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Endgames

Picture quiz

Black legs

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A 62 year old man with a 20 year history of chronic alcoholism presented to our hospital with severe diarrhoea. Since his company went bankrupt in 2008, he had been living on the streets without receiving welfare benefits. On examination, he was emaciated and gave off a pungent smell. He seemed to be alert but could not give a personal history. Neurological examination was unremarkable, although his deep tendon reflexes were reduced in all extremities. He had black discoloured skin lesions on both lower legs, below the hem of his knee length trousers (fig 1↓). Serum biochemistry showed decreased concentrations of niacin (2.1 µg/ml; normal 4.7-7.9) and thiamine (17 ng/ml; normal 28-56). A week after admission, when asked how he had spent the past few days, he answered without hesitation, "I returned from business yesterday. I'm going to play golf with a customer today." When asked 10 minutes later, he replied, "I was at home." Brain magnetic resonance imaging was performed (fig 2↓).

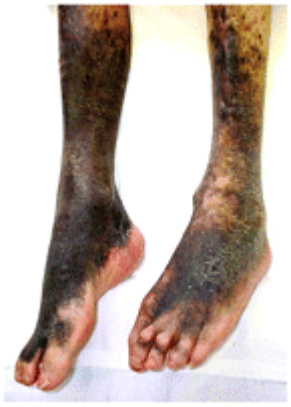

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Fig 1 Black discoloured lesions on the lower legs

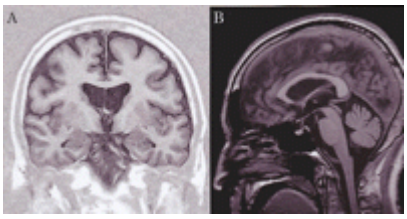

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Fig 2 (A) Coronal and (B) sagittal T1 weighted magnetic resonance imaging of the brain

Questions

1 What is the most likely cause of the skin lesions shown in fig 1?

2 What symptom can be deduced from his response to episodic memory questions a week after admission?

3 What does the brain magnetic resonance imaging scan show and what is the likely diagnosis?

4 How would you plan the management of this patient?

Answers

1 What is the most likely cause of the skin lesions?

Short answer

The bilateral skin lesions on the legs are most likely caused by pellagra.

Long answer

The most likely diagnosis is pellagra resulting from deficiency of niacin as a consequence of malnutrition and prolonged excessive alcohol consumption. Pellagra is mainly caused by lack of dietary niacin[1] or tryptophan (or both), which are precursors of nicotinamide,[2] in patients with chronic alcoholism, drug addiction, and malnutrition.[3] It is characterised by the "4Ds": dermatitis, dementia, diarrhoea, and death.[4] Dermatitis can be a pathognomonic finding that occurs bilaterally and symmetrically on body parts that have been exposed to the sun, such as the face, neck, the backs of the hands, and the legs. It usually begins with pigmentation on the healthy skin and deteriorates into scaliness, cracks, fissures, and blisters.[5] A clear line of demarcation is found between the morbid part and the healthy skin, and the affected area feels rough whereas the normal skin feels smooth. The sharp line between the black discoloured insteps and the healthy soles of the feet (fig 1) suggests that he wore flip flops most of the time. People with pellagra have variable psychotic symptoms including irritability, insomnia, depression, confusion, and amnesia, which lead to dementia.[5] His inability to give a personal history is consistent with retrograde amnesia—the impaired recollection of memories created before an important event. Diarrhoea is usually accompanied by bouts of intractable pain caused by mucous membrane lesions in the digestive organs, and this might have been related to the peculiar odour that he gave off. Pellagra is mostly found in countries where poverty and malnutrition are common. This disease may be on the increase in Japan, where the disparity between the "winners" and the "losers" is widening.

2 What symptom can be deduced from his response to episodic memory questions?

Short answer

The symptom is confabulation.

Long answer

Confabulation, which is classically defined as a falsification of memory in people with organic amnesia who have clear consciousness,[6] can explain the way his answer changed in only 10 minutes and his lack of insight into his memory problems. Confabulation was first reported in chronic alcoholism by Korsakoff.[7] Berlyne described two types of confabulation: momentary confabulation, which is provoked by interviewer questions and involves elements of real memory that are distorted in time and place; and fantastic confabulation,

which develops spontaneously, is not based on memories, and often includes wish fulfilling themes.[6] Confabulation is often regarded as pathognomonic of Korsakoff's syndrome.[8] It has also been reported in patients with brain lesions of the dorsomedial thalamic nucleus[9] and the posterior orbitofrontal cortex,[10] although the underlying anatomical localisation and mechanisms are controversial.[11] It is also unclear whether confabulation results from patients deliberately trying to hide their memory deficits or whether it is involuntary.[12] Although confabulation is often difficult to distinguish from delusions, brain magnetic resonance imaging can be used to investigate specific organic lesions in people with amnesia and confabulation.

3 What does the brain magnetic resonance imaging scan show and what is the likely diagnosis?

Short answer

T1 weighted images show enlargement of the third ventricle and atrophy of the mammillary bodies of the hypothalamus; this is indicative of Korsakoff's syndrome.

Long answer

Both coronal and sagittal sections of the T1 weighted image show marked atrophy of the mammillary bodies (fig 3A and B↓); the coronal section shows enlargement of the third ventricle (fig 3A), reflecting atrophy of the dorsomedial nuclei in the bilateral thalami. Atrophy in these brain regions is specific to the memory dysfunction found in Korsakoff's syndrome. Images from an alcoholic patient without amnesia show neither decreased volume in the dorsomedial thalami (fig 3C) nor atrophy in the mammillary bodies (fig 3C and D). Korsakoff's syndrome is characterised by anterograde or retrograde amnesia (or both), confabulation, and loss of insight.[13] Confabulation, a pathognomonic symptom of Korsakoff's syndrome,[8] became apparent in our patient a week after admission. The diagnosis was confirmed by decreased concentrations of serum thiamine. A diagnosis of both pellagra and Korsakoff's syndrome suggests that the patient not only had alcoholism but also severe malnutrition.

It is rare for Korsakoff's syndrome to develop after pellagra and not as a chronic neurological consequence of Wernicke's encephalopathy, which is chiefly caused by thiamine deficiency in those who misuse alcohol. The patient had none of the symptoms of the acute phase of Wernicke's encephalopathy, such as confusion, ophthalmoplegia, and ataxia,[14] so the diagnosis was not considered at the time of admission. The results of brain magnetic resonance imaging were also not consistent with this diagnosis because abnormal signal intensities in periaqueductal regions that are typical of Wernicke's encephalopathy were not seen (fig 3B).[14] It is possible however, that the patient had

developed encephalopathy before visiting the hospital, and that it might have led to Korsakoff's syndrome. Decreased deep tendon reflexes could be attributed to polyneuropathy resulting from thiamine deficiency, which is often coincident with Korsakoff's syndrome.

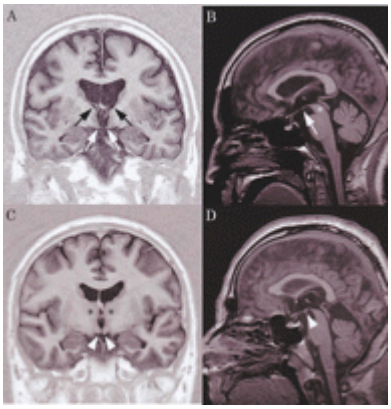

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Fig 3 (A) Coronal and (B) sagittal T1 weighted magnetic resonance imaging of the patient's brain showing marked atrophy of the bilateral mammillary bodies of the hypothalami (white arrows) and enlargement of the third ventricle, which suggests atrophy of the dorsomedial nuclei in the bilateral thalami (black arrows). No abnormal signal intensities in periaqueductal regions were detected (white asterisk). (C) Coronal and (D) sagittal T1 weighted MRI of the brain of an alcoholic patient who was non-amnesic showing neither decreased volume in the dorsomedial thalami (black asterisks) nor atrophy in the mammillary bodies (white arrow heads)

4 How would you plan the management of this patient?

Short answer

The patient needs both physical management and psychological care. He should be given oral or intravenous niacin for the pellagra and thiamine for Korsakoff's syndrome in combination with an alimentary diet. He should also be provided with a calm environment and sedative tranquillisers or hypnotics, to prevent mental disturbances including insomnia, anxiety, irritability, aggression, or violence.

Long answer

Inpatient care is recommended in such a serious case. Patients with pellagra may have

diseases associated with excess alcohol intake including hepatitis, liver cirrhosis, pancreatitis, and cerebrovascular or cardiovascular disease, so this should be investigated.[5] You should also check whether diarrhoea is caused by infectious gastroenteritis. Careful gastrointestinal examination is essential because people with pellagra often eat bizarre substances such as gravel and plaster (a phenomenon known as pica).[15] Electrolyte supplements, particularly magnesium and potassium, are often needed, because prolonged severe diarrhoea almost always disturbs the serum electrolyte balance. The intravenous route may be preferable, because these patients usually have sore mouths or painful glossitis. A single intravenous dose of glucose can precipitate exhaustion of thiamine, so thiamine should be given before glucose infusion. Within a few days of taking niacin, irritable patients become calm, and painful skin lesions and intractable diarrhoea also dramatically improve.[5] Healing of the mouth may promote eating, which will accelerate convalescence. In contrast, even prolonged thiamine replacement will not completely ameliorate the amnesia and brain lesions found in Korsakoff's syndrome. An integrated approach to treatment including referral to a rehabilitation programme can help prevent a relapse of alcoholism.[16]

Patient outcome

The patient remained in hospital for six months. His diarrhoea, dermatitis, disorientation, and peripheral neuropathy fully recovered, but he still could not completely recall his personal history. Provoked confabulation became milder but was still present despite long term administration of thiamine.

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Competing interests: All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: (1) No financial support for the submitted work from anyone other than their employer; (2) No financial relationships with commercial entities that might have an interest in the submitted work; (3) No spouses, partners, or children with relationships with commercial entities that might have an interest in the submitted work; (4) No non-financial interests that may be relevant to the submitted work.
Patient consent obtained.

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References

1. Koehn CJ, Elvehjem CA. Further studies on the concentration of the antipellagra factor. *J Biol Chem* 1937;118:693-9.[Free Full Text]

2. Ellinger P, Abdel Kader MM. Tryptophan as precursor of nicotinamide in mammals. *Nature* 1947;160:675.[Web of Science][Medline]

3. Pitche PT. Pellagra. *Sante* 2005;15:205-8.[Medline]

4. Hegyi J, Schwartz RA, Hegyi V. Pellagra: dermatitis, dementia, and diarrhea. *Int J Dermatol* 2004;43:1-5.[Web of Science][Medline]

5. Latham MC. Pellagra. In: Human nutrition in the developing world. 1997. www.fao.org/docrep/W0073E/w0073E00.HTM.

6. Berlyne N. Confabulation. *Br J Psychiatry* 1972;120:31-9.[Abstract/Free Full Text]

7. Korsakoff SS. Medico-psychological study of memory disorder. *Conscious Cogn* 1996;5:2-21.[CrossRef][Web of Science][Medline]

8. Kopelman MD. Two types of confabulation. *J Neurol Neurosurg Psychiatry* 1987;50:1482-7.[Abstract/Free Full Text]

9. Victor M, Adams RD, Collins GH. The Wernicke-Korsakoff syndrome and related neurologic disorders due to alcoholism and malnutrition. 2nd ed. FA Davis, 1971.

10. Schnider A. Spontaneous confabulation and the adaptation of thought to ongoing reality. *Nat Rev Neurosci* 2003;4:662-71.[CrossRef][Web of Science][Medline]

11. Dab S, Claes T, Morais J, Shallice T. Confabulation with a selective descriptor process impairment. *Cogn Neuropsychol* 1999;16:215-42.[CrossRef][Web of Science]

12. Gündoðar D, Demirci S. Confabulation: a symptom which is intriguing but not adequately known. *Turk Psikiyatri Derg* 2007;18:172-8.[Web of Science][Medline]

13. Mair WGP, Warrington EK, Weiskrantz L. Memory disorder in Korsakoff psychosis: a neuropathological and neuropsychological investigation of two cases. *Brain* 1979;102:749-83.[Free Full Text]

14. Zuccoli G, Pipitone N. Neuroimaging findings in acute Wernicke's encephalopathy: review of the literature. *Am J Roentgenol* 2009;192:501-8.[Abstract/Free Full Text]

15. Danford DE. Pica and nutrition. *Annu Rev Nutr* 1982;2:303-22.[CrossRef][Web of Science][Medline]

16. Kopelman MD, Thomson AD, Guerrini I, Marshall EJ. The Korsakoff syndrome: clinical aspects, psychology and treatment. *Alcohol Alcohol* 2009;44:148-54.[Abstract/Free Full Text]