Although the mechanism is not clear, it is of considerable importance to be aware of this phenomenon, so that the dosage of ethyl biscoumacetate may be adequate to control thrombo-embolic complications during hormone therapy. Unless absolutely indicated for their known specific effects, A.C.T.H. and/or cortisone should be withheld in the presence of thrombo-embolic complications.

Summary

An increased incidence of thrombo-embolic complications during A.C.T.H. and cortisone therapy was confirmed. During hormone therapy a higher dosage of ethyl biscoumacetate was needed to obtain plasma prothrombin activity at the optimum level.

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A CASE OF UVEITIS WITH DEAFNESS THE VOGT-KOYANAGI SYNDROME

BY

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Uveitis may be caused by many disease processes, but it was Vogt (1906) who first described a case of non-traumatic uveitis associated with alopecia and greying of the eyelashes and hair. Koyanagi (1929) reviewed the published reports of ten such cases and added six of his own. In his review he summarized a hitherto ill-defined syndrome of uveitis, deafness, alopecia, and loss of pigment in the skin and the hair of the scalp, eyebrows, and eyelashes, which has since been named after these two workers. There is a closely related disease, named after Harada, in which a low-grade uveitis is associated with bilateral detachment of the retina, deafness, alopecia, and pigmentary changes similar to those already described.

The following case of the Vogt-Koyanagi syndrome is described in order to stimulate interest in the early recognition of such cases, so that investigations of the cause may be carried out at an early stage in the disease and perhaps a more specific method of treatment found.

Clinical Picture

A stoker aged 41 was admitted to the National Hospital under the care of Dr. M. J. McArdle on April 9, 1952. There was no significant family history. Apart from a urethritis of uncertain cause seven years before, he had been in good health.

Three months before admission he noticed swelling of a left inguinal lymph node without apparent cause. Soon after

this he developed "a chill" with supraorbital headache and blood-streaked sputum on one occasion. Intermittent headache persisted for three weeks, during which time he noticed the insidious onset of misty vision, beginning in the right eye. Headache cleared spontaneously after a month, but vision slowly deteriorated. A month before admission he began to vomit, had right-sided tinnitus, and noticed difficulty in balancing. Two weeks later he became deaf on the right side, and a week afterwards deaf on the left also, by which time he had continual bilateral tinnitus.

On examination he was afebrile, but looked ill. His vision was R. 6/60, L. 2/60. Mr. Williamson Noble reported a bilateral granulomatous iridocyclitis with keratic precipitates and increase in ocular tension, particularly of the right eye. Haziness of the cornea prevented an adequate view of either fundus. Anosmia was not present. He was completely deaf in the right ear and could only just hear a loud voice with the left. There was no spontaneous nystagmus, although such had been observed just before admission. Caloric responses were absent (Miss Dix). The remaining cranial nerves were normal. There was no weakness, ataxia, sensory loss, or reflex abnormality in limbs or trunk, but the labyrinthine defects caused considerable dysequilibrium. There was no lymphadenopathy, and the chest and abdomen were normal.

Investigations.—C.S.F., April 10, 1952; pressure, 180 mm.; normal dynamics; 47 cells per c.mm. (93% lymphocytes, 7% monocytes); protein, 85 mg. per 100 ml.; Lange curve, 0112210000; W.R. (blood and C.S.F.) negative. April 23: pressure, 180 mm.; 34 lymphocytes per c.mm.; protein, 75 mg. per 100 ml.; glucose, 74 mg. per 100 ml.; chloride, 740 mg. per 100 ml.; no acid-fast bacilli seen; Löwenstein-Jensen culture and guinea-pig inoculation negative. May 17: pressure, 145 mm.; 18 cells per c.mm.; protein, 50 mg. per 100 ml.; Lange, no change. Full blood count, E.S.R. and serum protein were normal. Mantoux test was positive at 1 in 10,000. Blood agglutination test for brucellosis and dye and complement-fixation tests for toxoplasmosis were negative. X-ray examination of the skull, chest, hands, and feet (Dr. Davies and Dr. Thomson) revealed nothing abnormal. Urine: very faint trace of albumin; no sugar; centrifuged deposit contained a few leucocytes and red blood cells, but no casts.

Atropine drops were instilled into the eyes three times a day. In the next two days vision had deteriorated because of increased opacity of the media and raised ocular tension, but it subsequently began to improve. Although the cause of his meningeal reaction was uncertain he was given a course of penicillin (10 million units). Two weeks after admission he had complete and bilateral loss of cochlear and vestibular functions. Vision was R. 6/18 and L. 6/24. Progress was slow, and, since it was thought that the cause of his disease might be viral, a course of aureomycin (13.5 g.) was given. Mr. Keith Lyle saw the patient a month after admission and observed numerous posterior synechiae, pigment on the anterior lens capsule, turbid anterior chambers, keratic precipitates, and corneal oedema. Hyoscine $\frac{1}{2}$ % eyedrops were used, afterwards changed to lachesine 1%. Two days later, and about six weeks after admission, he was discharged home. Visual acuity was 6/24 in each eye, but he was deaf in both ears.

One month later his visual acuity was R. 4/60 and L. 6/24. He was admitted to King's College Hospital, under the care of Mr. Keith Lyle, on June 16, 1952. He had a severe bilateral iridocyclitis with raised tension in both eyes, and visual acuity was 6/24 in both eyes. He remained bilaterally deaf. No alopecia, poliosis, or vitiligo was observed on admission, but a few scattered hairs over the temples and some eyelashes turned white later. Diagnostic lumbar and anterior chamber punctures were made and the fluids examined at the Institute of Ophthalmology. No virus was detected. He was treated with cortisone drops and subconjunctival injections and atropine. Visual acuity fluctuated and a paracentesis of the right anterior chamber

had to be performed on July 30 to relieve ocular tension. This rose again some months later and he was readmitted for a right paracentesis on February 13, 1953; but raised ocular tension persisted, and required a right broad iridectomy *ab externo* for its relief in March. In May Mr. Keith Lyle performed a similar operation on the left eye for a similar persistently raised tension. The post-operative course was uneventful. Visual acuity was R. 6/18 and L. 6/9 unaided. At the time of writing both eyes were white and free from congestion. There has been no further return of cochlear or vestibular functions, and no alopecia or vitiligo has developed.

Discussion

Investigations of the above case excluded syphilis, tuberculosis, sarcoidosis, brucellosis, and toxoplasmosis as the cause of the symptoms and signs, and, although neither vitiligo nor alopecia was observed, this does not preclude the diagnosis of the Vogt-Koyanagi syndrome. In analysing 47 recorded cases Rosen (1945) found greying of the hair (poliosis) in 90%, alopecia in 73%, vitiligo in 63%, and deafness in 54%. The aetiology of the condition remains unknown, although the association of ocular disease with pigmentary changes and disturbance of hearing has long been recognized. Both Nettleship (1884) and Hutchinson (1892-3) described cases of spontaneous iridocyclitis associated with poliosis, but Vogt's (1906) case also presented alopecia, and it was Koyanagi's (1929) review which led to the recognition of the syndrome under discussion.

A similar disorder, known as Harada's disease, has been recognized since Salus (1932) referred to Harada's original description of a low-grade uveitis with bilateral detachment of the retina, and to the observations of other Japanese workers that such a syndrome may be associated with deafness, alopecia, and poliosis. Givner (1943) and others have since recorded similar cases, in some of which vitiligo has also been noticed. The similarity between the Vogt-Koyanagi syndrome and sympathetic ophthalmia has been commented upon by Parker (1931), Carrasquillo (1942), and Hague (1944), and the latter condition has been recorded with whitening of the eyelashes (Schenkl, 1873) and deafness (Snellen, 1881). In addition to the clinical similarities mentioned above, a meningeal reaction has been recorded in the Vogt-Koyanagi syndrome (Hague, 1944; Jaffé, 1950), Harada's disease (Walsh, 1947; Cowper, 1951), and sympathetic ophthalmia (Corcelle, 1947).

The precise aetiology of these disorders is uncertain at present, although there is sufficient likeness in their clinical appearances to suggest they have a similar cause. Allergy and infection have been suggested as the causes of sympathetic ophthalmia, although the factor of trauma is also present here. Woods (1936) considered allergy to be the predisposing factor in this disease, and Duke-Elder (1940) stated that the cause is almost certainly infective (probably an unknown virus inhabiting the conjunctival sac), allergic sensitization to uveal pigment being responsible for the condition in the non-injured eye. In his review of the aetiology of the Vogt-Koyanagi syndrome Jaffé (1950) refers to the concepts of allergy, virus infection, and endocrine disturbance, but the evidence for endocrine dysfunction in such cases suggests that it is fortuitous rather than causative, and sensitivity to uveal pigment in patients suffering from the Vogt-Koyanagi syndrome has been variable (Rones, 1932; Carrasquillo, 1942). Hague (1944) attempted to correlate a virus aetiology with an endocrine disturbance by postulating that the clinical picture could be produced by a discrete infective lesion in the hypothalamus, but this somewhat ingenious suggestion does not bear critical examination, and Cowper (1951) believes that there is a widespread involvement of the nervous system in the Vogt-Koyanagi syndrome, and that this condition and Harada's disease represent different aspects of a basic uveoencephalitis.

The experimental work carried out on these non-traumatic syndromes suggests there may be an infective

cause (Malbran and Muhlmann, 1936; Rados, 1940), and Friedenwald and McKee (1938) reported a case of endophthalmitis with a meningeal reaction, which they believed was almost certainly due to a virus, although they thought absolute proof was lacking because the virus isolated may have been native to the animals used in investigation.

Although there may be objections to the conclusions to be drawn from animal experiments in these two disorders of non-traumatic uveitis, there is more evidence in favour of a virus aetiology than anything else. The evidence at present available suggests that in these conditions and in sympathetic ophthalmia the most important factor is a virus infection, that allergy plays a part in the pigmentary disturbances, and that the various ocular manifestations depend upon the site of reaction in the uveal tract. Further progress can be made only by full and careful investigation in the early stages of the disease. The present case was not recognized as a case of the Vogt-Koyanagi syndrome before antibiotics were administered, and the negative viral investigations cannot therefore be taken as evidence against this mode of infection.

Treatment has, as yet, been of little avail in arresting the underlying disease process. There is a natural tendency towards spontaneous and good recovery of sight in Harada's disease, but in a group of 47 patients suffering from the Vogt-Koyanagi syndrome Rosen (1945) found that 30 had vision of 3/200 or less in each eye and only 7 had vision better than 20/50 in only one eye. Although deafness tends to disappear in most cases, in the one reported by Carrasquillo (1942) the auditory symptoms persisted, and this has been so in the case reported here. The syndrome therefore has a considerable morbidity. The present case is reported in order to stimulate interest in the condition and to encourage fuller use of future clinical material immediately it arises, particularly as the patients may be referred to an ophthalmologist, an otologist, a neurologist, or a general physician.

Summary

A case of the Vogt-Koyanagi syndrome is described. The points of similarity between this disorder and sympathetic ophthalmia and Harada's disease are given. As the aetiology of the condition remains unknown the importance of early investigation of future cases is emphasized.

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