

Headache and Confusion in a patient with Hereditary Haemorrhagic Telangiectasia

Dr Aurélie Baldolli

Maladies Infectieuses et Tropicales

Centre Hospitalo-Universitaire de Caen, France



Case report



- 62 year old man
- Medical history :
 - **Hereditary Haemorrhagic Telangiectasia (HHT)**
without any brain, pulmonary, hepatic or any other visceral arteriovenous malformation (AVM)
 - Asthma
- Farmer, pig breeder. No hunting
- No foreign travel at any time
- Animals : cows, dogs, cats
- Eat fruits and vegetables from his garden

Case report

December 2016 :

- Headache
- Confusion
- Gait disorders
- Left ptosis, dysathria, ataxia
- No meningeal stiffness
- No fever
- Cardio-pulmonary and abdominal examination normal

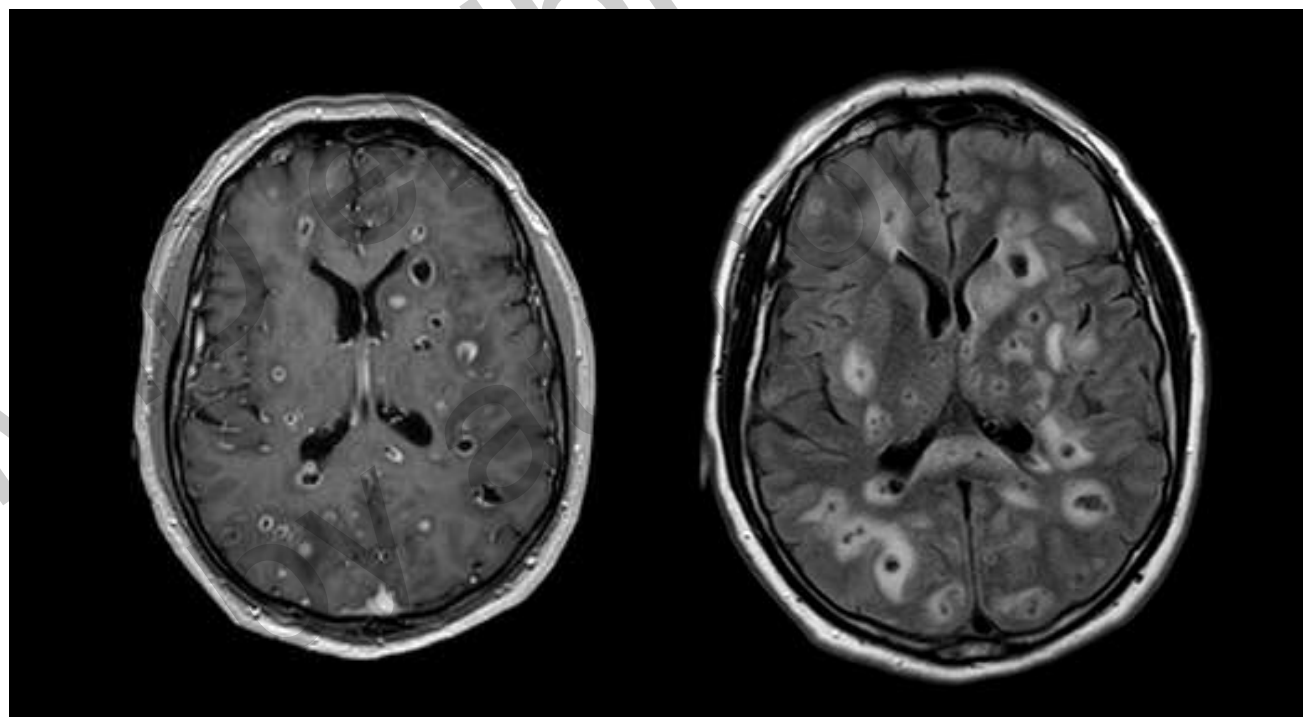
Day 0



Case report

T1-weighted contrast-enhanced FLAIR sequence

December 2016



Day 0

Case report

- Full Blood Count normal
- C reactive protein < 3mg/l (N<5mg/l)
- ALT, AST, bilirubin, ALP, GGT : normal
- Creatinine : 86 $\mu\text{mol/l}$ (N<100 $\mu\text{mol/l}$)
- Cerebrospinal fluid (LP) :
 - 230 leukocytes/mm³: 90% lymphocytes
 - Protein content 1 g/l, glucose 3,3mmol/l (glycemia : 5,5mmol/l)

A horizontal timeline arrow pointing to the right, with a vertical tick mark at the start. Below the arrow, the text 'Day 2' is written.

Day 2

Case report

Thoughts from the panel



Case report

- Lymphocytic meningitis
- Associated with atypical multiple cerebral abscesses

Empirical treatment : IV CEFOTAXIME and METRONIDAZOLE



Case report

Infectious Diseases work-up

CSF	Blood sample	Imaging
<p><u>Bacterial and fungal cultures,</u> <u>Nocardia spp, free-living</u> <u>amoebae:</u> negative/sterile <u>PCR :</u> Mycobacteria tuberculosis <i>Toxoplasma gondii</i> <u>Ag :</u> Cryptococcosis <u>Serology :</u> Cysticercosis</p> <p>= ALL NEGATIVE</p>	<p><u>Serological test :</u> <i>Coxiella burnetii, Rickettsia</i> <i>spp, Bartonella spp, Brucella</i> <i>spp, Treponema pallidum, HIV,</i> Cysticercosis, Toxocariasis <u>Ag:</u> <i>Aspergillus spp,</i> <i>Cryptococcus spp</i> <u>PCR :</u> <i>Toxoplasma gondii</i> <u>Blood culture :</u> sterile</p> <p>= ALL NEGATIVE</p>	<p><u>Body CT scan :</u> normal, no abscess, AVM, kidney, spleen stroke</p> <p><u>Transthoracic</u> <u>echocardiography :</u> normal, no endocarditis no right-left shunt</p>



Day 5

Case report

Infectious Diseases work-up

CSF	Blood sample	Imaging
<p><u>Bacterial and fungal cultures</u>, <i>Nocardia</i> spp, free-living amoebae: negative/sterile <u>PCR</u> : <i>Mycobacterium tuberculosis</i> <i>Toxoplasma gondii</i> <u>Ag</u> : Cryptococcosis <u>Serology</u> : Cysticercosis</p> <p>= ALL NEGATIVE</p>	<p><u>Serological test</u> : <i>Coxiella burnetii</i>, <i>Rickettsia</i> spp, <i>Bartonella</i> spp, <i>Brucella</i> spp, <i>Treponema pallidum</i>, HIV, Cysticercosis, Toxocariasis <u>Ag</u>: <i>Aspergillus</i> spp, <i>Cryptococcus</i> spp <u>PCR</u> : <i>Toxoplasma gondii</i> <u>Blood culture</u> : sterile</p> <p>= ALL NEGATIVE</p>	<p><u>Body CT scan</u> : normal, no abscess, AVM, kidney, spleen stroke</p> <p><u>Transthoracic echocardiography</u> : normal, no endocarditis no right-left shunt</p>



Day 5

Case report

Malignant disease

CSF	Physical examination	Imaging
<p><u>Cytology</u> : No suspect cells</p> <p><u>Flow cytometry</u> : No B or T-cell lymphoma</p>	<p><u>No melanoma</u></p>	<p><u>Body CT scan</u> :</p> <p>No lymph node, hepatosplenomegaly or tumour</p>

Autoimmune disease

Blood sample

Specific anti-nuclear antibodies, ANCA, ...
NEGATIVE



Day 5

Case report

- Aphasia and right hemiplegia



Case report

What would you do now ?



Day 5

Case report

- Aphasia and right hemiplegia

CORTICOSTEROIDS and ALBENDAZOLE were added



Case report

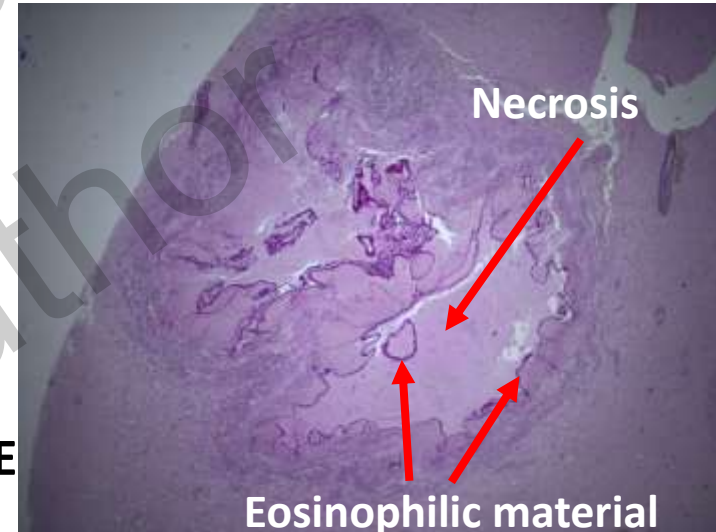
- Referred to our Infectious Diseases Department
- No clinical improvement
- **CORTICOSTEROIDS and ALBENDAZOLE were stopped**



Case report

- **Day 18** : 1st cerebral biopsy : non specific inflammation
- **Day 30** : 2nd cerebral biopsy
 - Necrotic tissue with **eosinophilic material composed of fragments of a laminated layer**
 - Periodic acid-Schiff stain and Grocott's methenamine silver stain **POSITIVE**
 - Universal bacterial PCR
 - Fungal and mycobacterial culture
 - PCR of *Mycobacterium tuberculosis*

NEGATIVE



Day 18 and 30

Case report

What is the diagnosis and what should be done?



Day 18 and 30

Case report

- Repeated blood testing for Toxocariasis, Amoebiasis, Cysticercosis, Trichinellosis : negative
 - ⇒ Biopsy highly suggestive of a tapeworm infection
 - ⇒ Autochthonous neurocysticercosis suspected again
 - ⇒ **ALBENDAZOLE 400mgX2 per day re-introduced**

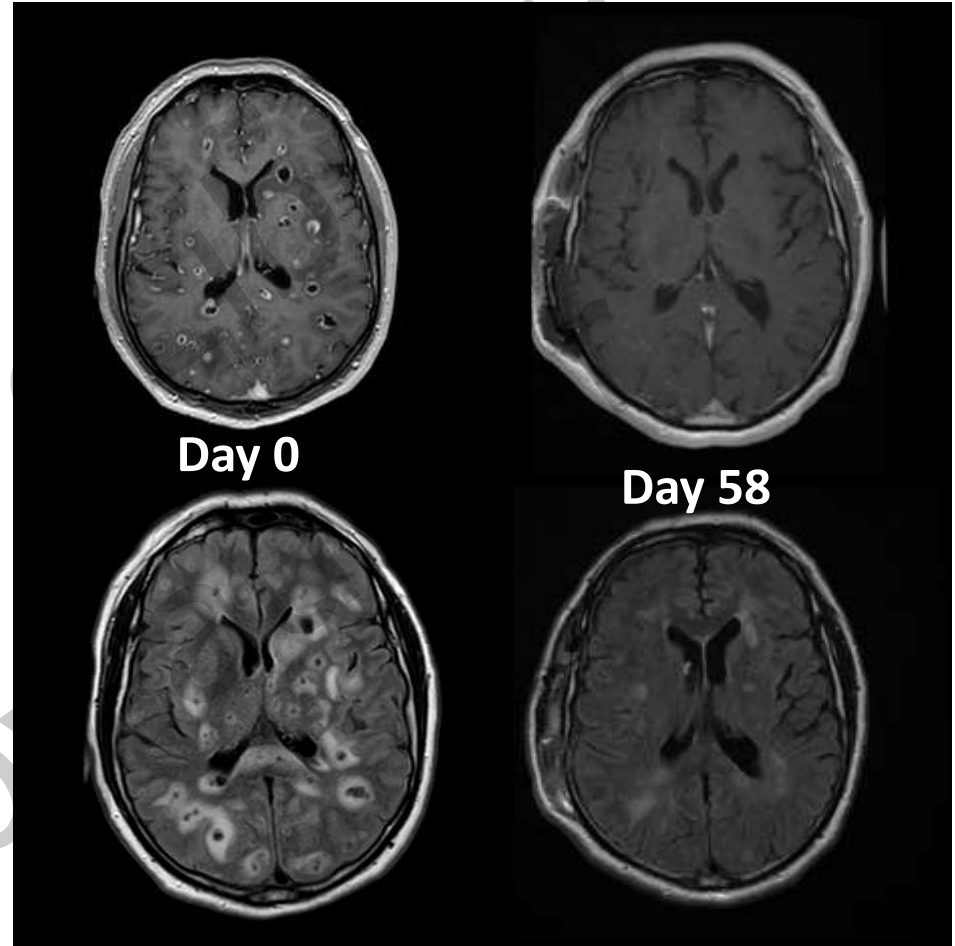


Day 18 and 30

Case report

4 weeks of treatment:
clinical and imaging
improvement

T1



Day 0

Day 58

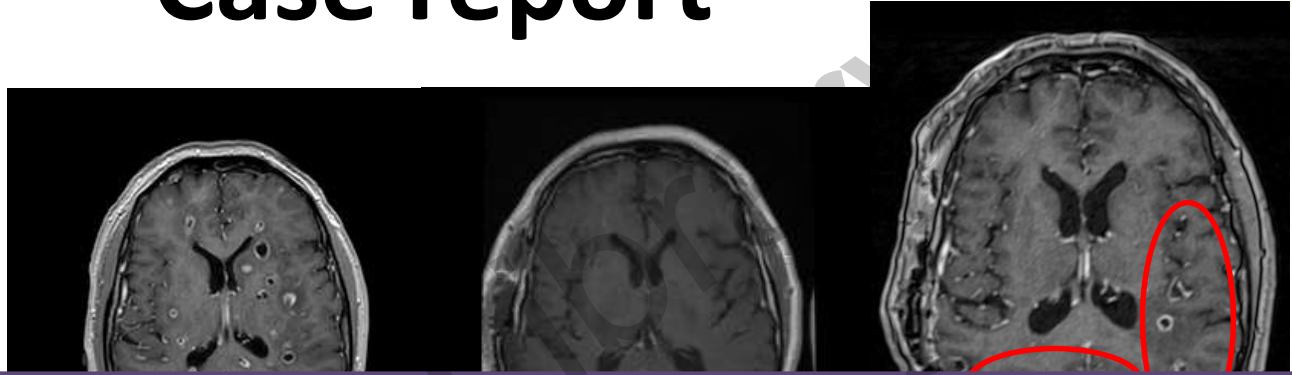
FLAIR



Day 58

Case report

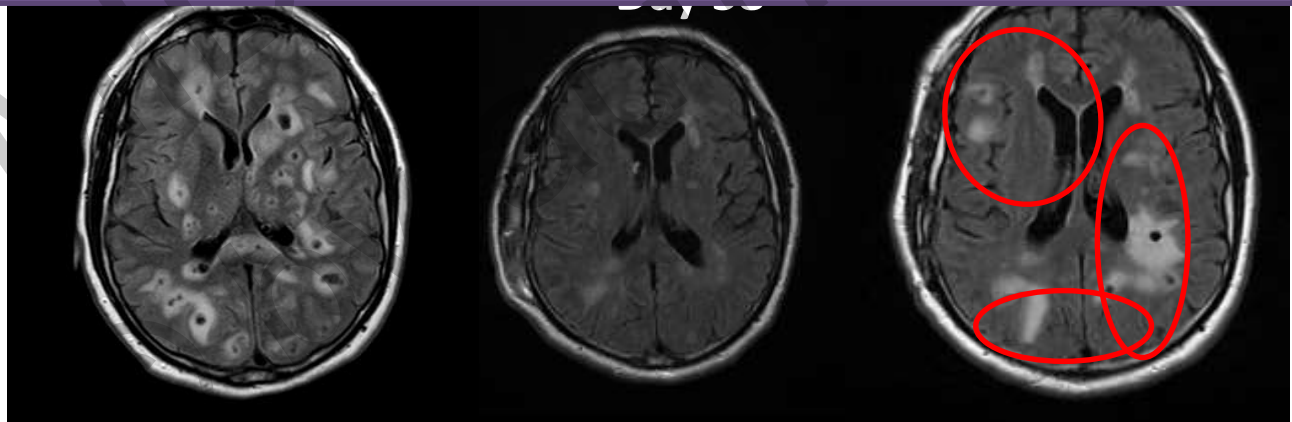
T1



Pan-cestode PCR biopsy: *Echinococcus multilocularis*

Weeks after
end of
treatment

FLAIR



Day 100



Case report

<i>E. multilocularis</i>	ELISA	Western Blot
December 2016	Index : > 3,5 Positive > 1	Negative
January 2017	Index : > 3,5	Bands 26-28 Kda Positive
May 2017	Index : > 3,5	Bands of 7,18, 26- 28 Kda Positive

Primary cerebral alveolar echinococcosis (AE)

ALBENDAZOLE 400mg X 2 per day



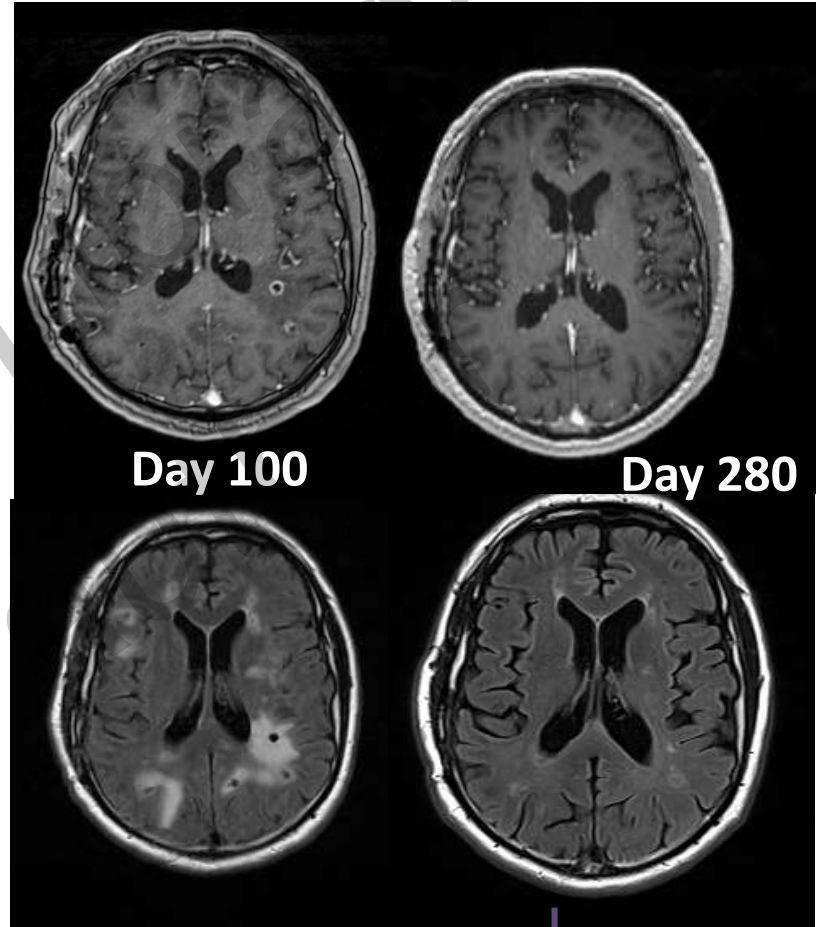
Day 100

Case report

After 6 months of ALBENDAZOLE :

- No relapse
- Well tolerated treatment

T1



Day 100

Day 280

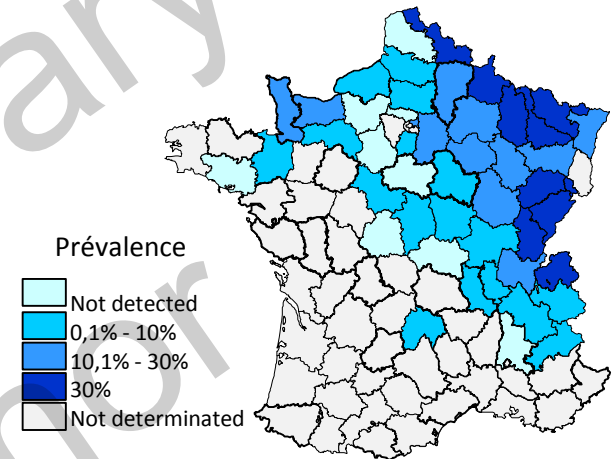
FLAIR



Day 280

Alveolar Echinococcosis (AE)

- Zoonotic infection : *E. multilocularis*
- Westward spread of *E. multilocularis* in foxes
- ↑ Incidence of human AE in France
- FrancEchino Register :
 - ✓ 1982-2017 : 735 cases
 - ✓ Annual incidence 2009 : 0,26 case /10⁶ inhab



Fox 2017



European Human AE 1982-2000

Boue et coll. Bull Epidemiol Hebd 14 septembre 2010

Grenouillet Bull Epidemiol Hebd 14 septembre 2010

Combes et al. Emerg Infect Dis. 2012

Piarroux et al. Euro Surveill. 2015; Emerg Infect Dis. 2013

Kern et al. Emerg Infect Dis. 2003

Alveolar Echinococcosis

- Only liver involvement : 62,8 %
- Primary extra-hepatic lesion without liver involvement : 2.3%
- Primary AE of brain is rare :
 - ✓ < 10 case reports
 - ✓ Not known to be associated with a specific strain
 - ✓ Unique or multiple lesions, usually supratentorial
 - ✓ Treatment : surgery when possible and/or long course of

ALBENDAZOLE/MEBENDAZOLE

Kern et al. Emerg Infect Dis. 2003

Debourgogne et al, J Clin Microbio 2013

HHT and Cerebral Abscesses (CA)

- Infections are associated with HHT in 13.6% of cases
- The risk of CA is estimated to be 100 times greater for HHT patients than the general population
- Cerebral abscesses :
 - ✓ 33% of all infections in HHT patients
 - ✓ *Streptococcus* species ++
 - ✓ Pulmonary arteriovenous malformation (AVM) : 100%
- Cerebral parasitosis not known to be associated with HHT

Dupuis-Girod et al. Clin Infec Dis 2007

Mathis et al Clin Neurol Neurosurg 2012

HHT and CA

- Our patient :
 - HHT definite diagnosis (repeated epistaxis, family history, mucocutaneous telangiectasia = 3 Curacao criteria)
 - No contrast CT scan AVM, no right-left shunt on TTE
 - Hypothesis : microscopic hepatic and pulmonary AVM driving larvae to the brain ?

Conclusions

- AE, still a rare disease, seems to spread farther than the classical areas
- CA due to echinococcosis are rare and may mimic a classical picture of neurocysticercosis
- Pancestode PCR on brain tissue should be part of CA work-up when the cause remains unknown

Acknowledgments

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Ze Normandy way of life



La vac



Le gros
ber



L'formage



Le
hauenet



L'mont



La bauge



L'canasson

Normandie
fort et vert

Heula 

CHU
CAEN NORMANDIE

**Thank you for your
attention**