Reminder of important clinical lesson

Progressive neuropsychiatric and brain abnormalities after smoke inhalation

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Summary

A 46-year-old man inhaled combustible smoke of unknown chemical composition for 15–20 min in an automobile body shop. Within 1 month, he noted headache, sadness, anergia, anhedonia, agitation, poor sleep and impairment of concentration, attention and learning skills. Three years later, mental status examination showed major depression and cognitive disorder manifested by apprehension, continuous sadness, agitation, exhaustion, difficulty with word finding, bradyphrenia, short-term and long-term memory impairment, and judgement impaired by impulsive and affect-laden reactions without reflection. Impairments were noted on neuropsychiatric tests, and positron emission tomography (PET) scan of the brain with ^{18}F -fluorodeoxyglucose showed globally decreased and heterogeneous metabolic activity in the entire brain. Treatment included sertraline, methylphenidate, valproic acid and topiramate. At 14 years after smoke inhalation injury, he had persistent cognitive impairment. Repeat brain PET scan showed areas of improvement and deterioration. This case shows long-term brain and psychiatric dysfunction resulting after toxic smoke inhalation, with some areas of the brain having progressive deterioration between years 3 and 14 after smoke inhalation.

BACKGROUND

This manuscript hypothesises that progressive brain injury, at least associated with inhalation of combustible smoke, presents progressive longitudinal impairment years after the acute trauma resolved. There are collated statistical data to state that there is an increased risk of seizure and dementia after closed head injury. To my knowledge, there is no metabolic study over 11 years to calculate the percentage of positive or negative changes. Brain tissue varies in vulnerability to inhalation injury. This manuscript argues that some tissue is vulnerable to progressive deterioration because mitochondrial respiratory was compromise causing oxidation of DNA that consequently permanently altered cell function. The case of a healthy man, well regarded in his community, successful at work, is used to demonstrate metabolic variances between 3 and 14 years post-injury.

CASE PRESENTATION

A 46-year-old man had a smoke-inhalation injury while working in an automobile body shop. For undetermined reasons, an automobile interior precipitously ignited, and black smoke filled the garage; the patient attempted to extinguish the fire and he inhaled combustible smoke of unknown chemical composition for 15–20 min. He had no previous history of medical, neurological or psychiatric problems except for pneumonia (age, 16 years), hypercholesterolaemia, mild obesity and tobacco abuse (stopped 3 years earlier).

For 3 days after smoke inhalation, he was hospitalised with severe chest pain, severe dyspnoea and cough that produced black, slimy sputum. Blood tests, cardiac studies and chest radiographs were normal. Discharge diagnoses included chest pain and acute tracheal bronchitis secondary to smoke inhalation.

Within the first few months after the smoke inhalation injury, he was treated with daily prednisone to control pulmonary symptoms. During the subsequent 3 years, he developed chronic pulmonary disease and had multiple hospitalisations for pneumonia.

By 1 year after injury, he also developed moderate obstructive sleep apnoea (overnight sleep study: disturbance index increased from 24 to 49 events per hour with severe oxygen desaturation [68%]), which was improved with bi-level positive airway pressure (disturbance index, 1.8 events per hour; nadir oxygen saturation, 94%).

Within 1 month after the smoke-inhalation injury, the patient presented with sadness, headache, anergia, anhedonia, agitation, poor sleep and impairment of concentration, attention and learning skills. Three years later, mental status examination showed apprehension, depression, agitation, exhaustion, difficult word finding, bradyphrenia, short-term and long-term memory impairment and judgement impaired by impulsive and affect-laden reactions without reflection. Psychiatric clinical diagnosis included major depressive disorder (single episode, moderate) and cognitive disorder secondary to brain injury. A positron emission tomography (PET) scan with ^{18}F -fluorodeoxyglucose (FDG) showed globally decreased heterogeneous metabolic activity in the entire brain (figure 1). Neuropsychiatric testing showed multiple functional abnormalities (table 1).

Repeat neuropsychiatric testing 2 years later (5 years after smoke inhalation injury) showed weaknesses on the Wechsler Adult Intelligence Scale (third edition) WAIS-III in short-term auditory memory, visual motor speed and rote copying skills. On the Wechsler Memory Scale (third edition), there were six indices that were markedly decreased, including Visual Immediate Index (score, 68),

Figure 1 The positron emission tomography scan of the patient (age, 49 years), 3 years after combustible smoke inhalation. There was globally decreased and heterogeneous metabolic activity in the entire brain. The orbital frontal lobes and temporal poles had symmetric but decreased metabolic activity.

Immediate Memory Index (score, 69), Visual Delayed Index (score, 65), Auditory Recognition Delayed Index (score, 55), General Memory Index (score, 62) and

Working Memory Index (score, 74). The patient was denied vocational retraining, because of cognitive loss.

Table 1 Results of neuropsychiatric testing in a 46-year-old man at 3 years after smoke inhalation injury*

Neuropsychiatric test	Result*
Beck depression inventory-II score*	30 points
Purdue pegboard performance	
Right (dominant) hand	23rd (slow movement)
Left (non-dominant) hand	12th (very slow movement)
Bimanual dexterity	
Right (dominant) hand	5th
Left (non-dominant) hand	8th
Rey osterrieth complex figure test†	
Visuospatial construction abilities	<1st
Visuospatial memory (immediate, delayed and free recall)	66th (each)
Ruff 2 and 7 selective attention test‡	19th
Conner continuous performance test (visual attention)	2nd
Brief test of attention (auditory attention)	2nd
Wechsler Memory Scale (third edition) (memory abilities)§	Average range
Cambridge Automated Neuropsychological Test Assessment Battery (CANTAB)	
Spatial location memory subtest	34th
Visual pattern recognition memory subtest	3rd
Delayed matching to sample subtest	4th
Wisconsin card sorting task	
Performance subtest	Normal
Number of problems solved	11th
University of Pennsylvania Smell Identification Test (UPSIT)¶	58th

*Beck score reported as points (threshold for severe depression, 29; maximum, 63); all other test results reported as percentile or descriptive score.

†Validity of performance supported by memory error patterns.

‡Impaired because of slow-processing speed rather than inaccuracy.

§Validity of performance was supported by two subtests of the Wechsler Memory Scale (third edition) being forced choice tests, which can reveal malingering.

¶Validity of performance supported by UPSIT incorporating a malingering threshold through forced choice response of 25% not approached by the patient.²

TREATMENT

Psychiatric treatment included (1) sertraline (100 mg daily), which caused improved symptoms of depression; (2) methylphenidate (sustained release, 60 mg daily), which caused improved focus of concentration; and (3) valproic acid (1500 mg daily), which controlled rage but caused major weight gain; valproic acid was replaced with topiramate (200 mg daily), which continued the control of rage. Improvements with psychopharmacological treatment were evident within 6 weeks of treatment onset. Other medication included albuterol, pravastatin, alendronate, valdecoxib, doxycycline, glucosamine and chondroitin sulphate.

OUTCOME AND FOLLOW-UP

After 14 years of psychiatric treatment, the patient still had major cognitive loss, requiring his wife to take over the executive functions of the home and compelling him to resign from active leadership in two national organisations. Follow-up evaluation with brain PET scan at 14 years after the inhalation injury showed areas of improvement and deterioration. There was loss of glucose uptake and metabolism in the corpus callosum (left, -31%; right, -21%), left and right orbital frontal lobes (each, -27%), globus pallidus (left, -24%; right, -18%), left and right putamen (each, -15%) and thalamus (left, -7%; right, -18%). There was improvement of glucose uptake and metabolism in the temporal pole (left, 47%; right, 60%), occipitotemporal region (left, 9%; right, 44%), pons (left, 6%; right, 35%), superior parietal lobule (left, 15%; right, 31%), cerebellum (left, 11%; right, 23%) and right and left angular gyrus (each, 21%). No area returned to normal control values. The right side of the brain had less metabolic insult than the left side at 3 and 14 years.

DISCUSSION

The etiology of brain and neuropsychiatric dysfunction is inferred from the chronological progression of the clinical syndrome after smoke inhalation. The original injury to the brain most likely resulted from hypoxia and neurotoxicity. However, subsequent bouts of pneumonia and the development of obstructive sleep apnoea may have further compromised brain function. By 3 years after the inhalation of toxic smoke, the patient had stability of pulmonary function and was being treated with bi-level positive airway pressure for obstructive sleep apnoea. The need for steroids to help pulmonary function is another potential contributing factor because of the potential effect of steroids on brain tissue.

At 3 years after inhalation injury, depression and cognitive dysfunction were documented with neuropsychiatric testing, mental status examination and an FDG PET scan. Depression does not explain the specific deficits of brain metabolism. However, depression and brain dysfunction occurred after toxic smoke inhalation.

Comparison of the clinical status of the patient at 3 and 14 years after inhalation injury showed that he had improved mood and affect control but ongoing cognitive impairment at 14 years. Metabolic changes of the brain between 3 and 14 years after injury showed areas of the brain that improved and other areas that deteriorated. The right side of the brain had less metabolic insult than the left side at 3 and 14 years, perhaps because of vascular differences.

Theoretically, the neural circuitry of the globus pallidus and putamen to the thalamus, and then to the cortex, may predict deterioration in temporal pole metabolism. However, the results in this patient could not validate the explanation that specific brain regions may have deteriorated because of a chain reaction from deterioration of another region.

Previous animal studies have shown that oxidative DNA damage caused by inhibition of mitochondrial respiratory complexes may contribute to neuronal dysfunction and

progressive brain injury.^{1 3} The patient's course of illness between 3 and 14 years after inhalation injury may have resulted, in part, from impaired mitochondrial respiration and oxidative DNA damage. Some regions of the brain may have been more or less vulnerable because of differences in vascularity, myelination and sensitivity to neurotoxins, resulting in diverse, dissimilar areas of damage.

This case demonstrates that a smoke inhalation injury may be associated with permanent metabolic changes in vulnerable regions of the brain. Patients who have brain trauma from smoke inhalation may have ongoing deterioration years after the injury.

Learning points

- ▶ Combustible smoke contains macromolecules.
- ▶ After the acute event, there is a risk of progressive brain metabolic dysfunction.
- ▶ Mood disorder occurs after some brain insults, including combustible smoke inhalation and requires chronic treatment especially in patients who have suffered vocational and avocational losses.

Competing interests None.

Patient consent Obtained.

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