Toxicology and Industrial Health
25(9-10) 577–581

DOI: 10.1177/0748233709348393
tih.sagepub.com

Neurologic and neuropsychiatric syndrome features of mold and mycotoxin exposure

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Abstract

Human exposure to molds, mycotoxins, and water-damaged buildings can cause neurologic and neuropsychiatric signs and symptoms. Many of these clinical features can partly mimic or be similar to classic neurologic disorders including pain syndromes, movement disorders, delirium, dementia, and disorders of balance and coordination. In this article, the author delineates the signs and symptoms of a syndrome precipitated by mold and mycotoxin exposure and contrasts and separates these findings neurodiagnostically from known neurologic diseases. This clinical process is designed to further the scientific exploration of the underlying neuropathophysiologic processes and to promote better understanding of effects of mold/mycotoxin/water-damaged buildings on the human nervous system and diseases of the nervous system. It is clear that mycotoxins can affect sensitive individuals, and possibly accelerate underlying neurologic/pathologic processes, but it is crucial to separate known neurologic and neuropsychiatric disorders from mycotoxin effects in order to study it properly.

Keywords

Pain syndrome, chronic fatigue, myalgia, tremors-jerking, weakness

Introduction

The effects of various molds and mycotoxins have been observed for eons in domesticated animals. As commercial mass processing of animal feeds and rearing of livestock ensued, mold contamination avoidance strategies arose to decrease product and stock losses and to reduce risk of contamination of public food supplies. With the combination of more tightly sealed structures for energy saving and water damage to buildings, humans have become more frequently exposed to molds and mycotoxins. Hence, it is not unexpected that beyond the more obvious respiratory and dermatologic effects of mold exposure, susceptible individuals would also be showing signs and symptoms of central and peripheral nervous system effects.

For several reasons, the neurologic and neuropsychiatric effects of mold and mycotoxins in humans have been less well-studied, and in some circles, controversial. First of all, the nervous system is extremely complex and there is a wide range of individual variation in how the central nervous system, the peripheral nervous system, and the autonomic nervous system react to biologically toxic molecules. Secondly, there is a wide range of biotoxins molds produce and many combinations of molds that can grow within a water-damaged structure. Hence, with a huge individual and organism diversity, almost an endless number of combinations of exposure-reaction profiles will occur. And, lastly, in recent decades, most of the attention brought to focus upon humans with exposure to water-damaged buildings has been in the legal arena. In this naturally adversarial legal milieu, scientific methods can be obfuscated and often all parties can become discredited and/or dismissed. The process can then lead to individuals and resources abandoning the area of study. Even with the clinical variability and

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the dearth of formal study within the medical community, and despite the legal clamor, the preponderance of recently growing data suggests very strongly that for selected sensitive or vulnerable individuals there are clear neurologic and neuropsychiatric effects of mold and mycotoxin exposure that in some cases can lead to severe and permanent deficits. It is for this reason then, that in the pages to follow, I will outline some preliminary clinical observations and symptoms of a syndrome that are meant to further the scientific study into the nature of these phenomena.

Methods and clinical setting

Having dual training in Psychiatry and Neurology (Johns Hopkins) and having had faculty experience directing an academic pain center (Blaustein Pain Treatment Center/JHH/Neurology) I commonly am asked to consult and treat complex and unusual cases at our Atlanta clinic, the Independent Neurodiagnostic Clinic. Several years ago, Dr Donald Dennis (ENT) began sending us patients in one such group: chronic fungal sinusitis (CFS) cases with peculiar pain complaints. In addition to pain syndromes, many also had unusual disorders of cognition, movement, and balance. As we will see below, symptomatic treatment of the pain generators was quite successful, but what was of particular interest was the reduction of not only the pain generators, but of many of the movement, balance, and cognitive disorders when the underlying CFS and the systemic fungal syndrome (SFS) were treated in tandem with treating/biobalancing the home environment for mold.

Over the years, then with additional patients from Dr Dennis and other physicians and sources, we have seen a wide variety of neurologic and neuropsychiatric signs and symptoms. These clinical features can be diffuse in their presentations, but can also be more focal depending upon the neurologic system affected. Since the nervous system is really a balance between excitation and inhibition, one can see amplification or diminution of normal neurological activities, as well as precipitation of neural activity well beyond expected limits.

In our discussion below, we will look first at more focal presentations, and then later at more ''diffuse'' presentations. The goal is to begin working on defining systems of a syndrome or clusters of signs/symptoms, and then to look at possible improvements in measurement and testing, and ultimately to illustrate neuroanatomical/clinical and neuropathophysiologic components of the disorders. Of interest also, of course, is to delineate these mold and mycotoxin-induced signs and symptoms from classic neurologic disorders.

Local and focal pain syndrome complexes

Migraine and atypical facial pain

The inflammatory sinus changes with CFS can induce referred atypical facial pain of a nociceptive type and respond to antinociceptive medications. Branches of the trigeminal nerve can become focally irritated or permanently damaged, creating secondary focal atypical trigeminal neuropathic pain, which can be responsive to anticonvulsants and tricyclics. Especially in patients with a diathesis toward migraine, but even in patients with no prior history of headache, we can frequently see common migraine (without aura or complicated features usually) develop. The better the inflammatory process is managed in the sinuses, the more easily the migraines are managed with prophylactic medications such as calcium channel blockers and tricyclics. Abortives can also help.

Pharyngitis and glossopharyngeal neuralgia

Postnasal drainage from inflamed sinuses, as well as local throat irritation from direct mold or mycotoxin exposure, again, are simple mucosal inflammatory nociceptive pain generators. However, that inflammation can irritate the throat's innervations and a neuropathic pain can evolve. It can then, once instigated, be more easily precipitated with much lower levels of stimulation and can act as an allodynic neuropathic process. Elimination of the inflammation and using nociceptive and antineuropathic medications can greatly reduce the pain.

Local head and neck myalgias

All of the inflammatory, nociceptive, and migraine pain generated in the head and throat can feed into cranial nerve and upper cervical root pain pathways and myofascial pain loops. Secondary local increased muscle tone, spasm, and local trigger points can develop into independent facial, temporal, suboccipital, and cervical myofascial pain syndromes. These in turn can feed into some of the shoulder-stabilizing muscles such as the trapezii, levator scapulae, Romberg muscles, etc. Removing the primary pain

generators can sometimes eliminate the myofascial component, but in chronic cases and/or susceptible individuals, the myofascial syndrome can gain a 'life of its own' self-perpetuating even if the main or original mold or mycotoxin-induced irritants are removed. Medications for muscle spasm and neuromuscular mobilization technique can be very helpful here.

Inflammation induction of distant and diffuse pain

Any inflammatory process in the body, including CFS, can induce diffuse myalgias and arthralgias. Inflammatory cytokines and circulating immune complexes can reach any joint or muscle or connective tissue in the body by way of the circulatory system. And again, once instigated, these can be self-perpetuating. The nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and adjuvant analgesics such as tricyclic antidepressants, antiepileptic drugs, and SSRIs/SNRIs can be extremely helpful in these more widespread pain syndromes. Always, however, lessening and/or removing the primary inflammatory source is crucial to clinical improvement.

Unusual neuropathic focal pain patterns

Single or multiple peripheral nerves can become painful occasionally, or a distal painful peripheral neuropathy can be seen. We also rarely see dorsal root ganglia involvement (e.g. bilateral L1, L2, L3). Certainly, microvascular compromise must be considered as a possible mechanism. At any rate, these neuropathic pain features generally respond to an antineuropathic multimedication co-pharmacy regimens.

Pain treatment guidelines

Identification of the nociceptive, myofascial, and neuropathic pain generators and treatment of them with an appropriate co-pharmacy and physical program is important. However, treating the underlying CFS and clearing/treating/biobalancing the environment are necessary to eliminate the external stimulus for the various pain generators. Often, then, the medications can be reduced or discontinued.

Disorders of movement

With CFS, mold, or water-damaged building or mycotoxin exposure, we can see tremors, jerking movements, spastic dysphonia, tic-like motions, and idiopathic paroxysmal unique involuntary movements. The curious thing about these movements is that they are similar to, but not stereotypical of, well-defined neurologic signs such as chorea, hemiballismus, Parkinson's tremor, myoclonic jerks, etc. Being similar but not exactly alike classical neurologic findings, and lacking other 'classical' neurologic-associated signs can influence clinicians to suspect a psychiatric source. However, mimicking (consciously or subconsciously) these odd movements would be difficult, and sometimes impossible to do. Other neurologic features such as strength, reflexes, and sensation are almost always normal.

These unusual signs generally suggest an alteration of regulation of motor function rather than focal neurologic damage. This may be why we see signs similar to some classic neurodegenerative disorders, but not exactly the same. There may be a demodulation of cellular function rather than specific motor subsets of cells that are becoming impaired and/or dying.

Another confusing process, also, is the fact that with abnormal movements, though they may begin involuntary, the motor system reflex or the patient consciously and voluntarily will try to alter or normalize or control the initiated abnormal action. This is more possible to modulate in an impaired rather than damaged motor syndrome. Being able to exert some voluntary control, however, can lead to misinterpreting the entire process as psychiatric.

Medications that modulate 'classic' movement disorders such as anti-parkinsonian medications do not help, but taking the patient out of the contaminated environment almost always down-regulates the abnormal movements. Also, unfortunately, this can also be misinterpreted as a psychiatric response to reward with 'secondary gain', and since we can be affecting multiple neurologic motor systems simultaneously, we can see a very mixed clinical picture with tremor, choreiform, cerebellar, balance signs, etc., all manifesting variably and simultaneously.

Balance and ataxia

Imbalance and gait ataxia are seen much more commonly than pure cerebellar findings in these patients. Balance relies on multiple sensory inputs (visual, proprioception, vestibular, etc.), the pyramidal motor

system, and multiple extrapyramidal and cerebellar modulating systems. Having so many sites susceptible to attack makes imbalance a common symptom; having a fair amount of redundancy makes the symptom somewhat more manageable. And again, medications are ineffective and symptom resolution generally comes only when body and environment are cleared and corrected, respectively.

Since any one of many systems, if affected, can affect balance, it can be an early measurable sign and a good variable to follow. What balance as a neurologic sign lacks in specificity, it makes up for in its sensitivity. Balance and ataxia also may be more measurable and quantifiable than many of the other motor and sensory signs and symptoms.

Focal disorder overview

Not uncommonly, we will see a fluctuant variety of these focal system dysfunctions in one patient. With the exception of the pain syndromes, these abnormalities are not pharmacologically treatable. However, very reliably they fluctuate with treatment of the underlying process (such as CFS) and the signs reliably defervesce when the patient is removed from exposure, and recrudesce when re-exposed.

Clinically, one wants to 'rule out' classical neurologic disorders by clinical exam and testing and trial treatments, and at the same time, make a 'diagnosis of inclusion' by reducing signs/symptoms with treatment of the sinus or systemic fungal disorder and by elimination of the environmental exposure. Reactivating the signs and symptoms by re-exposure then gives further causal relationship confirmation.

Diffuse neuropsychiatric syndromes from mold/mycotoxin exposure

Mental confusion can be seen in patients exposed to mold and mycotoxins; in some instances, it can become a fixed clinical state. A common label affixed to these altered mental states is 'Brain Fog'. While brain fog may be illustrative and an easily understood metaphor for patients to understand, it is a moniker that can lead the patient to be seen as melodramatic and the clinician as unscientific. Therefore, we will focus on the neurologic and neuropsychiatric mycotoxin and mold-induced forms of delirium and dementia.

Temporary malfunction of the attention, cognitive and memory systems, of the brain is usually called delirium. In our patients susceptible to mold exposure, we see varying degrees of altered mental status, usually with altered attention, blunted executive function, and faulty short-term memory. The patient's intelligence and personality can mediate a delirium in either a positive or negative fashion. The patient experiences delirium as 'being less sharp than usual' with mild cases (like being 'off' with a viral flu and fever), to cases of experiencing a moderate confusion clearly recognized by the patient as an altered mental state with diminished mental capacity (such as moderate alcohol intoxication), to finally, a very confused and nearly nonfunctional mental state that can further induce catastrophic decompensating behaviors, recognizable to others.

Classic of delirium, these alterations of mental status wax and wane. Clearly in part, this can occur when exposed (or improved when isolated from exposure) and generally patients get back to normal mental baseline at times. This pattern can go on over time, but if sensitivity and susceptibility worsen and/or exposure becomes more continuous or stronger, the periods of normal function lessen and a chronic state of confusion and/or brain malfunction can be established as a new impaired baseline. In most patients, this is still a physiologic imbalance and if exposure is stopped and treatment started, patients can still, in most cases, return to their normal status.

If, however, repeated physiologic alterations occur within the brain's neuron and/or supportive cells (e.g. astrocytes, oligodendroglia, etc.), and/or the brain's protective structures (e.g. blood brain barrier), to a degree they only partially recover, then we have a net loss of brain function with some mild memory or cognitive changes. However, brain function loss beyond this mild form is seen as true dementia. Depending upon underlying pathophysiologic mechanism, the dementia can be static or progressive, worsening with more cellular damage or death.

Due diligence clinical workup

With delirium, we can have a very wide range of medical disorders that can produce 'encephalopathic' or delirious profiles, and those disorders and entities need to be pursued as best as is practical. Generally, these deliriums are reversible, and their causes are well-illustrated in the neurologic and psychiatric textbooks. If these causes of delirium can be demonstrated as noncontributory, then removal of the patient from the environmental source with clinical improvement and then reexposure with clinical

worsening can help document causality. And one does, of course, need to keep in mind psychiatric disorders such as somatization and conversion.

Out of the early diagnostic categories of 'senile dementia' and 'pre-senile dementia' have emerged Alzheimer's, CNS vasculitis, Creutzfeld-Jakob disease, frontotemporal dementia, multi-infarct dementia, etc. Many, if not most, can be ruled in by clinical and neurodiagnostic maneuvers such as MRI, EEG, PET scanning, etc.

We do not, as yet, have a set of diagnostic maneuvers to 'rule in' a mycotoxin-induced dementia. In my experience, thus far, when CFS is improved and the patient's environment is treated/biobalanced and the delirium has improved, but there is still a memory/cognitive deficit remaining, that ''dementia'' has been the least likely to improve of all the mold-induced phenomenon. Most patients tend to get some better with treatment and elimination of exposure, but most do not return to pre-exposure baseline. They do tend to stabilize and, in the near term, do not tend to progress. Thus far, I have not seen the various 'Alzheimer's drugs' improve patients' memory or cognition.

Conclusion and recommendations

Overall, as in many neuropsychiatric and neurologic diseases, the beginning of delineation of a spectrum of disorders starts with the following:

1. Observations that denote a possible unique group of disorders.
2. Clinical and testing processes to eliminate classic and/or known disorders.
3. Delineation of syndromal features that facilitates:
    a. Correlation to possible existent animal disorders/models.
    b. Neuroanatomic localizations of sites of effects.
    c. Delineation of testing methods to further localization of pathologic processes.
    d. Finally, neuropathophysiologic theories of mechanism of disease.

Currently, in our clinic, we are just beginning the methodical process of syndromal definitions and 'rule-out' testing. It is likely that with such wide individual susceptibility (none to severe), and with so many mold species and multiple mycotoxins per species, we will see a wide range of pathophysiologies active. These could include direct neuron effect, alteration of support cells, microvascular changes, etc.

However, with a systematic process, perhaps we can at least begin to illustrate the differences of mold/mycotoxin/water damaged building exposure effects from classic neurologic/neuropsychiatric disorders, look for more specific useful diagnostic maneuvers, and in addition, see how much, if at all, mold mycotoxin contributes to causality or acceleration of known neurologic disorders.

Acknowledgments

Examination, testing, and treatments were paid for by patients, their medical or Workers' Compensation insurance, or by a claimant or defense law firm. All patients were seen in the normal course of clinical practice.

Conflict of interest statement

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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