Kveim Test Reactivity in Melkersson-Rosenthal Syndrome (Cheilitis Granulomatosa)

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The relation between the Melkersson-Rosenthal syndrome (MRS) and sarcoidosis is unclear. The Kveim test, a test for sarcoidosis, was performed in seven patients, two with complete and five with abortive forms of Melkersson-Rosenthal syndrome. All were found to be negative. Serum levels of angiotensin converting enzyme and calcium were normal. These facts make it unlikely that MRS is a type of sarcoidosis. (Received January 19, 1985.)

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The classical triad consisting of intermittent or permanent facial nerve paralysis, lingua plicata and recurrent facial oedema is known as the Melkersson-Rosenthal syndrome (MRS). Initially Miescher's cheilitis granulomatosa was considered as a separate entity, but today, most authors consider the disease as a monosymptomatic form of the syndrome (1).

The etiology of MRS has remained an open question and there are many etiological hypotheses. Some authors (2–4) contend that MRS, respectively cheilitis granulomatosa, is a peculiar variant of sarcoidosis. Their opinion is based on the histological appearance of the granulomas often found in the oedematous tissue of lips and/or face.

In order to investigate if MRS is related to sarcoidosis we have tested seven patients with complete or abortive forms of MRS with the Kveim test. Also angiotensin-converting enzyme in serum (SACE) and serum calcium were measured.

MATERIAL AND METHODS

Subjects

The study included seven patients, five males and two women in the age range 41–73 years and with a 6–58 years duration of disease. Two had the complete MRS, two had macrocheilitis and lingua plicata and three had macrocheilitis only. Five of the patients had been treated surgically for persistent macrocheilitis. Two of the patients were relatives. In five of the patients the histopathological examination of the resectate from the lips showed oedema and mononuclear inflammatory cells, but epithelioid cells were only found in two of them. In one patient, not operated, a biopsy showed lymphocytes and oedema and one patient was not examined histologically.

The Kveim test

The Kveim suspension was prepared from a sarcoid spleen as earlier described (5) and 0.2 ml was injected intracutaneously in the thigh. The test was read macroscopically after 6 weeks and at the same time a punch biopsy was taken for histological examination. Only focal epithelioid-cell collections were regarded as positive (6).

Blood analyses

SACE levels were measured in all seven patients by the spectrophotometric method of Lieberman. Normal values (mean ± 2 SD = 8–32 U/ml) for SACE were determined in 102 healthy controls (25–50 years old, 40 women and 62 men). Also serum calcium was analyzed (normal range 2.20–2.60 mmol/l).

RESULTS

In all seven investigated patients, Kveim tests were negative, SACE and serum calcium were within normal range.

DISCUSSION

The etiology of MRS remains speculative. The hypothesis of a disturbance of the autonomous nervous system has been put forward by Hornstein (1). In the literature also the following etiological candidates are found: Allergies of various types, infections and sarcoidosis.

The histological picture of oedematous tissues can be divided into two types, the sarcoid type and the lymphoedematous type (7). The finding of epithelioid cell granulomas has led a group of authors to believe that MRS is a variant of sarcoidosis (2–5). On the other hand Mazurkiewicz (8) comparing the nosological criteria of sarcoidosis and MRS was unable to reveal a common pathogenic denominator of both diseases. Pontén & Thyresson (9) also found that the granulomas of MRS differed from those of tuberculosis, sarcoidosis and lupoid rosacea, by their strong tendency to a perivascular arrangement, particularly around lymph channels.

However, the histological picture with granuloma formation is a relatively common immunologic expression. The diagnosis sarcoidosis is often accepted if certain clinical, radiological and functional criteria are fulfilled. Sarcoidosis is a multisystem granulomatous disorder of unknown etiology. Strictly scientifically the diagnosis should be supported by histological evidence of widespread non-caseating epithelioid-cell granulomas in more than one organ or a positive Kveim skin-test. The specificity and sensitivity of the Kveim reactions is still controversial. There are a few clinical trials where up to a quarter of the controls have achieved a positive test but most investigators report less than 4% positive tests in controls (10). The sensitivity seems at least partly to depend on disease duration and stage, e.g. if the only radiological change is bilateral hilar gland enlargement as is common at early stages, 92% of the tests may become positive. If, however, there are only parenchymal changes of the lungs and signs of shrinkage, about 37% of the tests will turn out positive (5). Our seven patients had long-lasting diseases which might have reduced the probability of getting positive Kveim tests if MRS is a variant of sarcoidosis.

Several investigators have noticed elevated SACE in sarcoidosis but there have also been reports on raised levels in other diseases with granuloma formation (11). In 10–15% of patients with sarcoidosis an elevation of calcium in serum can be seen (12). In the present study normal levels of SACE and calcium in serum were found. Thus our findings failed to support the hypothesis that there is a connection between the sarcoidosis and MRS.

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