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A 44 year old woman was admitted to our clinic because of progressive multiple sclerosis. One year before admission she had developed parasthesias of the legs, and subsequently of the arms. She became incontinent for urine and feces, and had complained of numb feelings and muscle cramps in her legs. The medical history mentioned hypertension for which she used propranolol and hydrochlorothiazide. The family history was negative for multiple sclerosis. On examination there was vertical nystagmus, slight paresis of the right arm, lid lag, incoordination of the arms, and loss of sensation from a mid-thoracic level. The tendon reflexes of the legs were very brisk, and both plantar responses were extensor. Examination of the CSF showed eight white cells/mm³ (all lymphocytes), and an immunological production of IgG and IgM. Brain MRI and the cervical part of the spinal cord showed multiple white matter lesions. Additional investigations excluded other diseases—for example, borreliosis and lupus erythematosus. A 10 day treatment with daily administration of 1000 mg methylprednisolone divided doses was started. Methylprednisolone was given in its injectable form, methylprednisolone sodium succinate, which hydrolyses to methylprednisolone in the body. The infusion period was one hour. Because of cystitis she also received trimethoprim. One day after the intravenous methylprednisolone treatment course had ended, the patient developed generalised urticaria which disappeared after a few days, and which could have been induced by either drug. After informed consent of the patient it was decided to give the patient the next two doses of 500 mg dose of intravenous methylprednisolone in isotonic saline. How­ever, minor risk, we gave 4.0 mg intravenous clemastine, and no side effects were observed. The reactions found, we measured blood concentrations not exceeding 6.5 mg/l, which is less than those measured in patients receiving high dose intravenous methylprednisolone with no adverse reactions.6

Reviewing the literature we found only one case report of a patient with multiple sclerosis who developed an anaphylactoid reaction to intravenous methylprednisolone.7 This patient had a positive skin test for methylprednisolone, and a radio allergosorbent test (RAST) for IgE antibodies was positive. No information regarding the RAST procedure was mentioned.

Mild side effects to oral or intravenously administered corticosteroids in patients have been found but occur infrequently (0.3% of the patients). 8 Risk factors for developing allergic reactions after receiving intravenous methylprednisolone are asthma and aspirin intolerance.9 Our patient had no history of asthma or allergies.

Skin tests have been used to investigate the nature of side effects to intravenous methylprednisolone.10 We showed that skin tests are unreliable as they also gave positive reactions in the healthy volunteers. The “allergic” reactions are probably not due to IgE antibodies, but could have been caused by fast administration of methylprednisolone leading to high plasma concentrations. However, raised concentrations were not found. The histamine release reaction for methylprednisolone sodium succinate was not indicative of an IgE mediated reaction, but rather due to a (dose related) toxic effect of methylprednisolone on the basophil granulocytes.

In conclusion, the clinical symptoms which developed during high dose intravenous methylprednisolone are rare, but can be dangerous. Therefore, patients with multiple sclerosis who receive an intravenous methylprednisolone treatment for the first time should be carefully monitored. According to this case, the mechanism of the reaction seems to be IgE independent, and may have been induced by toxic concentrations of methylprednisolone on the basophil granulocytes. Skin testing with methylprednisolone is unreliable, and should be interpreted with care.
Unilateral auditory hallucinations: ear or brain?

Brašić and Perry* convincingly describe a boy with unilateral otopathic auditory hallucinations. However, their literature review is very much focused on the CNS causes for auditory hallucinations other than from a hyperactive ear. They also do not cite a misleading, postulating dubious CNS causes or brain?

Brasic and Perry et al reviewed musical hallucinations. In their paper starts: "Unilateral auditory hallucinations: ear or brain?" and not the neocortex. This is not evidence that auditory hallucinations are generated in the brain; instead, it is consistent with peripheral impulses funnelling up via the thalamus.

The volunteers of Ketter et al *-consistently (29 out of 32 subjects) reported procaine induced auditory hallucinations (unformed buzzing, ringing, or electronic sounds)*. They considered procaine a selective limbic activator, even though no change in cerebral blood flow corresponded to the "auditory hallucinations". In an ear, nose, and throat clinic the above noises would definitely be labelled tinnitus, and an obvious peripheral cause usually found. In line with procaine causes cochlear hyperactivation (increased wave I and II amplitude in dogs); in view of the link between epilepsy and the ear, it is noteworthy that the EEG changed from an awake pattern to seizure activity.

The 1968 review of sensory deprivation by Perlsta et al was cited as an example of auditory hallucinations from sensory disinhibition. I reviewed some of this literature, concluding that for musical hallucinations there is as much evidence for ear disease and labyrinthe hyperactivity as when they occur in all other conditions and diseases. Deprivation is a rare occurrence; deafness (especially white noise is used to mask environmental sounds, whereas if all background noises are reduced, normal subjects will start to have tinnitus. I recently tested a 16 year old dyslectic patient who had never known silence ("there was always a permanent noise running through it")., yet his EEG never differed from normal. Sensory deprivation is more likely than deprivation, as in fact misprinted! A similar case to that of Brasic and Perry throws considerable light on pathophysiological processes involved. Both were tormented by voices of demons leaving symptoms of unilateral ear disease; saw things that never existed; andated; had "fey visions (fire surrounded by cockroaches, devil transforming into burning wisp of straw); possible fluid in one middle ear (blocked grommet plus air-bone gap; fluid discharge from one ear). Conspicuously omitted was any mention of tinnitus, the most likely generator of the auditory hallucinations. Fortunately, the other case was Martin Luther, who clearly described ringing in his ears, unendurable buzzing, thundering, cracks, thumps, etc. Once, he had a musical hallucination (bells of specific church towers) which woke him in bed because of noises in his head. Curiously, Luther did not have a simple demonic or religious explanation for his torments. Instead he blamed Satan for his Meniere's symptoms (headache, episodic vertigo, tinnitus), in which he recognised caused his hallucinations. In fact his symptoms were typical of Meniere's disease, a well known condition which caused tinnitus.

Letters, Book reviews