
Historical View

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The other physician behind the use of colchicine for the treatment of familial Mediterranean fever

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One of, if not the most, quoted papers in FMF is the seminal article by Sohar, Gafni, Pras and Heller in the American Journal of Medicine in 1967 (1). This paper, based on the authors' meticulous clinical observations on nearly 500 patients with familial Mediterranean fever (FMF) has, over the last four decades, been a most valuable source of reference for both clinicians and scientists. In the Sohar article one finds not only very useful information on the myriad of clinical presentations of FMF but also gets introduced to some notable and far-reaching views on the pathogenesis and genetics, including the recently revisited concept of autosomal dominant transmission. However, there is one, from the standpoint of the medical historian, rather interesting note in this article. In the section devoted to the treatment the authors first quote a long list of remedies reported to be not useful and then continue with their own experience with both IV and oral colchicine and say that this drug is of no help in FMF, either.

In 1972 Dr. Goldfinger of the Massachusetts Hospital in Boston publishes perhaps one the most famous letters to the editor ever in the New England Journal of Medicine (2). His letter "Colchicine for Familial Mediterranean Fever" describes five patients with FMF all prescribed colchicine and all of whom make a remarkable recovery from their illness once this age-old medicine is prescribed. Everybody even remotely familiar with medicine and most importantly the FMF patients and their families now know that this time honoured gout-drug is the remedy for FMF. It not only stops the very debilitating attacks of serositis but also prevents the emergence of amyloidosis, the most dreaded complication. This latter effect seems also to be true even



Fig. 1. Prof. Emir Özkan.

in the small percentage of patients among whom the attack preventing effect of colchicine is not that pronounced. There is little doubt that we and our patients owe a lot to Dr. Goldfinger.

However, what is not widely known about this wonderful colchicine-FMF story is the contribution of another physician from a part of the globe as far from Boston as the Eastern end of the Mediterranean sea from the western end of the Atlantic Ocean. Dr. Emir Özkan (Fig 1), a professor of Medicine in the Department of Cardiology in the Medical Faculty of University of Istanbul is from Sivas, a town in Mid Eastern Anatolia not only the heartland of Turkey but also epidemiologically the heartland of FMF (3). As a physician of Anatolian background he feels responsible not only to patients with cardiological problems, his main line of work, but he cannot turn down also the substantial number of patients from his homeland that come with other complaints to seek the help of their native who has made the megapolis. Among these patients, as expected, there is a substantial number with FMF and Dr.

Özkan, along with several of his colleagues apparently prescribe colchicine and salicylamide to these patients with remarkable good outcome. They go on to publish their findings on the treatment of FMF in an article entitled "A New Approach to the Treatment of Periodic Fever" in the December 1972 issue of the Medical Bulletin of Istanbul Medical Faculty (Fig. 2) (4). From the note on the first page we understand that the authors submitted this article on April 17, 1972, some 8 months before the appearance of the Goldfinger article in the *New England Journal of Medicine* which appears in the same month (December 21st issue) of the said journal.

In short Özkan and colleagues report their very favorable experience with the combination of colchicine (0.025 mg/kg/day) and salicylamide (20 mg/kg/day) in 14 patients with FMF. Of interest is the fact that one of their patients with renal amyloidosis and nephrotic syndrome had a complete disappear-

ance of proteinuria after 6 months of treatment.

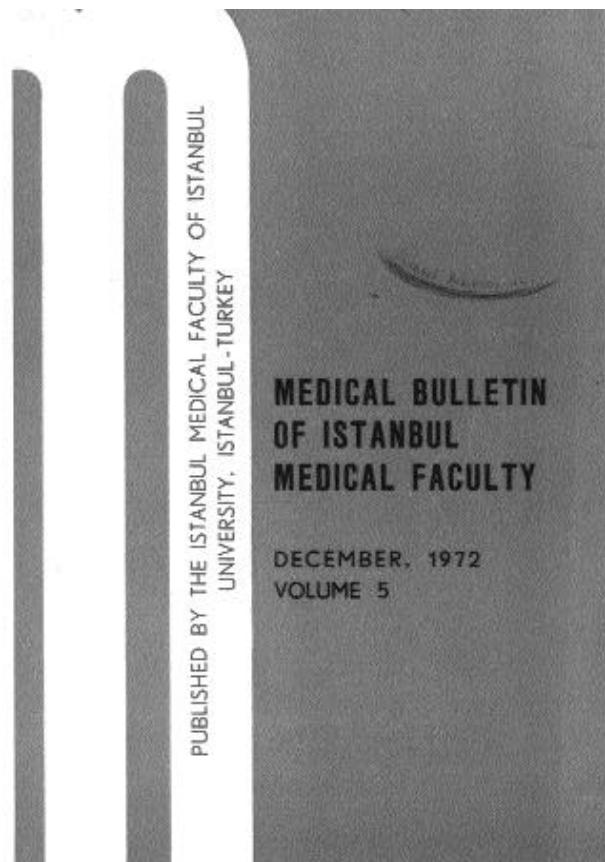
During the Second International Congress on Familial Mediterranean Fever in Antalya in May 2000, the organizers felt that a tribute must also be paid to Dr. Emir Özkan. In fact during the closing ceremonies an award called the "Goldfinger-Özkan award" was given to that person who contributed most significantly to the "clinical science and management" of FMF.* The first Goldfinger-Özkan award went to Dr. Mehmet Tunca for his work in the acute phase response and interferon treatment of FMF. Prof. Özkan died in a sea accident in 1987. His wife had already passed away and they had no children. We all feel that the Goldfinger-Özkan award has been and will continue to be a humble tribute to this very fine and innovative physician-teacher.

**In fact during the closing ceremonies two separate awards were given to the distinguished and dedicated students of*

FMF. Another award, named after H. Heller, was given to that person that had contributed most to the "basic science" of FMF, was received by Dr. Isabelle Touitou for her original and continuing contribution to the discovery of the genetics of FMF. Dr. Daniel Kastner had been the recipient of the first "Heller award" given during the First International Congress on Familial Mediterranean Fever, held in Jerusalem in 1997.

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A NEW APPROACH TO THE TREATMENT OF PERIODIC FEVER

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Periodic fever is a disease frequently observed in Turkey on which numerous reports have been published (1, 2, 3, 4, 5, 6, 7, 8, 9).

As it is well known, the various types of treatment applied in this disease have been far from being successful (10, 11, 12, 13, 14, 15). Recently, we have tried a combination of colchicine and salicylamide in 14 cases of proven periodic fever and have followed up the patients for periods of time varying between 10 to 28 months. As we have observed noteworthy changes both in the clinical and laboratory findings of the patients we find it worthwhile to report the preliminary results of this trial.

MATERIAL and METHODS

Cases: Our series consisted of 23 males and 1 female patient diagnosed to suffer from periodic fever according to the classical criteria accepted for the disease. The age of onset of the disease, as obtained from the history given by the patients, varied from 1 to 28 years (mean 11 years). The period of the time which had elapsed from the onset of the disease to the time of the initial examination was between 2 to 49 years (mean 15 years). All patients were referred to our clinic with the presenting symptoms of chest pain, abdominal pain, joint pain, fever, headache, nausea and vomiting, diarrhea, constipation, low back pain or a combination of these (Table 2). Some of the patients had received unsuccessful interventions.

The age and sex of the patients are shown in table 1. The laboratory and clinical findings of the patients during an acute attack are summarized in table 2. In one patient (case 10) the blood sedimentation rate remained increased following an acute episode and in another case (case 11), a nephrotic syndrome developed. This patient was previously reported as "amyloidosis due to periodic fever" by Özer et al (6).

* Received for publication April 17, 1972.

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Fig. 2. The paper by Prof. Emir Özkan reporting on the successful treatment of FMF with colchicine published in the December 1972 issue of the *Medical Bulletin of Istanbul Medical Faculty* (reproduced with permission from *Medical Bulletin of Istanbul Medical Faculty*).