Biyomedikal Dergilere Gönderilen Makalelerin Uyması Gereken Standartlar • Amerikan Dermatoloji Akademisi Burs Duyurusu ve formu • International Investigative Dermatology 98 • 15-17 Mayıs Graz'da yapılan Dermatopatoloji Toplantısı • "The Renaissance of Dermatology" Uluslararası Toplantısı • Tıpta Görsel Estetik ve Dermatoloji • Dermatopatoloji Derneği 1994-1997 Dönemi Faaliyet Raporu

Dermatopatoloji Bülteni

Turkish Journal of Dermatopathology is an electronic journal
http://www.ato.org.tr/konuk/tdp/

Cilt/Volume 7
Sayı/Number 1-2
Yıl/Year 1998

TURK J DERMATOPATHOL 1998; 7: 48-51

Sarcoidosis: searching a proof for an old hypothesis

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ÖZET

Sarkoidoz: Eski bir varsayıma yeni kanıtlar ararken

Sarkoidoz, non-kazeifiye epitelioid hücre granulomlarının oluşumu ile karakterize etyolojisi belirlenememiş bir sayrılıkdır. Sayrılığın etyolojisinde mycobacterium türlerininde rol oynayabileceği üzerinde durulmaktadır. Klinik ve histopatolojik özellikleriyle sarkoidoz tanısı alan nazolabial sulkuslarda eritemli zeminde yerleşmiş küçük papulaların gözlendiği 19 yaşında bir kadın olgu sunulmaktadır. Olgunun biyopsi materyalinden yapılan polimeraz zincir reaksiyonu tekniği ile lezyonlarda mycobacterium tuberculosis DNA'sı saptanmıştır.

Anahtar Sözcükler: Sarkoidoz, Polimeraz zincir reaksiyonu, Mycobacterium tuberculosis

SUMMARY

Sarcoidosis is a multisystemic disease of unknown etiology, which is characterized by the formation of non-caseating epithelioid cell granuloma. Because of the similarities in clinical and histopathological features between sarcoidosis and tuberculosis, it has been thought that mycobacterium species might be an etiologic agent. We report a 19-year-old woman, presenting small papules over erythematous skin on nasolabial folds diagnosed as sarcoidosis clinically and histopathologically. Mycobacterium tuberculosis DNA was detected in the lesion by polymerase chain reaction technique.

Key words: Sarcoidosis, PCR, Mycobacterium tuberculosis

Sarcoidosis is a multisystemic disease of unknown etiology, which is characterized by the formation of non-caseating epithelioid cell granuloma. The predilection sites are lungs, lymph nodes, skin and eyes. The onset is often between the ages of 30 and 50 years (1,2).

HUTCHINSON described the skin lesions of the disease in 1877.1 In 1899, BOECK reported the first unequivocal case of sarcoidosis and called the lesions "multiple benign sarcoid of the skin" (1,2) because of the clinical similarity to lupus vulgaris (1). In 1914, SCHAUMANN recognized the multisystemic course of the disease and called it "lymphogranulomatosis benigna" (1,2).

The etiology of sarcoidosis is still unclear. Because of the similarities in clinical and histopathologic features between sarcoidosis and tuberculosis, it has been hypothesized that mycobacterium species might be involved as an etiologic agent. In recent years there were some reports about detection of mycobacterial DNA in sarcoidal granulomas by polymerase chain reaction (PCR) (3,4). In this article we report a case of sarcoidosis that mycobacterium tuberculosis DNA was detected by PCR technique.

CASE REPORT

A 19-year-old woman presented with a complaint of small papules on erythematous skin around the nasal alaes for one year. She had been treated with topical corticosteroids, but there was not any response. Her medical history was noncontributory and there was no familial history of sarcoidosis and tuberculosis.

Dermatologic examination revealed multiple pinhead sized, red papules on erythematous skin involving nasolabial folds and nasal alaes (Fig. 1.). Yellowish-gray lupoid infiltration was detected by diascopy. The pröbe phenomenon was negative. General physical examination was normal.

Presented as a poster at the Second Regional Clinicopathological Colloquium of the International Society of Dermatopathology

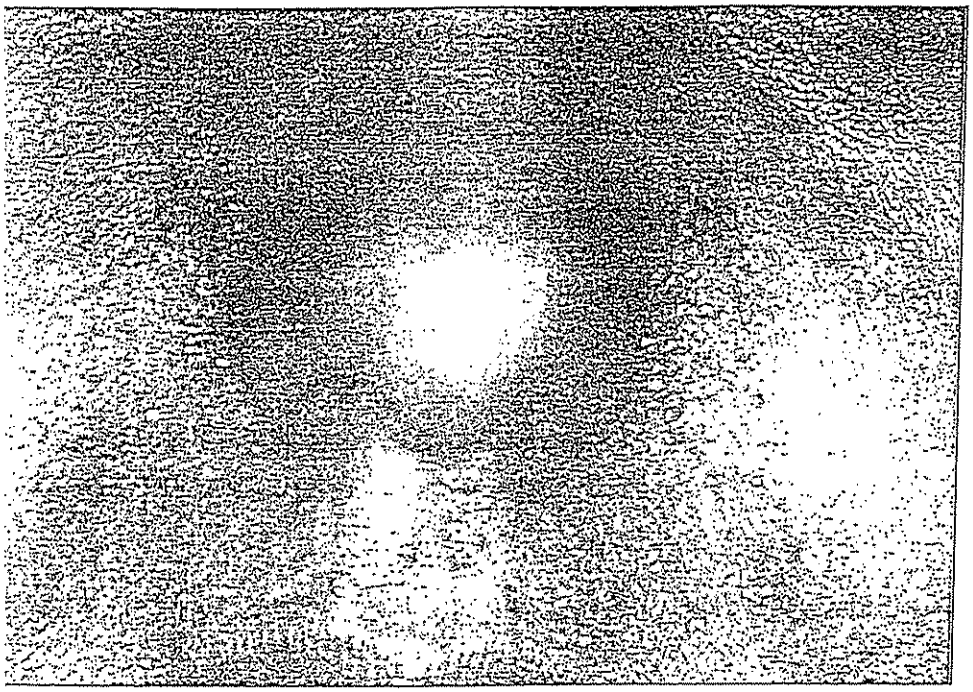

Figure 1. Multiple pinhead sized, red papules on erythematous skin involving nasolabial folds and nasal alaes.

he result of the laboratory tests including X-ray examiation of the lung, erythrocyte sedimentation rate, mplete blood cell count, liver function tests, serum lcium and phosphate levels, urinalysis and electrocarogram were normal. PPD was anergic.

skin biopsy specimen was obtained from a papule at e right nasal alae. Horny plugs and slight orthokeratos in the epidermis and granulomas containing mphocytes, histiocytes and Langhans giant cells in the rmis were seen (Fig.2). Acid-fast bacilli were not deted by Rhodamin-Auramin staining.

CR technique:

rmalin fixed paraffin embedded skin biopsy sample is used for PCR. Seven micrometer sections were cut d three sections were placed into 1.5 ml Ependorf tu-. DNA was extracted using standard phenol-chloroprm procedure (5). The primers originally designed by enach et al (6) were used for the amplification. The ay detects a 123 bp region from the M. tuberculosis mplex specific insertion sequence IS 6110. Amplifiion reaction were performed in final volume 50 μl ntaining, 1XPCR reaction buffer (50 mM Tris HCl 9.0). 20 mM (NH4)2SO2. 1%Triton X 100), 1.5 M MgCl 200 μM each dNTPs, 20 pmol each primers enosys Biotechnologies Ltd, London, UK) 1.25 U of polymerase (Appligene Inc. CA, USA) and 10 μl A sample. The DNA sample was denatured at 94°C for 5 min, and then 35 amplification cycles were performed as follows: 2 min of annealing at 68°C, 2 minutes of primer extension at 72°C and 7 minutes of final extension at 72°C were performed with an automated thermal cycler (M.J Research Inc. PTC 100, USA). Controls with purified M. tuberculosis DNA, without DNA and human leukocyte DNA were used. After amplification 10 μl of the reaction mixtures were electrophoresed on ethidium bromide containing 2% agarose gel and visualised by uv translumination (Fig. 3).

CONCLUSION

Sarcoidosis, a disease of unknown etiology could be interpreted as a chronic immunologic reaction directed against one or more persistent antigenic stimuli (7). Mycobacteria, especially M. tuberculosis, have repeatedly been considered as a causative agent of sarcoidosis because of the clinical and histopathologic similarities between sarcoidosis and certain forms of tuberculosis (4,7). Detection of mycobacteria in sarcoidosis by microscopy or by cultural isolation have been generally difficult (7) and given unsatisfactory results (8).

PCR affords a highly sensitive means of detecting DNA of various infectious organisms (4) especially mycobacteria that require long periods of time for culture (4,9). The use of PCR in M. tuberculosis infections provides a rapid diagnosis (4,10).

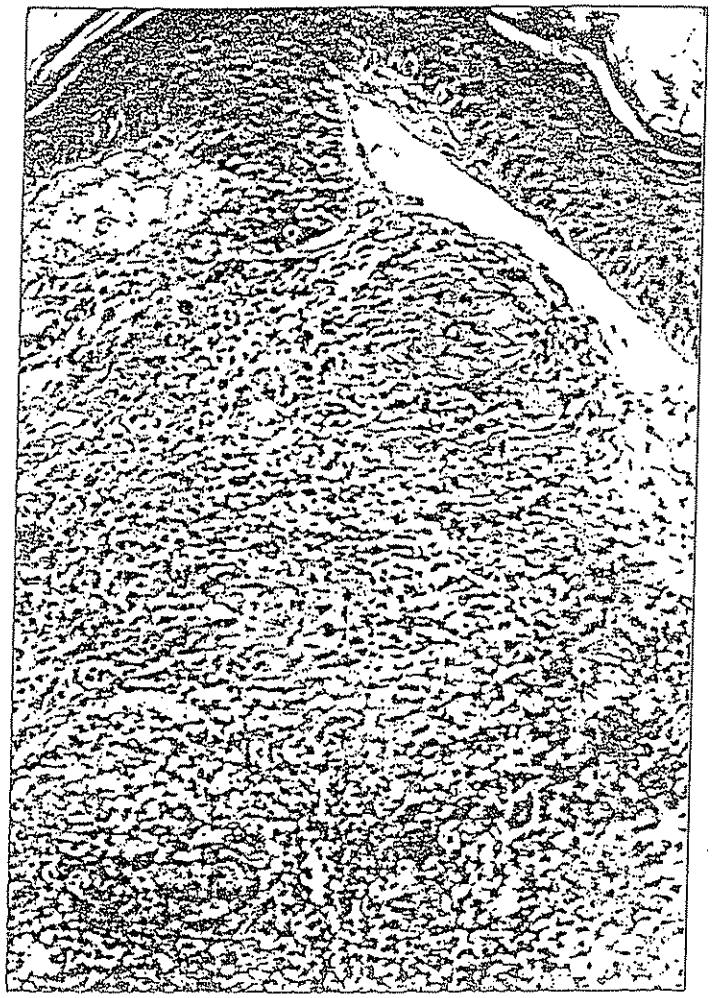

Figure 2. Non-caseating epithelioid cell granuloma in the dermis (Hematoxylin-eosin, x200)

There were many reports about M. Tuberculosis DNA amplification using PCR in sarcoidosis (3,4,7,8,11). While SABOOR et al. found M. Tuberculosis DNA in half of their 20 patients with sarcoidosis (11), RICHTER et al. reported negative results from their 23 patients with sarcoidosis and only in one patientí s lung tissue they could detect mycobacterial DNA (3). POPPER et al. found mycobacterial DNA in 2 cases from 15 cases of sarcoidosis. They offered that presence of mycobacterial DNA, at least the cell-wall-deficient forms, were responsible agents for some cases of sarcoidosis (8). GHOSSEIN et al, detected negative results with mycobacterial PCR from tissues of patients with sarcoidosis. They did agree with the view that very few, if any, mycobacterial organisms exist in granulomatous tissues from patients with sarcoidosis. They suggested that sarcoidosis was a delayed hypersensitivity reaction to degraded mycobacterial antigens rather than an active mycobacterial infection (4).

In this article we report a case of sarcoidosis that mycobacterium tuberculosis DNA was detected by PCR technique. It is controversial that M. Tuberculosis is an etiologic agent in sarcoidosis or not, yet. Mycobacterial DNA assesment by PCR-technique in large series of sarcoidosis may be helpful to understand, what is the role of mycobacteria in the etiopathogenesis of sarcoidosis.

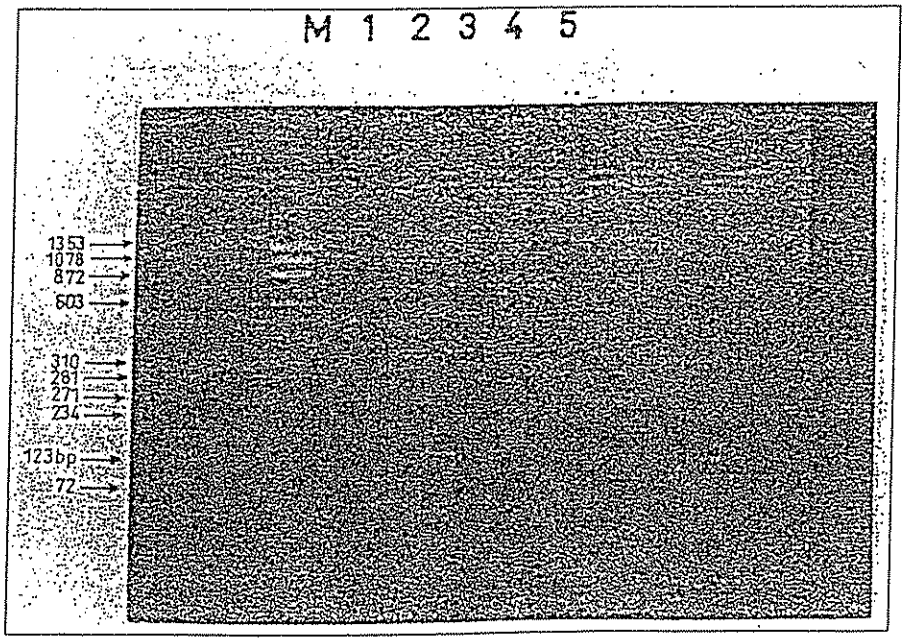

Figure 3. Amplification product (123 bp) of M. tuberculosis by PCR from formalin fixed paraffin embedded skin biopsy sample. Lane M: Hae III digested (X 174 as a molecular size marker lane 1: negative control (noDNA), lane 3: positive control (M.tuberculosis from culture), lanes 4: positive (case with sarcoidosis), lane 5: positive (case with tuberculosis meningitis)

REFERENCES

1. Braun-Falco O, Plewig G, Wolff HH, Winkelmann RK. Dermatology 3rd edition. Berlin, Springer Verlag 1991; 937-942.
2. Kerdel FA, Moschella SL. Sarcoidosis; an updated review. J Am Acad Dermatol 1984; 11: 1-19.
3. Richter E, Greinert U, Kırsten D, Rüsch-Gerdes S et al. Assesment of Mycobacterial DNA in cells and tissues of mycobacterial and sarcoid lesions. Am J Respir Crit Care Med 1996; 153: 375-380.
4. Ghossein RA, Ross DG, Salomon R, Rabson AR. A Search for Mycobacterial DNA in Sarcoidosis using the Polymerase Chain Reaction. Am J Clin Pathol 1994; 101: 733-737.
5. Greer CE, Peterson SL, Kiviat NB, Manos MM. PCR amplification from paraffin-embedded tissues. Am J Clin Pathol, 95: 117-124.
6. Eisennach KD, Cave MD, Bates JH, Crawford JT. PCR amplification of mycobacteria by amplification of mycobacterial DNA, Mol Microbiol, 1989; 3: 843-849.
7. Degitz K. Detection of Mycobacterial DNA in the skin; etiologic insights and diagnostic perspectives. Arch Dermatol 1996; 132: 71-75..
8. Popper HH, Winter E, H"fler G. DNA of Mycobacterium tuberculosis in formalin-fixed, paraffin-embedded tissue in tuberculosis and sarcoidosis detected by Polymerase Chain Reaction. Am J Clin Pathol 1994; 101: 738-741.
9. Eisennach KD, Cave MD, Bates JH, Crawford JT. Polymerase Chain Reaction amplification of a repetitive DNA sequence spesific for Mycobacterium tuberculosis. J Inf Dis 1990; 161: 977-981.
10. Perosio, PM, Frank TS. Detection and species identification of mycobbacteria in paraffin sections of lung biopsy specimens by the Polymerase Chain Reaction. Am J Clin Pathol 1993; 100: 643-647.
11. Saboor SA, Johnsonn NM, McFadden J. Detection of mycobac-