P 21 Don't know was it means, don't know whether it exists, but I know it is in English (or French)

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Pure alexia is a reading deficit following occipitotemporal lesions. In the most severe cases the capacity to read isolated letters is lost. Most patients have residual implicit reading abilities, testimonied by the preserved capacities to make lexical and semantic decision tasks with quickly presented stimuli. Here we describe a patient with pure alexia who showed striking preservation of the ability to identify the language in which words were written while he performed at chance in tasks usually preserved in pure alexic patients. To our knowledge, this residual visual word processing ability in pure alexic patients has only been mentioned by Cohen and Dehaene (2000) in patient VOL with pure alexia.

Reading abilities were assessed by using several tasks including lexical, semantic, emotional decision and language decision on words, sentences and texts. The patient was able to decide the language (French or English) in which a shortly (400 ms) visually presented word was written, even if he made close to 93% errors in reading. Reaction times in reading were slow (mean reaction time, 2300 ms for correct answers). In lexical decision (400 ms) the patient performed above 90% when pseudowords were orthographically illegal; but 46% errors when the pseudowords were orthographically legal. When asked to make a semantic and an emotional decision on rapidly presented words, A. N. responded at chance level. In language decision on individual words he made 80% correct and his mean reaction time ranged from 950 to 2300 ms. Performance was neither influenced by word frequency nor by word length. Language recognition was influenced by orthographic regularities as A. N. performed 54% correct when words were orthographically legal French and English words. For sentences and texts, performance was not influenced by syntactic legality.

Together, these results indicate that A. N.'s residual ability in language decision was most likely due to a preserved ability to extract and recognise combinations of letters, specific to a given language.

Neurologist-in-training

The aim of this section is to prepare the neurologist-in-training for the FMH examination, to confront her or him with specific problems of everyday neurological practice and to give him or her updates on recent controversies in clinical neurology.

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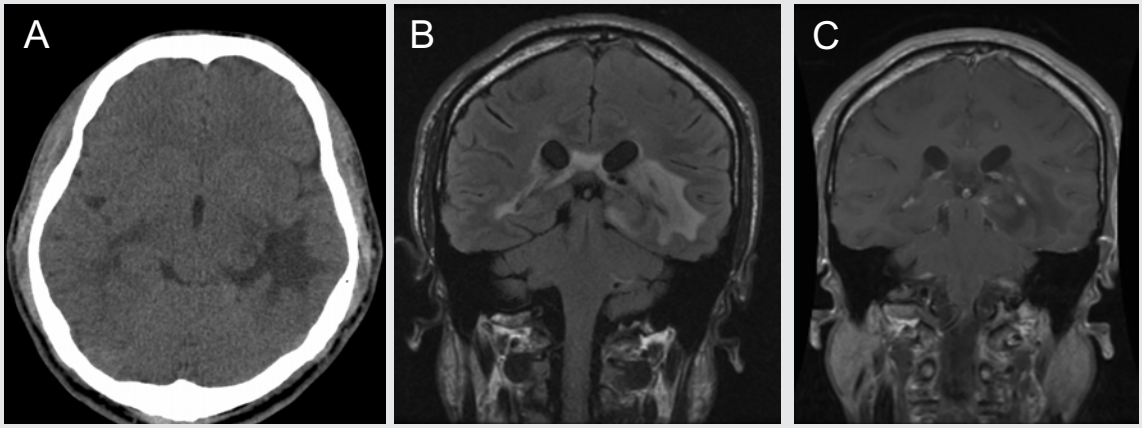
Case vignette

The 54-year-old right-handed male patient originated from Malaysia but had been working for many years in Canada as a professor of technical sciences. Currently, he made a tour throughout Europe after a one-year sabbatical in Germany. At the evening before the admission his wife noticed that he could not memorise new information and repetitively asked the same questions. The neurological examination on the next morning revealed a reduced digit span (0), loss of anterograde memory and impairment of retrograde memory covering several years. There were no other neurological deficits, physical examination and routine laboratory work-up (including white and red cell count, CRP, TSH, liver and kidney parameters) revealed no abnormalities. The resident in the emergency room suspected a transient global amnesia (TGA) and proposed a clinical follow-up in 24 hours without further examinations.

Question 1

Which clinical finding indicates that this initial appraisal might not be correct?

Neuroradiology



Computed tomography (A) demonstrated a hypointense lesion in the left temporal lobe. Magnetic resonance imaging (MRI) shows extension of the lesion into the hippocampal formation and to the opposite hemisphere in T_2- and flair images (B). In addition, there is an inhomogeneous gadolinium enhancement (C).

Question 2

What are the three most important differential diagnostic thoughts when you see such a lesion pattern?

Additional examinations

A cerebro-spinal fluid (CSF) examination was performed immediately after the MRI examination revealing a cell count of 450/µl whereof 95% monocytes. There was an elevated CSF protein of 10.5 g/L (normal 0.15–0.45) and CSF lactate of 10.2 mmol/L (normal 1.2–2.1), as well as reduced CSF glucose of 1.1 mmol/L (normal 40–60% of serum glucose which was 5.3 mmol/L). In the blood, white and red cell parameters, CRP and LDH revealed normal values.

Question 3

In respect of your differential diagnostic thoughts and these CSF findings, which additional examinations would you perform?

(For correct answers, see page 344)

Epicrisis

HIV testing was negative. CSF cultures and microscopic examinations did not reveal evidence for aerobic and anaerobic bacteria as well as M. tuberculosis. PCR examinations for human herpes viruses and M. tuberculosis were negative. Direct microscopy for fungal elements as well as fungal cultures was negative. However, *Cryptococcus neoformans* antigen was positive (1:512) confirming the diagnosis of a *cryptococcal meningoencephalitis*. Further evaluation revealed a stay in Vancouver island one year ago where *Cryptococcus neoformans* var. *gattii* is endemic which is pathogenic also for immunocompetent persons. Treatment with flucytosine (5-FC) and amphotericine B was initiated. The condition of the patient did not further deteriorate and he was repatriated to Canada from where a gradual remission with minor neuropsychological sequels was reported.

Take-home message

- → **Search for red flags also in apparently clear diagnosis!**
- → **Structural brain lesions may cause TGA-like syndromes.**
- → **Fungal encephalitis may arise in immunocompetent persons without major general symptoms.**

Suggested reading

1 Hodges JR, Warlow CP. The aetiology of transient global amnesia. A case-control study of 114 cases with prospective follow-up. Brain. 1990;113:639–57.

2 Sander K, Sander D. New insights into transient global amnesia: recent imaging and clinical findings. Lancet Neurol. 2005;4:437–44.

3 Quinette P, Guillery B, Desgranges B, de la Sayette V, Viader F, Eustache F. Working memory and executive functions in transient global amnesia. Brain. 2003;126:1917–34.

4 Batchelor T, Loeffler JS. Primary CNS lymphoma. J Clin Oncol. 2006;24:1281–8.

5 Taillibert S, Chodkiewicz C, Laigle-Donadey F, Napolitano M, Cartalat-Carel S, Sanson M. Gliomatosis cerebri: a review of 296 cases from the ANOCEF database and the literature. J Neurooncol. 2006;76:201–5.

6 Idnurm A, Bahn YS, Nielsen K, Lin X, Fraser JA, Heitman J. Deciphering the model pathogenic fungus *Cryptococcus neoformans.* Nat Rev Microbiol. 2005;3:753–64.

7 Hoang LM, Maguire JA, Doyle P, Fyfe M, Roscoe DL. *Cryptococcus neoformans* infections at Vancouver Hospital and Health Sciences Centre (1997–2002): epidemiology, microbiology and histopathology. J Med Microbiol. 2004;53:935–40.

Neurologist-in-training

Answer 1

TGA is characterised by sudden onset of antero- and retrograde amnesia without change of consciousness or loss of self-awareness lasting for 1 to 24 hours. Cognitive impairment is limited to amnesia, there is no recent history of head trauma or seizures, and there are no neurological symptoms beside dizziness, vertigo or headache. Although TGA produces a profound impairment of long-term episodic memory, the working memory is usually spared. Therefore, the observation of a reduced digit span in our patient is an unusual finding in TGA.

Answer 2

1. Cerebral lymphoma
2. Gliomatosis cerebri
3. Encephalitis

Answer 3

1. *Cerebral lymphoma* may be found in immunocompetent persons but is more frequently associated with immune deficiency. Therefore, HIV testing is mandatory. Because the CSF cell count is >100/µl, fluorescence-activated cell sorting (FACS) may be feasible to detect a clonal expansion of lymphocytes. Positron emission tomography (PET) with methionine and/or glucose may demonstrate hypermetabolism of the lesion. If FACS examination is negative or not feasible, histological examination of a brain biopsy specimen has to be performed in a non-eloquent brain area to confirm the diagnosis.
2. *Gliomatosis cerebri* is defined as a diffuse neoplastic glial cell infiltration of the brain. Since CSF cell count is usually <50/µl, the diagnosis of gliomatosis cerebri is less likely in the present case. CSF cytology and FACS do not give additional diagnostic information. Methionine and/or glucose PET may demonstrate hypermetabolism of the lesions. Histological examination of a brain biopsy specimen performed in a non-eloquent brain area has to be carried out to confirm the diagnosis.
3. *Encephalitis/cerebritis:* HIV testing has to be done to determine a possible immune deficit. The high protein and lactate level together with the clearly decreased glucose level in the CSF strongly argue against *autoimmune encephalitis* such as sarcoidosis, histiocytosis or viral encephalitis with herpes simplex virus (HSV) or varicella-zoster virus (VZV), respectively. On the other hand, *cerebral tuberculosis* has to be considered and respective CSF examinations including Ziehl-Nelson staining, PCR as well as cultures for M. tuberculosis have to be performed. Finally, a *fungal encephalitis* has to be considered and CSF examination for fungal elements, fungal cultures and determination of cryptococcal antigens have to be carried out.