into the third ventricle almost to the level of the foramen of Monro. A frontal craniotomy showed the optic nerves and chiasm to be elevated by a craniopharyngioma that was subtotally resected. The lamina terminalis was opened, and cyst fluid and wall were resected. Postoperative medications included thyroid hormone, hydrocortisone, and testosterone.

On May 6, the patient's visual acuity had improved to 20/15 in the right eye and 20/20 in the left, and no visual field defect could be found on formal testing, even with objects as small as the 1-mm white object at 2 meters. The rest of the findings were unchanged. Between May 10 and June 15, he received 4,600 rads to five cranial portals. These portals were arranged in a coronal arc—right lateral skull, left lateral skull, right coronal oblique, left coronal oblique, and saggital coronal. Field size was 6×5 cm. On June 2, the findings of the ocular examination were unchanged except for the presence of 2 mm of exophthalmos of the left eye. This was not accompanied by any congestion of the conjunctiva or distention of the veins of the fundus. Orbital resiliency was unremarkable, and the eye seemed to protrude straight out. The exophthalmos was noticeable on casual inspection. Two months later the visual acuity had improved to 20/15 in both eyes, and the proptosis had completely cleared. Although vision began to fail in both eyes and his scotoma reappeared in July 1973, the proptosis has not reappeared.

COMMENT

If exophthalmos develops in a patient who has been treated for perichiasmatic neoplasm, it is apt to cause alarm. The physician may assume that the exophthalmos is due to further growth of the tumor or that it is a complication of surgery or irradiation. Recurrence of tumor could produce proptosis by invasion of the orbit through the optic canal or superior orbital fissure, or by compressing the cavernous sinus and causing congestion of the orbit. A similar mass effect could occur with a postoperative cyst, abscess, granuloma, or hematoma. Such masses situated above the orbit could remold the orbital roof and constrict the orbital contents. Radiation therapy could conceivably cause proptosis by fibrosis or edema in the orbit or cavernous sinus. However, the chronology of events and the subsequent courses of the three cases in this report make it unlikely that growth or swelling of the tumor was responsible. The exophthalmos first appeared in each patient at a time when visual function was improving. It receded spontaneously in two patients and has remained unchanged in the third. The irradiation is unlikely to have been at fault since proptosis was present in one case prior to the start of therapy. The proptosis was mild, but in two of the three patients it was evident by inspection. In the third, it was detected only by measurement. Because exophthalmometry was done at each examination, before and after surgery, it is possible to be reasonably certain that the changes were significant. Furthermore, since the preoperative measurements were known, the disparity between the two eyes could be confidently ascribed to exophthalmos rather than enophthalmos.

To my knowledge, there are no prior descriptions of this type of exophthalmos, and there have been no cases in my experience other than those mentioned. The mechanism that is responsible for it is obscure, and attempts to identify features of these cases that might provide clues have been frustrating. However, regardless of what causes this type of exophthalmos, it is benign and should not in itself prompt reevalution of the patient.

Anticonvulsant Nature of Marihuana Smoking

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• **Marihuana smoking, in conjunction with therapeutic doses of phenobarbital and diphenylhydantoin, was apparently necessary for controlling seizures in one 24-year-old epileptic patient.**

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ANECDOTAL accounts of beneficial therapeutic effects of *Cannabis sativa* have been known throughout recorded history.[1] The classic description by O'Shaughnessy[2] in 1842 of the ameliorative effects of marihuana extract on "infantile convulsions," "hydrophobia," and "lockjaw" invite speculation as to the anticonvulsant effect of the drug. Other 19th century physicians reported that marihuana preparations were of benefit in controlling various spastic and seizure states,[3,4] although entirely useless in states of "true chronic epilepsy" such as petit mal.[4] Synthetic derivatives of Δ^9-tetrahydrocannabinol, the main psychoactive ingredient of marihuana, have been reported to be of value in the treatment of human epilepsy, al-

though explicit details are absent in the abstract-report.[5] Finally, there is also a published report in which grand mal convulsions in a 20-year-old man were exacerbated by smoking marihuana.[6]

These references are essentially the only available literature on the relationship between marihuana and human convulsions, which obviously indicates a paucity as well as a contradiction of information. The following case report describes the possible beneficial effect of marihuana in human epilepsy.

Report of a Case

A 24-year-old man has been seen in a neurology outpatient clinic for a period of eight years for control of his epileptic seizures. His history included febrile convulsions at 3 years of age and epileptic seizures since the age of 16. Since that age, the patient has been taking diphenylhydantoin sodium, 100 mg four times a day, and phenobarbital, 30 mg four times a day. Control of seizures with this regimen was incomplete, and the patient complained of attacks about once every two months. From the age of 16 to 22, the incidence of seizures increased to one attack per month to one per week.

At 22 years of age, the patient began smoking marihuana (two to five joints per night) while continuing the prescribed anticonvulsant drug therapy. During this period, attacks did not occur as long as the patient continued to take the combination of all three drugs. The patient's condition could not be maintained on marihuana alone, because on two occasions he experienced an attack three to four days after running out of his prescribed medication.

Neurological work-up has recently been done on the patient and he has been thoroughly interviewed, because of the possible association between marihuana and epilepsy. The patient was found to have abnormal paroxysmal bursts of spike and slow-wave electroencephalographic discharges bilaterally, and his condition was diagnosed as grand mal epilepsy. The patient showed no other physical or emotional disability and did not admit to smoking cigarettes, drinking alcohol, or taking any other drugs. Plasma level of diphenylhydantoin was 7.4μg/ml; phenobarbital level was 11μg/ml; and folic acid, 4.5μg/ml.

The patient apparently complies with his dosage regimen, since he has a history of regular clinic visits and refilled drug prescriptions.

Comment

This case suggests that marihuana may possess an anticonvulsant effect in human epilepsy. Previous reports have alluded to this possibility.[1-3,5] Moreover, the antiseizure properties of Δ⁹-tetrahydrocannabinol have been demonstrated in a wide variety of experimental animal species.[7-9] It has been shown in laboratory-animal seizure models that the tetrahydrocannabinols show a differential activity against major seizures without altering the sequelae of minor seizures.[7] Thus, the present case appears to bear out the prediction from the animal studies while at the same time possibly explaining marihuana's observed lack of effect in petit mal epilepsy.[4]

Theoretical calculations can be made to elucidate the probable blood level range for Δ⁹-tetrahydrocannabinol. A sample of the patient's marihuana was analyzed for tetrahydrocannabinol content by gas chromatography, and was found to contain 1.2% by weight total cannabinoids. One twelfth of the total cannabinoids, or 0.1% by weight, was accounted for by Δ⁹-tetrahydrocannabinol. Assuming 1 gm of marihuana per joint and correcting for pyrolysis (50%) and lung-absorption losses (20%), the inhalation dose of Δ⁹-tetrahydrocannabinol to the patient (weight, about 65 kg [143 lb]) would be 6.15μg/kg. It is known that doses of 5μg to 7μg/kg of Δ⁹-tetrahydrocannabinol produce psychological and physiological effects in steady marihuana smokers.[10] Moreover, after an intravenous bolus of Δ⁹-tetrahydrocannabinol, marihuana smokers show lower blood levels and shorter half-lives (28 hours) for the drug than nonusers (half-life, 57 hours).[10] Since the half-life is 28 hours in steady smokers and this patient used two to five joints per evening, little of the drug would be eliminated and the blood levels would be expected to climb rapidly during the evening.

The subtherapeutic blood level of diphenylhydantoin in this patient, 7.4μg/ml (normal range, 10 to 25) was not unexpected, since phenobarbital is known to induce the formation of enzymes that metabolize diphenylhydantoin. Even when the blood levels of diphenylhydantoin are less than the normal range, the combination of the two drugs is known to be clinically effective.[11] The blood level of 11μg/ml of phenobarbital found in this patient is within the normal therapeutic range (10 to 20).

In summary, marihuana smoking in conjunction with routine doses of phenobarbital and diphenylhydantoin was apparently necessary for controlling seizures in one 24-year-old patient. However, the present case is in direct contrast to the single previously reported case of marihuana smoking exacerbating seizures in one patient with grand mal epilepsy.[6] The possibility that Δ⁹-tetrahydrocannabinol or other cannabinoids may be useful or detrimental in major seizures needs further investigation.

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The analysis of marihuana for tetrahydrocannabinol was performed by Pharm Chem Laboratories, Palo Alto, Calif.

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