinary, Cardiopulmonary& abdominal examinations were all normal.

Oral cavity: oral Candidiasis

Laboratory evaluation

CBC:

- **WBC=2400 (Lymph:15%)**
- **HGB= 10**
- **PLT=106000**

- **ESR:18**
- **CRP: 7**
- **Urea & Cr: NL**

- **LFT: NL**
- **Serum VDRL: neg**
- **HIV Ab : Reactive**
- **HCV Ab: neg**
- **HBS Ag: neg , HBS Ab: 2, HBC Ab:neg**
- **Brain CT Scan: NL**

Laboratory evaluation

Lumbar puncture:

WBCs: 360cell/mm^3 (with lymphocytic predominant)
RBC :280cell/mm^3
protein:150 mg/dl
Glucose : 70 (simultaneous blood glucose: 100)

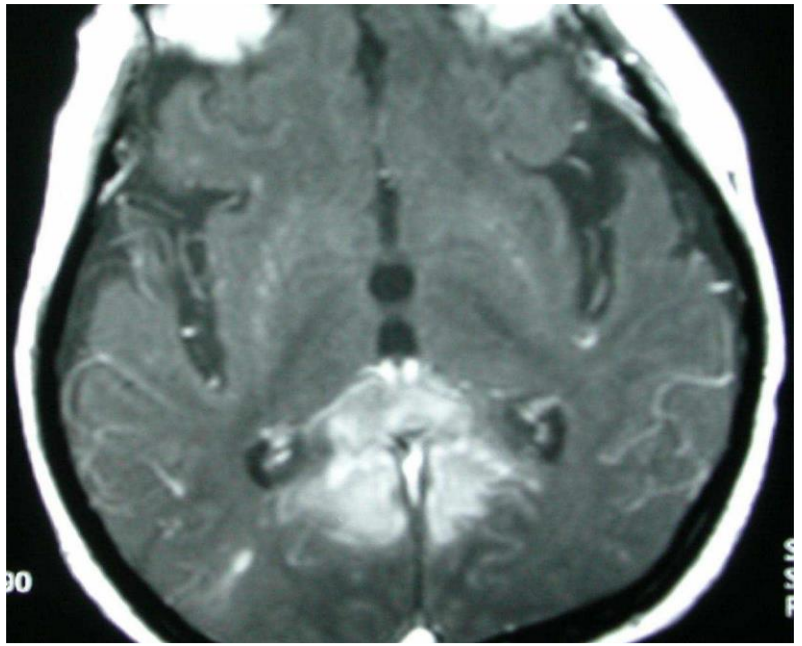
Cerebrospinal fluid sample sent for : HSV PCR, VZV PCR, EBV PCR, CMV PCR , TB PCR, cytology

Patient Process

- He was administered IV acyclovir for suspected (HSV) encephalitis.
- Antiepileptic medication for seizure control
- brain MRI was Requested.

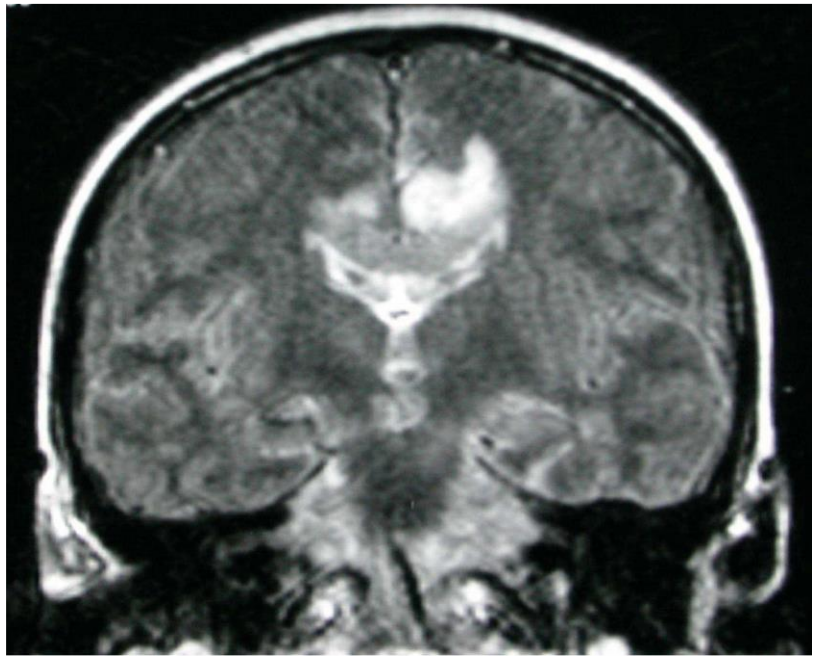
Patient Process

T1 weighted MRI of Brain post-gadolinium (axial) demonstrating enhancement of the corpus callosum.



Patient Process

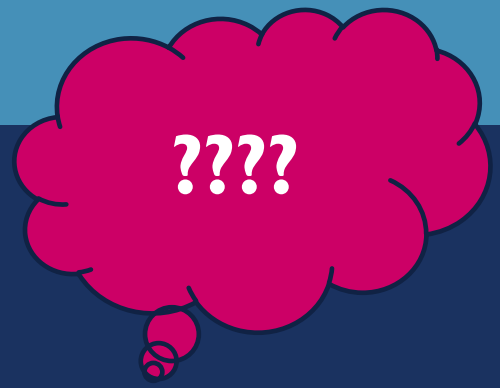
T2 weighted MRI Brain (sagittal) demonstrating hyperintensities in the splenium and body of the corpus callosum symmetrically extending into the posterior parietal-occipital lobes and with vasogenic edema.



Patient Process

Second day of hospitalization

- The initial MRI interpretation by radiology was most consistent with a "butterfly glioma."
- He became a candidate for brain biopsy.



Differential diagnosis for the patient ????

Patient Process

Third day of hospitalization

Papulopustular and vesicular lesions appeared on the trunk, limbs, and face.

A diagnosis of varicella encephalitis was made.

Patient Process

Fourth day of hospitalization

CSF HSV PCR: Neg
VZV PCR: Pos
EBV PCR: Neg
CMV PCR : Neg
TOXO PCR: Neg
TB PCR: Neg
cytology : Neg

- Continue IV Acyclovir
- Start Corticosteroids (Dexamethasone)

CD4 Count = 54

Patient Process

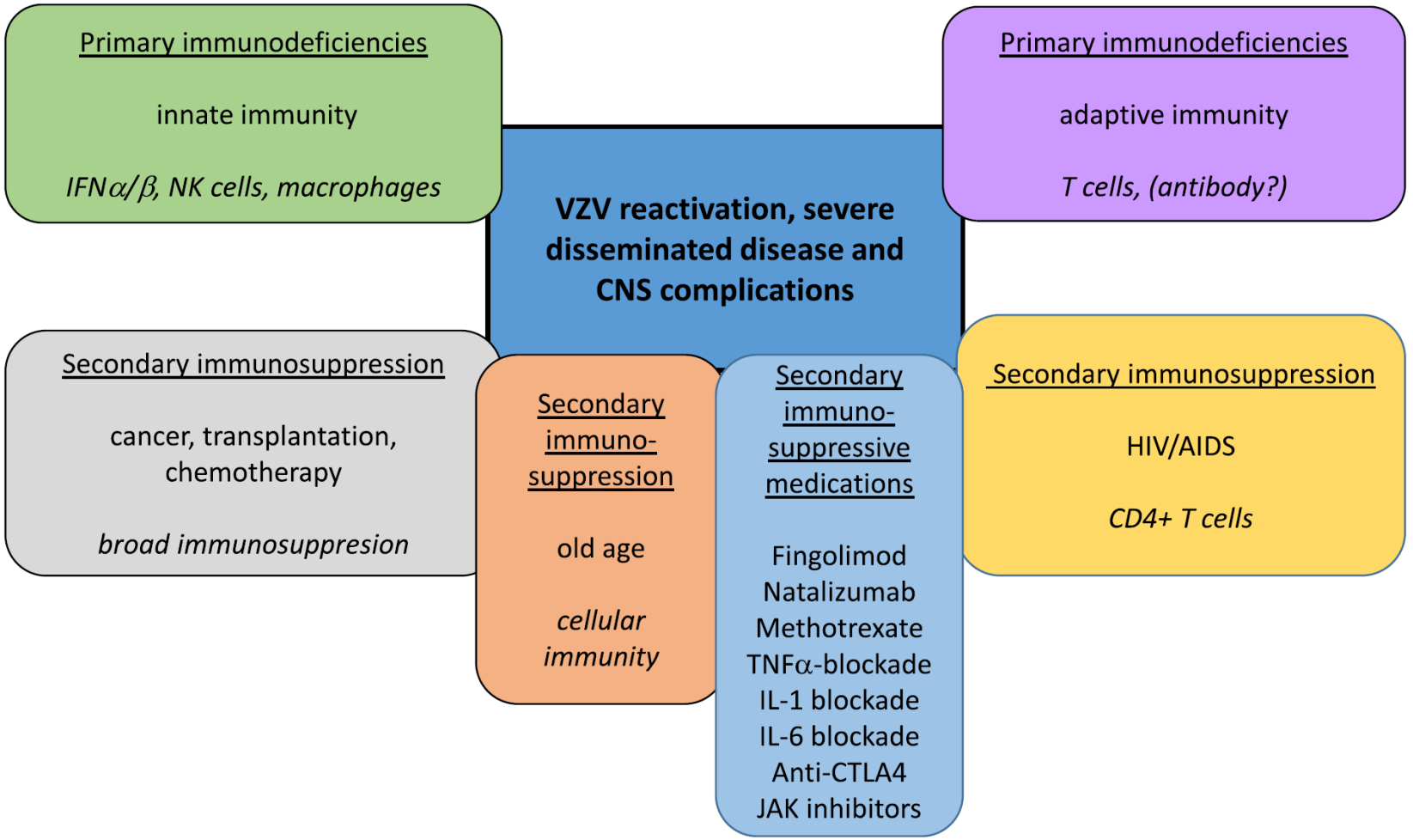
- The patient's neurological status gradually improved after 5 days of treatment & His headache disappeared completely after 10 days.
- Treatment with IV acyclovir for 14 days was completed and the patient was discharged with oral valacyclovir for 7 days and referred to the HIV clinic for Primary care & Start ART .
- Clear improvement of the imaging alterations described in the control brain MRI 3 months after hospitalization, with the disappearance of the lesions located on the corpus callosum region.

Discussion

DISCUSSION

- **Varicella-zoster virus (VZV) infection usually presents with a typical skin rash, either as primary varicella or reactivation as herpes zoster.**
- **However, in immunocompromised patients, particularly those with HIV/AIDS, VZV can present with atypical manifestations including encephalitis without skin lesions (up to one-third of cases). This makes diagnosis more challenging, as the classical dermatological clue is absent and leading to delayed diagnosis.**
- **CSF PCR for VZV remains the gold standard diagnostic tool in such atypical cases.**

Host Factors Predisposing To VZV Reactivation, Severe Disseminated Disease & CNS Complications



HIV/AIDS

During the emergence of HIV and AIDS, it became clear that VZV is a cause of CNS infection in HIV-infected individuals with severely impaired CD4 T cell immunity.

Chronic VZV encephalitis is seen almost in AIDS patients and manifests with multifocal lesions in the white matter with small vessel vasculitis and demyelinization as well as ischemic and hemorrhagic infarcts.

several cases of VZV aneurysmal vasculopathy have been reported, and indeed it is possible that many cases of HIV-associated vasculopathy are in reality cases of VZV vasculopathy.

Other Neurological Manifestations Of Primary Varicella Zoster Virus Infection

- The incidence of neurological manifestations associated with VZV is 1-3 per 10,000 cases.
- Both primary VZV infection (chickenpox) and VZV reactivationcan cause various neurological manifestation .
- Neurological manifestations following primary VZV infection are uncommon (0.01-0.03%).

Table 1: VZV neurological manifestations[1,4-8]

Primary VZV manifestations	Manifestations of VZV reactivations
Meningoencephalitis	Herpes zoster
Cerebellitis	Postherpetic neuralgia
Guillain barre syndrome	Cranial nerve palsies zoster paresis
Neuromyelitis optica	Vasculopathy
Acute disseminated encephalomyelitis	Meningoencephalitis
Vasculopathy	Cerebellitis
	Myelopathy
	Multiple ocular disorders
	Zoster sine herpete and Retinitis.

Cerebellar ataxia and encephalitis are seen frequently; while transverse myelitis, aseptic meningitis, Guillian-Barré syndrome, rarely can be observed .

Encephalitis

- Varicella encephalitis typically presents with fever, headache, altered mental status, and seizures, usually associated with characteristic vesicular rash.
- Encephalitis-related VZV is reported to be more common in children than in adults , typically developing five to seven days after rash onset.
- However, in immunocompromised patients, skin lesions may be absent in up to one-third of cases, leading to delayed diagnosis.

Acute Cerebellar Ataxia (ACA)

Most common neurological complication in children.
A ratio of 1 in 4000 children are affected with ACA by varicella zoster Infection.

- **Usually appears 1–3 weeks after rash**
- **Symptoms: sudden onset of gait disturbance, tremor, dysarthria, nystagmus**

- **Usually self-limiting, good prognosis**

Other Neurological Manifestations

Stroke / Vasculopathy

- **VZV can infect cerebral arteries → large- or small-vessel vasculitis**
- **May cause ischemic stroke, hemorrhagic stroke, or TIA**
- **Often occurs weeks to months after infection**

Transverse Myelitis

- **Rare , Rapid Onset**
- **Motor Weakness: Progressive weakness and, in some cases, paralysis in the legs.**
- **Sensory Disturbances: Numbness, tingling, or loss of sensation below the level of the spinal cord injury.**
- **Bowel and Bladder Issues: Loss of control over urination and bowel movements.**
- **Can be monophasic or relapsing**

Guillain–Barré Syndrome (GBS)

- Autoimmune demyelinating neuropathy post-infection
- While it's uncommon, GBS can be triggered by either primary varicella infection or the reactivation of the varicella zoster virus.
- as progressive muscle weakness and paralysis, areflexia, possible respiratory compromise.

- Diagnosis involves tests like cerebrospinal fluid (CSF) analysis and nerve conduction studies
- Treatment may include intravenous immunoglobulin (IVIg) or plasma exchange, with cases often showing good recovery.

KEY MESSAGES

absence of skin lesions does not rule out VZV encephalitis especially in immunocompromised / HIV-infected patients.

Clinicians should maintain a high index of suspicion in immunocompromised patients presenting with acute encephalitis

With early diagnosis and appropriate treatment the neurological manifestations due to primary VZV infection had good prognosis.

Live attenuated varicella vaccine, will help in preventing VZV infection and reducing the complications associated with it.

Any questions?