Vogt-Koyanagi-Harada syndrome, a rare association of Hodgkin's disease

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Summary: Vogt-Koyanagi-Harada syndrome (VKHS) is a well-documented clinical entity. We report the case of a 24 year old man who, within 5 months of the diagnosis of VKHS, developed Hodgkin's disease. Like VKHS, the aetiology of Hodgkin's disease is unknown. A viral factor has been suspected in the pathogenesis of both conditions. Similar immunological abnormalities have been described in both, and may be important predisposing factors.

Introduction

Vogt-Koyanagi-Harada syndrome (VKHS) is a well-documented clinical entity, mainly in Japanese literature. It was described by Vogt in 1906,¹ Harada in 1926² and Koyanagi in 1914³ and 1929.⁴ Initially the Vogt-Koyanagi syndrome was considered as a separate entity from Harada's disease. The former consists of bilateral non-traumatic anterior uveitis, poliosis, vitiligo, alopecia and deafness. The latter is characterized by bilateral non-traumatic posterior uveitis and retinal detachment. In 1951, Cowper⁵ embraced the two diseases as a single clinical entity. The American Uveitis Society⁶ established the following diagnostic criteria: (1) no previous eye trauma; (2) posterior uveitis; (3) one or more of the following: bilateral iridocyclitis, papillitis, meningoencephalitis, pleocytosis of the cerebrospinal fluid, deafness, alopecia, poliosis and vitiligo.

Cipriani *et al.*⁷ reported a case of VKHS occurring in a patient who was treated for Hodgkin's disease 10 years previously. We report, here, a patient who, within 5 months of the diagnosis of VKHS, developed Hodgkin's disease, despite appropriate treatment of the former.

Case report

A 24 year old man was admitted with an 8-day history of headache, nausea and vomiting, and a 2-day history of deafness, dizziness and oscillopsia. On examination, he had bilateral acute red eyes

with circum-corneal injection. He had bilateral fatiguable horizontal nystagmus. Fundoscopy revealed bilateral papilloedema with clouding of the media. Bilateral sensorineural deafness was present. Computerized tomography of his head was normal. Audiograms revealed profound hearing loss of 70 decibels bilaterally.

Five days after admission his visual acuity had deteriorated alarmingly to 6/60 bilaterally. His brother noticed that his previously blue eyes had turned green. His pupils had become irregular, and detailed ophthalmic examination revealed bilateral anterior and posterior uveitis with papillitis, macular oedema and vitritis. Topical steroids and mydriatics were prescribed.

Lumbar puncture revealed no excess of white cells. Chest X-ray was normal. Toxoplasma and viral serology was negative, including herpes simplex, cytomegalovirus and human immunodeficiency virus. The diagnosis of Vogt-Koyanagi-Harada syndrome was made and treatment started with intravenous hydrocortisone four times daily, changing after a few days to prednisolone orally 100 mg/day. His condition improved rapidly and the dose of prednisolone was gradually reduced.

Two months after presentation, his visual acuity had improved to 6/5 bilaterally. Four months after diagnosis, while on prednisolone 7.5 mg/day, he presented with left supra-clavicular lymphadenopathy which was biopsied. The histological appearances were those of nodular sclerosing Hodgkin's disease (high grade, lymphocyte depleted subgroup). Chest radiographs showed a large left parahilar mass, with bilateral para-tracheal lymphadenopathy. Computerized tomography of his abdomen was normal. His disease was staged at 2A. In view of the unfavourable histology and the bulky disease he was treated with chemotherapy.

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Discussion

Vogt-Koyanagi-Harada syndrome (VKHS) is a clinical diagnosis.⁶ Cerebrospinal fluid pleocytosis strengthens the diagnosis but is not an absolute necessity. Our patient fulfilled the criteria laid down by the American Uveitis Society.

The aetiology of VKHS is unknown. It has been suspected to be a viral-induced⁸ autoimmune disease.⁹⁻¹¹ The disorder affects tissues having a common embryological origin; the uvea, leptomeninges, the melanoblasts, ocular pigments and auditory labyrinth pigments all originate from the neural crest. Autoantibodies to melanin^{12,13} and myelin¹⁴ have been described, accounting for the cutaneous and neurological manifestations respectively. Based on a surface marker, peripheral blood lymphocytes, which sometimes exhibit a suppressor function, were reduced in number in VKHS.¹⁵ VKHS has also been reported in association with ulcerative colitis,¹⁶ and with hypothyroidism and diabetes mellitus.¹⁷

Epstein-Barr virus^{18,19} and vaccination²⁰ have been implicated in the pathogenesis of some cases of Hodgkin's disease. An imbalance between helper and suppressor immune activity (the latter being weak) has also been proposed as a predisposing factor in the development of Hodgkin's

disease.²¹ Hence there are immunological similarities between VKHS and Hodgkin's disease.

Hodgkin's disease has been shown to be the initiating cause of autoantibody production in immune thrombocytopenia,²²⁻²⁵ haemolytic anaemia²⁶ and autoimmune neutropenia.^{27,28} Insulin-receptor antibody has also been reported in Hodgkin's disease.^{29,30} It is, therefore, possible that Hodgkin's disease could induce the production of autoantibodies to melanin and myelin too.

It is very unlikely that our patient had central nervous system invasion by Hodgkin's disease rather than VKHS. Central nervous system invasion is a very uncommon complication of Hodgkin's disease and is usually found only late in the illness. In a series of more than 2,000 patients,³¹ only 12 had central nervous system invasion and, indeed, only 34 cases have been reported in the last 60 years.^{32,33} Our patient developed VKHS more than 4 months before the diagnosis of Hodgkin's disease.

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