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Ototoxicity and neurotoxicity from exposure to a mixture of organic solvents and noise, a case report

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ABSTRACT

Background: Neuropsychological alterations and decreased hearing, are related to organic solvents (OS) exposure; and if noise is present it potentiates the hearing damage. **Aim:** to evaluate neuropsychological performance and hearing of a 50 years old worker, occupationally exposed to OS mixtures for 26 years (toluene, ethyl acetate and isopropyl alcohol) and noise > 85 dB (A). **Design of study:** Report of a case assessed by Neuropsychological tests, CT and SPECT studies of hearing and clinic-occupational history. **Results:** He presented, loss between 35 to > 55 dB HL of his hearing in both ears, both in low frequencies (125 Hz-2 kHz) as well as the treble ones (3-8 kHz), in relation to his age. There was an otoacoustic emissions absence at the same frequencies. He showed cerebellar atrophy, cognitive, motor and emotional disorders. **Conclusions:** We Integrated diagnosis of: moderate to severe hearing loss, mental and behaviour disorders due to the simultaneous exposure to noise and an OS mixture, mainly toluene. It should fully evaluate workers exposed to noise and OS.

Keywords: Ototoxicity, neurotoxicity, toluene, noise, emissions otoacoustic audiometry.

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INTRODUCTION

The central and peripheral nervous system damage caused by chronic occupational exposure to organic solvents (OS) such as: toluene, xylene, styrene, trichloroethylene, among others. Either uniquely in mixtures are well known. They are widely used in various production processes, and are volatile and highly lipophilic as well with the capability of being absorbed through the respiratory tract and skin (WHO, 1989; Juntunen J, 1993; Viaene MK, 2002). For more than 30 years, they have been associated with hearing damage as well, potentializing their effects along noise exposure (Sliwinska-Kowalska et al, 2001; Morata TC, 2003; Vyskocil et al, 2012).

Ototoxic and neurotoxic clinical manifestations are diverse: fatigue, memory disorders, concentration difficulty, emotional disturbances, some intellectual functions disturbances, velocity nerve conduction decrease and reduction of its scope in motor nerves, alterations in contrast vision, dyschromatopsies, neuroimaging and neuropsychological changes; lower performance in various tests; as well as hearing loss, absence of otoacoustic emissions, latency speed and breadth of auditory evoked potentials decrease and behavior of central auditory processing tests abnormalities (WHO, 1989; Juntunen J, 1993; OSHI, 1998; Viaene MK, 2002; Lataye and Campo, 1997; Sulkowski et al, 2002; Chang SJ et al, 2006; Fuente A, 2010; Fuente A et al, 2012; Fuente and McPearson, 2012). Experimental and epidemiological studies have shown the toluene and noise synergy which potentiates damage to the auditory system (Lataye and Campo, 1997; Morata TC, 2003) these neurological and hearing damages intensity, will depend on the OS toxicological characteristics, its mixtures, the exposure intensity and frequency, as well as individual susceptibility (Viaene MK, 2002; Vyskocil et al, 2012).

We describe a worker´s case exposed chronically to an organic solvent mixture - mainly toluene-, ethyl acetate, isopropyl alcohol and noise probably intensities greater than 85 dB (A); who presented irreversible ototoxicity and neurotoxicity clinical manifestations.

CLINICAL CASE

A 50 years old man, without relevant family history of hearing loss or recreational activities at-risk for otoneurological and neurotoxic pathologies.

Pathologic personal background. - Use of Ototoxic drugs and infectious otitis denied. Occasional smoking (12 p/year) for 20 years, occasionally alcohol intake for 16 years (1 p/month) without reaching drunkenness, suspending it 15 years ago. Traumatic brain injury 30 years ago, without loss of alertness. Chronic degenerative diseases denied.

Occupational background. – He worked in a manufacturing company of printed rolls and packaging of polypropylene and polyethylene bags for 26 years.

Organic solvents and noise-mixture exposure. - At the age of 24, he was adjutant general packaging of coils assistant for six months. Subsequently, as inks assistant during a year, preparing 15 drums a day with OS mixture. Then, as a web-fed-printing assistant for three years, he used to clean printing trucks in an industrial washing machine containing solvents. He joined for a year, blades-laundering area with OS, 15 to 20 times a day. Their fifth job he weighted rolls, for six months. For a year he would measure ink viscosity, managing OS from three different web-fed-printing machines. His seventh job supplying rolls to the web-fed-printing for three years. He aided the operator (first assistant) and the one who would supply rolls to the web-fed-printing for ten years. And finally, in his ninth job was a machine operator, reviewing the OS, printing, the ink levels, the material´s image, programming machines, placing the role, took measures and tones, and began printing for six years.

During the 9 jobs, he was exposed to higher toluene steamers concentrations, mixed with ethyl acetate and isopropyl alcohol, as well as inks which could contain lead. The rolling mill machines and printing, according to the worker, they prevented verbal communication within 1 meter of distance and they had to speak out louder, so that the noise was probably > 85dB (A). He was not provided with any personal protective equipment for 24 years, and only in the last two years he was given ear plugs, mask, and gloves.

Current condition. - it started 13 years ago, referring slow and progressive decrease bilateral hearing with left dominance, without apparent cause, adding continuous left treble tinnitus, with ipsilateral otic fullness. It evolved with tinnitus persistence, with left dominance, bilaterally exacerbating at the end of the workday.

10 years ago he presented recent memory disorders, and occasional dysesthesias in hands and feet. A year ago, he presented colors discrimination disorders, oppressive and moderate-intensity bi-temporal headache; balance disorders by perceiving his body turned, exacerbated with head position changes, vertigo which lasts a few seconds triggered by cephalic position changes which conditions instability limiting his displacement. The symptoms increased, adding a right leg muscle weakness, the reason why he was hospitalized.

EVALUATION AND RESULTS

Auditory function. – He presented permeable external auditory canals and tympanic membranes intact. Tympanometry in both ears curve (s) type Jerger, normal compliance and present stapedial reflex. Hearing loss was recorded in all frequencies (125 Hz to 8 kHz) with an audiometric ototoxicity-like curve and hearing damage induced by noise, with an 8 KHz recovery. The audiometric curve expected, according to this patient´s age (50 years old) was estimated, in accordance with ISO 7029:2000 (E) (Fig. 1). The logoaudiometry showed voice perception to 60 dB HL, the right ear 80% and 50% the left ear. In both ears, there is a large response amplitude decrease in the otoacoustic emissions, at 500 to 8000 Hz frequencies (Fig. 2). The auditory evoked potentials of stem brain (AEPSB), waves latency times and intervals inter-waveform, were normal according to age and sex. The final diagnosis was bilateral moderate ototoxic hearing loss (CIE-10 H91) due to organic solvents and noise occupational exposure.

Neuropsychiatric assessment. - Patient was alert, cooperative, was unstable and dependent on a family member, hearing loss behavior. Serious tone voice, adequate intensity hyporinophonic tone. Speak: language with question-answer latency phase delay. Speaking slowly, hypotimic affection, emotional lability (easy tears and despair). Attention and concentration, decreased; fixation memory deficiencies of evocation and abstraction.

We analyzed his emotional status with the Q-16 questionnaire (Marthiowtz, 1985), with a neuropsychiatric symptoms increase (n = 11) 16. Also, we applied to him the Derogatis & Spencer´s brief symptoms inventory, (1982), showing an increase in symptoms such as: Somatization disorder, obsessive-compulsive, depression, anxiety, paranoia and additional symptoms (referred to in Van Wendel et al, 2000). With these previous studies, we could diagnose anxiety and depression mixed disorder (ICD-10 F412) secondary to organic solvent occupational exposure.

Neuropsychological performance. - We evaluated cognitive, motor-cognitive, motor, and affective domain performance. In relation to the cognitive area: Wechsler digits and symbols test, (1981) assessed visual memory, motor-vision tracking, motor perceptual speed and sustained concentration, which was decreased (n = 25 vs. n = 47). Lewis & Kaple´s, monitoring test (1977), evaluated sustained attention, and it showed a decrease with more time for his performance (180.04 vs 198.4 sec.) (Referred to in Van Wendel et al, 2000). WAIS: 68 total

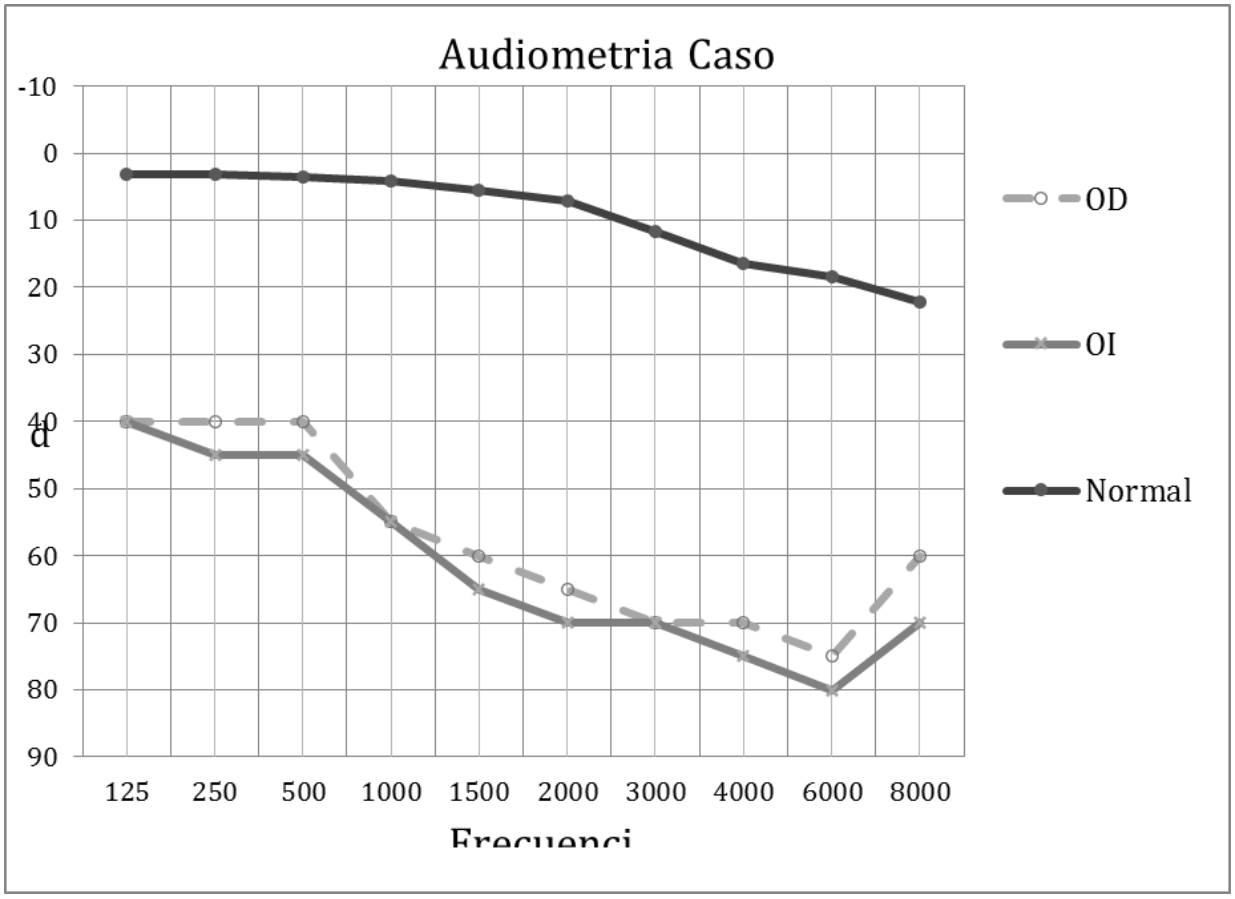

Fig. 1 audiometric curves: expected to 50 years of age and which resulted from 26 years to noise and organic solvents mixture exposure

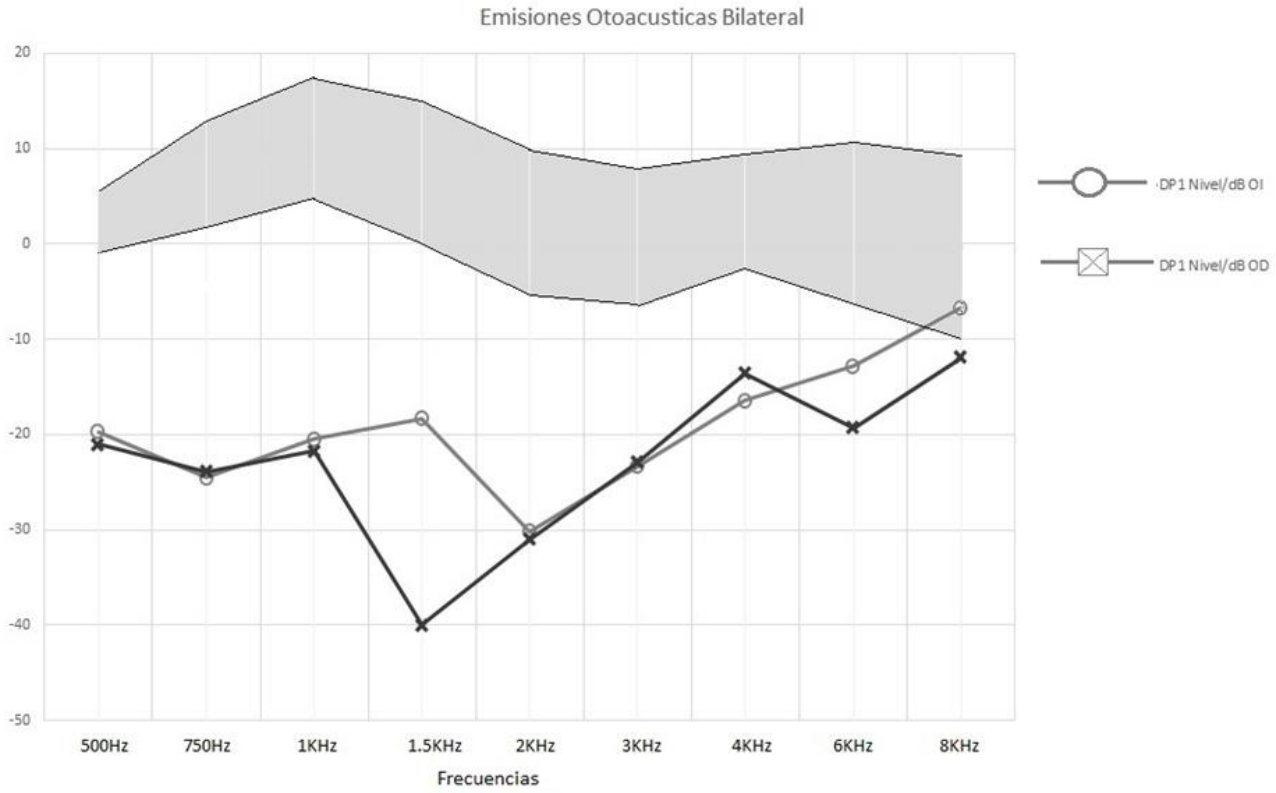

Fig. 2. After exposure bilateral otoacoustic emissions for 26 years to noise and organic solvents mixture.

IQ, verbal area 70, 69, damage index - 16% (emotional) performing area. Bender obtained a 10 total score, motor-vision alteration indicators.

Clinical neurological assessment. – Spontaneous and sight evocated nystagmus were negative, without any positional nystagmus evidence. Head shaking and pushes were negative, metrics and dysdiadochokinesia, Romberg sign was positive, tandem test unstable, Unterberger-Fukuda was negative, Babinski-Weil star lateralize to the right. During the electronystagmography he presented seeking saccades with bilateral hypometria. Intact thoracic limbs with normal tone and trophism, Daniel´s manual muscle strength 5/5, psychomotricity slightly increased due to tremor. Intact pelvic limbs, with normal tone and trophism, Daniel´s manual muscle strength 5/5, full sensibility, patellar reflex with bilateral pendulum sign, Lasegue, Bragard, Patrick and Hoover signs were negative. Limb´s electromyography was normal.

Neuroimaging. - SPECT/CT brain perfusion, we observed severe Thalamic and left caudate nucleus hypoperfusion, multiple moderate to severe ischemia areas, in left superior parietal gyrus, calcarine sulcus and left temporal association cortex, suggestive multi-ischquemic disease pattern is observed. The brain CT, presented subtle cerebellar atrophy. With data from previous tests and the chronic OS occupational exposure we could integrate mental and behavior disorders diagnosis due to volatile solvent use (ICD-10 - F188).

Visual evaluation. - The visual acuity 20/40 right eye (.) 20/30 and 20/50 left eye (.) 20/40. Color discrimination, with D-15 Lanthony test (Bowman, 1982), showed a bilateral confusion chromatic index slight increase, with 1.28 in right eye and 1.25 in left eye (normal value is 1). These results are considered normal. (Referred to in Van Wendel et al, 2000). The Ishihara test, turned out normal.

Biological-determination. - For having handled inks containing lead we determined the lead level in blood resulting in 38.22 µg/dL.

Environmental-determinations. - The company did not provide neither historical nor punctual results, about organic solvents concentrations or noise levels.

DISCUSSION

Considering the hearing, he should have at his age (50 years) (Fig. 1), the lost threshold average in frequencies from 125 to 8000 Hz, in both ears is greater than 38 dB (A). Thresholds average on all frequencies from the right ear was 47.9 dB (A) and the left ear 51.4 dB (A); Although the bilateral loss average in high frequencies - 3 to 8 kHz - was greater than 51 dBA vs the low - 125 to 2000 Hz, RE = 45.6 dB (A) and LE = 48.9 dB (A). These losses were corroborated with an otoacoustic emissions absence by products of distortion (Fig. 2) on the same frequencies.

Our results are similar to those observed in the experimental study of Lataye and Campo, (1997); where rats were simultaneously exposed to toluene and noise, presenting greater hearing loss in low and high frequencies, compared to those with only toluene exposure (2000 ppm) and others with only noise exposure (92 dB), where only high frequencies were affected. As a result, external hair cells (OHC) loss of functionality and/or destruction is probably present in the worker studied, as it shows the same in Lataye and Campo study (1997), with hair cells loss, in a 60 %:OHC1 and 86 %:OHC2, affecting 18-24 kHz frequencies; and 41%: OHC1 and 74 %:OHC2 affecting 4-5 kHz frequencies; and OHC3 loss of 89 to 98%, both in the mild and low frequencies.

As well as Morata et al., (1993) and Chang et al., (2006), reported 11 times more risk of hearing loss in workers exposed simultaneously to toluene and noise compared with those exposed only to OS or noise. This also occurred in two studies by Sliwinska-Kowalska

et to the, (2001 and 2004). The first observed greater hearing loss in 61.5% of the group occupationally exposed to OS mixture and noise; and the second reported five times more risk of hearing loss in those occupationally exposed to OS mixtures with xylene and noise, and 20 times more risk of hearing loss in workers exposed to noise and estireno, toluene and n- hexane, toluene mixtures (2005). In these studies the hearing loss was greater in high frequencies (3-8 kHz).

According to normal results of the AEPSB which are similar to those achieved in tests with rats exposed to toluene. In other words, there were not observed any significant differences between absolute latencies, inter-wavelength and amplitude intervals, uniaurals or interaurals, which suggests the damage lies apparently only in the cochlea (Vyskocil et al, 2012).

In the same way, Draper and Bamiou, (2009) and Fuente et al, (2012), have reported some cases of irreversible hearing loss from chronic occupational exposure to xylene. These two case reports also recorded increases in 1 to 6 kHz frequencies, but with moderate damage (> 25 dB to 50 dB), in contrast to the serious damages observed in our case. These differences may be due to a shorter exposure to low concentrations of xylene and xylene (6 months); and there was no simultaneous exposure to noise > 85dB. And in our case, perhaps the greater toxicity of toluene, simultaneous noise exposure > 85dB, as well as a chronic and increased respiratory and dermal occupational exposure to the OS.

When toluene and noise are present there is a synergistic effect of hearing damage. Some authors suggest that the probable mechanism of toluene is its inhibition of acetylcholine receptors, located on the medium olivo-cochlear beam, which in turn it regulates cochlea external hair cells contraction (Fuente and McPearson, 2012). Route of toluene intoxication is via blood by the stria vascularis, through the external spiral groove, reaching the Hensen´s cells. These cells are in close contact with Deiters´ cells, which are located in the lower part of the external hair cells, (Campo et al, 1999). Evidence suggests that in workers with simultaneous toluene exposure > 50 ppm and noise > 85 dB, hearing damage is irreversible (Schaper et al, 2008).

The patient also presented cognitive, emotional and motor functions impairment, widely pointed out by OS exposure (WHO-European, 1989 ;) Viaene MK, 2002). In addition, the worker had concentration changes, memory, psychomotor speed decrease in, decreased mental flexibility, mood swings, personality changes, diffuse pain, and sleep difficulties. Some reports refer to cases also presented signs of spasticity, ataxia, polyneuropathy, intentional tremor, distal peripheral reflexes decreased, among others (Viaene MK, 2002). Psychomotor speed is the first neuropsychological function deteriorating, after ten years exposure, followed by the attention and memory. Also, our case report presented these signs and symptoms.

Moreover, our case showed severe hypoperfusion on thalamic region and left caudate nucleus, as well as mild to severe multiple ischemic areas on upper left parietal gyrus, calcarine sulcus and left temporal association cortex. CT showed cerebellar atrophy. A wide literature review conducted by Viaene (2002) reported the presence of cortical and subcortical atrophy in axial CT, data similar to those observed in the present case. There is documented evidence since last century that chronical occupational and environmental organic solvents exposure or mixtures, causes permanent damage to central and peripheral nervous system. For that reason working meetings have been developed in Europe in order to determine the clinical criteria to diagnose it (Gilioli R, 1993). We consider that these meetings to define the algorithm of diagnosis and treatment of diseases associated with simultaneous noise and OS exposures should take less industrialized countries into account such as Mexico, in such a way, any

clinical criteria changes for diagnosis and treatment are global.

CONCLUSIONS

In the present case report, there was a history of simultaneous chronical occupational OS mixture exposure (mainly toluene) and noise > 85dB (A) which generated synergies damage and ototoxic moderate to severe hearing loss and chronic disorders due to neurotoxicity (psychiatric, and neuropsychological).

These health issues are complex to evaluate because of its insidious neuro-ototoxicity clinical manifestations (WHO-European, 1989; Juntunen J, 1993; Vyskocil et al, 2012), and because of extended latencies to its clinical manifestation. The occupational exposure reconstruction led us to the diagnosis, even though, it is difficult to do so because of the lack of information from the company about concentrations and frequency of OS exposure and noise intensities over the worker´s occupational history.

Therefore, his diagnoses are essentially based on the meticulous reconstruction of chronical occupational noise and OS exposure, narrated by the worker, and the evidence given by scientific literature on similar cases, this is corroborated with the hearing assessment, neuroimaging studies, and performance on neuropsychological tests (Vyskocil et al, 2012; OSHI, 1998).

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