



Dramatic efficacy of Vemurafenib on psychiatric symptoms revealing BRAF^{V600E} Erdheim-Chester Disease

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Disclosure



- The authors declare no competing financial interested related to this work.



Presentation plan

- Background
- Case presentation
- Discussion
- Conclusion



Background

- Erdheim-Chester disease is a rare histiocytosis¹
 - Long bone osteosclerosis
 - Peri-nephric fat infiltration : “hairy kidney”
 - Vascular sheathing
 - Compatible histology
 - Frequent MAP-kinase pathway gene involvement
 - 60% *BRAF*^{V600E} mutation



Background

- Neurologic involvement: 20-40% ^{1,2,3}
 - Tumoral
 - Vascular
 - Degenerative (less frequent than LCH)
- Clinical features:
 - Cerebellar disability+++
 - Dysarthria
 - Seizure
 - Diabetes insipidus



Background

- Magnetic resonance imaging patterns^{1,2,3}:
 - T2 hyperintense lesions
 - brain parenchyma= cerebellum , brain/spine parenchyma
 - Meningeal structures: dura, hypothalamic-pituitary-adrenal axis
 - Vascular sheathing
 - Osseous involvement = sinus
 - Possible cerebellar atrophy

Background



- Neurological signs are heterogenous
- Psychiatric signs are not described in the spectrum of neuro-ECD



Case presentation

- 81 years old woman
- Central retina vein occlusion 15 years earlier
- Addressed to the hospital for acute dyspnea
- Acute cardiac failure
- Pericardial effusion requiring surgery



Neurological features

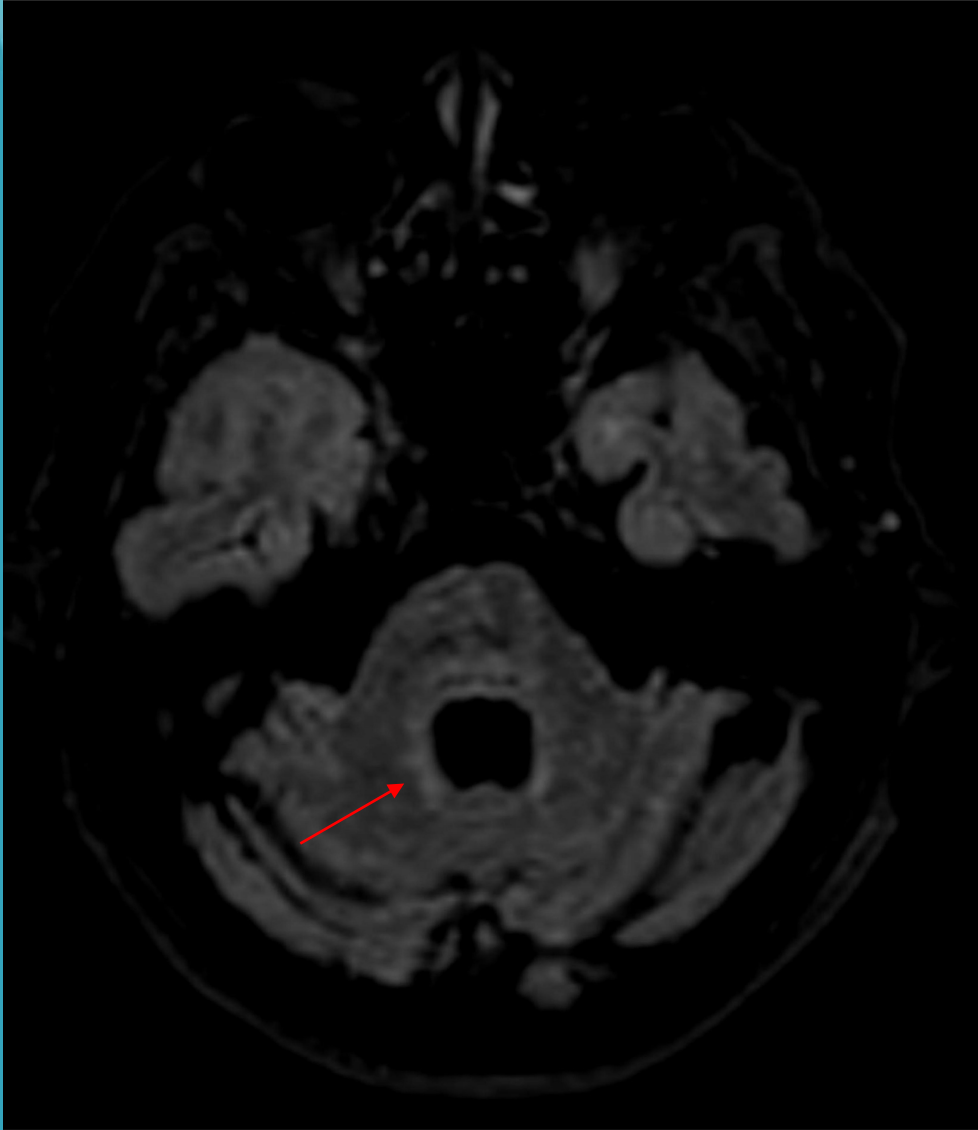
- 8 months ago in Lyon hospital:
 - Delirium with auditive and visual hallucinations
 - Static and dynamic cerebellar syndrome
 - Normal cerebral CT and electroencephalogram
 - Normal blood samples analysis
 - = elderly cognitive decline.
- Treatment with Olanzapine



Neurological features

- Physical examination:
 - Cerebellar disability: Scale for Assessment and Rating of Ataxia (SARA) score = 14
 - Mild cognitive impairment : Mini-Mental State Examination (MMSE): 22/30

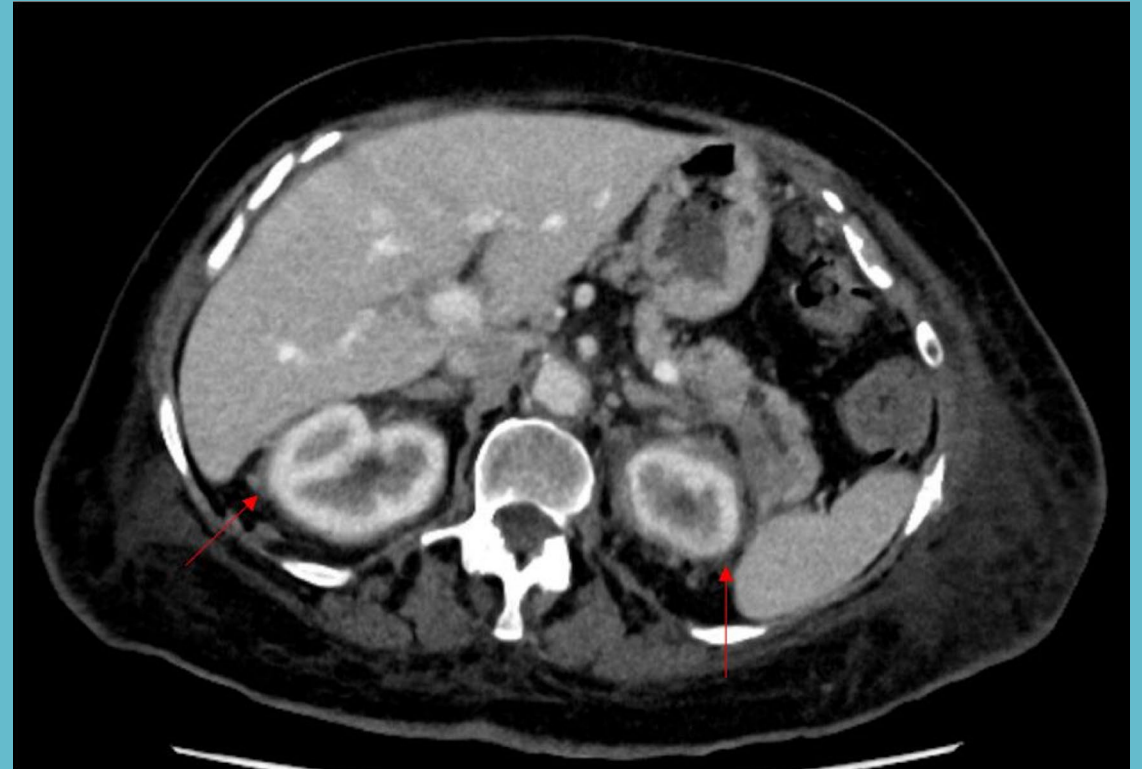
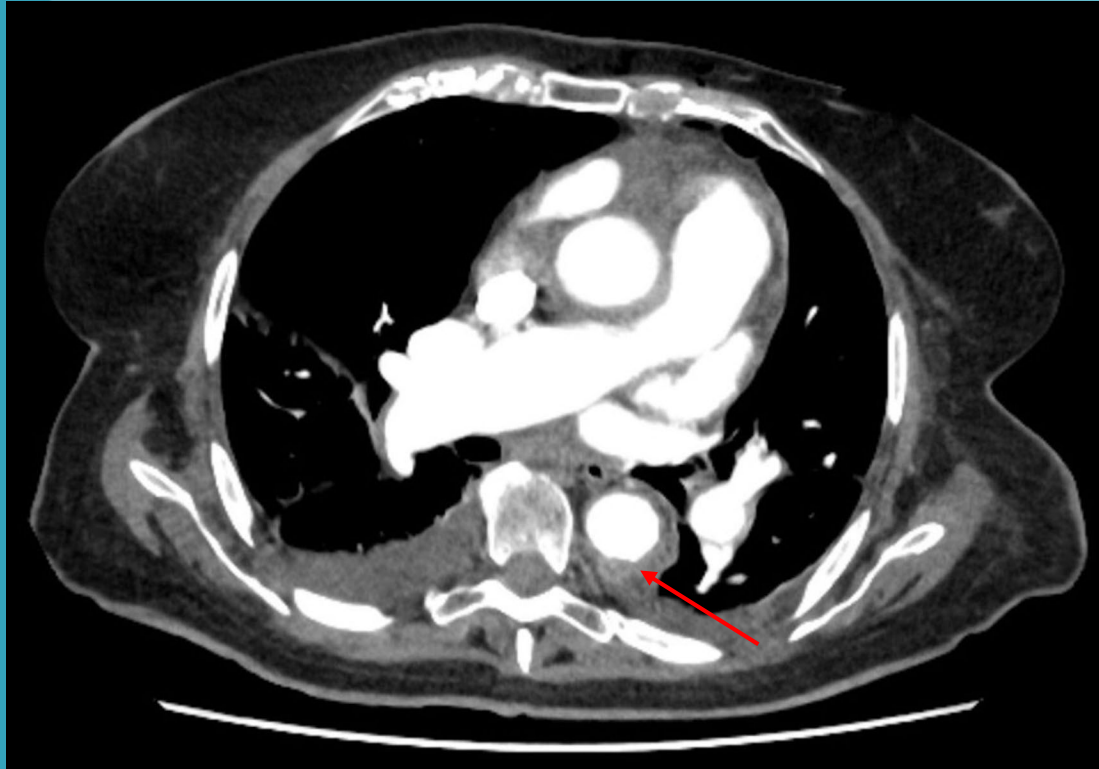
Neurological features



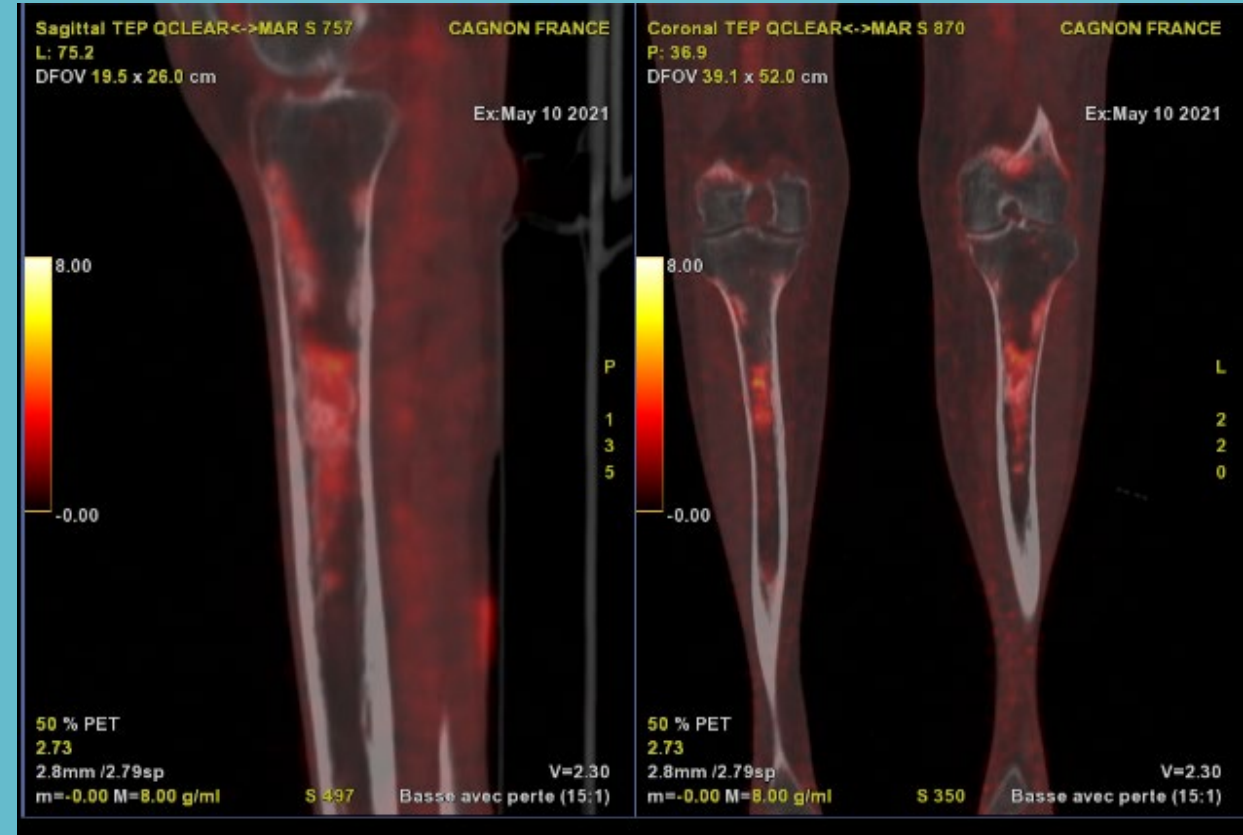
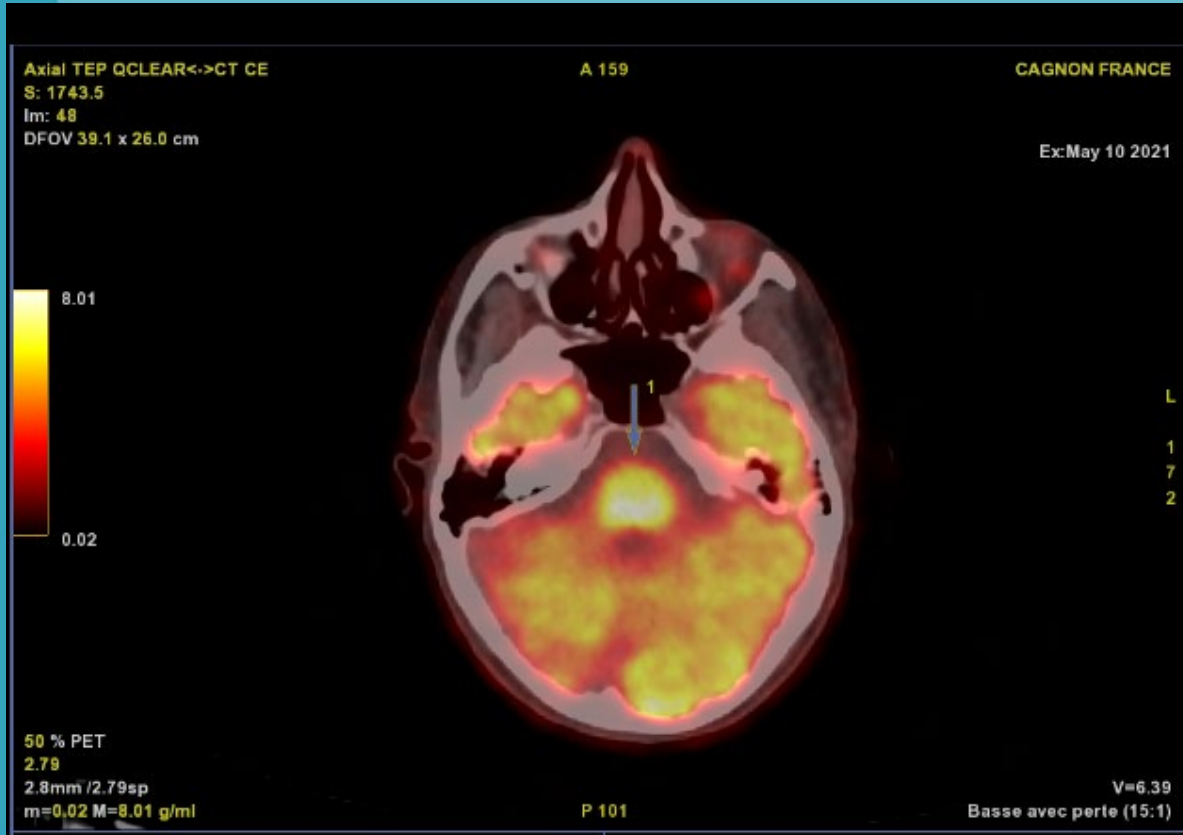
Lumbar puncture:

- 1 leucocyte/mm³ (N<5)
- Protein level: 0.48 g/L (N<0.60)
- Negative bacterial and viral culture with PCR analysis
- Oligoclonal bands negative
- Antibodies associated with paraneoplastic syndrome negative
- Tau protein level: 274 ng/L (N<400)
- phosphorylated isoform: 33 ng/L (N<60)
- Neopterin level: **9.4 nmol/L (N<5)**

Supplementary examination



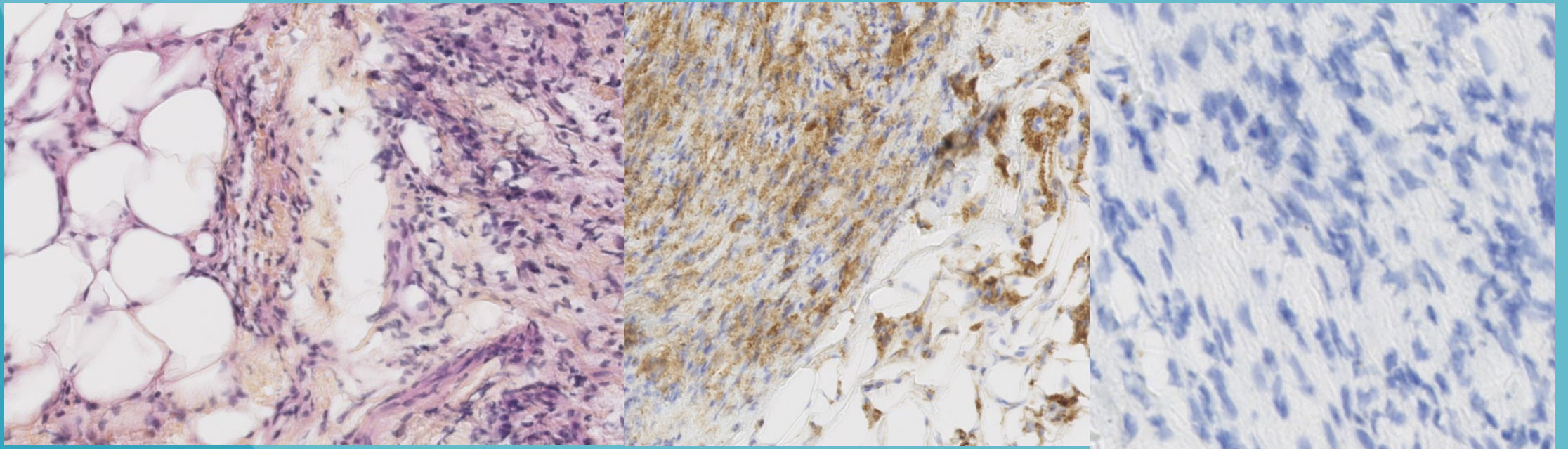
Supplementary examinations



Supplementary examination



Peri-nephric fat biopsy:





Erdheim-Chester disease

- Long bones osteosclerosis
- Hairy kidney
- Coated aorta
- Right atrium tumor
- Neurological involvement?
- *BRAF*^{V600E} by pyrosequencing

Treatment



- Interferon 180 μ g/weeks twice
- Vemurafenib 240 mg: 2-0-2

Outcomes



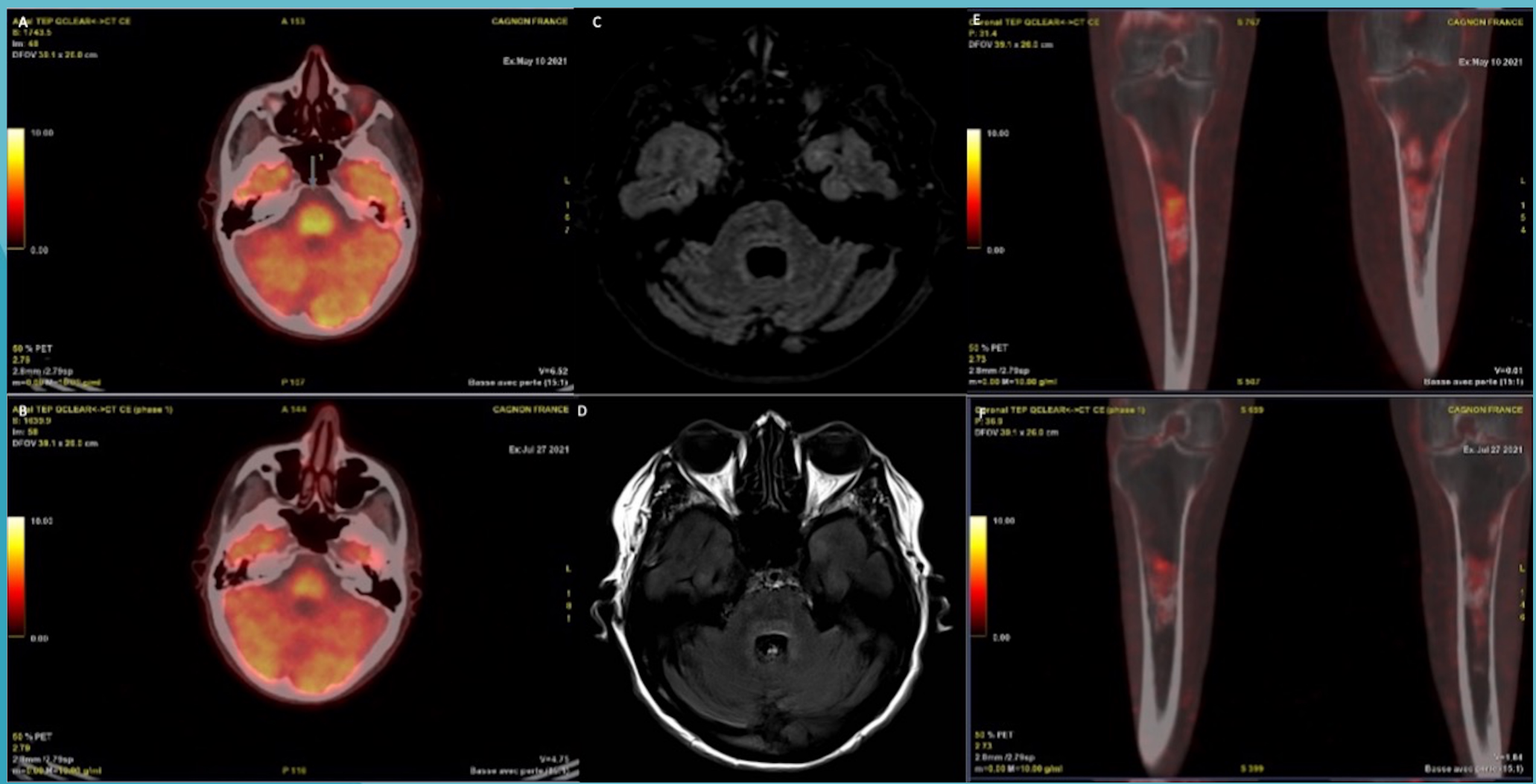
- Regression of psychiatric symptoms 7 days after peg-interferon
- Abolition of delirium ten days after targeted therapy



Outcomes

- 8 weeks follow-up:
 - No delirium
 - Mild improvement of cerebellar disability: 12
 - Mild cognitive improvement: MMSE 26/30
 - Imaging improvement

Outcomes





Discussion

- Presentation of neuro-ECD with psychiatric symptoms as first onset
- Interpretation of cerebellar disability in cognitive decline
- Favorable outcome with targeted therapy



Discussion

- **Neopterin:**

- Neurological biomarker of cerebral inflammation
- Caused by viral infection and macrophage activation in microglia
- Marker of neuro-histiocytosis in the settings of sterile culture?



Conclusion

- Delirium as first manifestation of neuro-ECD
- Importance of neurological examination for cerebellar disability
- Dramatic improvement with targeted therapies
- Role of neopterin in neuro-ECD?