| K562 cell line | | | | | |
|---|---|---|---|---|---|
| Patient | | | Control | | |
| 25: 1 | 50: 1 | 100: 1 | 25: 1 | 50: 1 | 100: 1 |
| 37 | 41 | 44 | 8 | 17 | 35 |
| 36 | 48 | 54 | 19 | 44 | 56 |
| 29 | 30 | 52 | 0 | 12 | 14 |
| 38 | 44 | 66 | 0 | 11 | 19 |
| 24 | 30 | 57 | 14 | 24 | 34 |
| 32.8 | 38.6 | 54.6 | 8.2 | 21.6 | 31.6 |
| ±6.1 | ±8.2 | ±8 | ±8.4 | ±13.5 | ±16.4 |
| <0.01 | <0.025 | <0.025 | | | |

# Cytoplasmic Tubular Structures in the Diagnosis of Oral Discoid Lupus Erythematosus

Morten Schiødt and Lis Andersen

*Department of Oral Medicine and Oral Surgery, University of Copenhagen, Rigshospitalet, Department of Oral Pathology, Royal Dental College, Copenhagen, and Departments of Oral Pathology and Electron Microscopy, Royal Dental College, Aarhus, Denmark*

Received January 20, 1981

*Abstract.* Biopsies from oral lesions of 5 patients with discoid lupus erythematosus (DLE), 5 with lichen planus (LP), 5 with leukoplakia (LEUK) and 3 patients with uncertain diagnoses termed DLE?, LP? were examined in the electron microscope for presence of cytoplasmic tubular structures (CTS) in vascular endothelium. Five vessels were examined in each of two randomly selected sections from each biopsy, without knowledge of the clinical diagnosis. All five DLE biopsies showed presence of CTS in 4–9 out of 10 vessels, as compared with none of 10 vessels in biopsies from LP or LEUK, the difference being significant. Further, CTS occurred in 4 out of 10 vessels in one DLE?, LP? biopsy from a patient with serologic signs of systemic lupus erythematosus. As CTS seem to be absent in oral lesions of LP and LEUK, which are the most important differential diagnoses for oral DLE, the identification of CTS in vascular endothelium using electron microscopy may be an auxiliary diagnostic procedure in oral DLE.

*Key words:* Lupus erythematosus, discoid; Lichen planus; Leukoplakia; Oral manifestations; Tubular structures

Cytoplasmic tubular structures (CTS) in vascular endothelial cells is a characteristic feature of skin lesions of discoid lupus erythematosus (DLE) and systemic lupus erythematosus (SLE), but CTS may also occur in other conditions (1–3). The CTS have been reported under various terms, such as paramyxovirus-like structures (3), tubuloreticular inclusions (2) and intra-endothelial tubular aggregates (1). The origin of CTS is not known. Recently such structures have been described in oral lesions of DLE (5). The diagnostic significance of the presence of CTS in the oral mucosa is not known either.

The purpose of the present study was to examine the frequency of the presence of CTS in oral lesions of DLE, compared with the frequency of CTS in oral lesions of lichen planus (LP) and leukoplakia (LEUK), which are the most important differential diagnoses for oral DLE. Furthermore, the relation between presence of CTS and deposits of immunoglobulins at the basement membrane zone is examined.

## MATERIAL AND METHODS

The material consisted of representative 5 mm punch biopsies from oral lesions of buccal mucosa of each of the following groups of patients: 5 DLE, 5 LP, 5 LEUK, and 3 DLE?, LP? Patient data are given in Table 1. The diagnosis was based on clinical and histopathologic features. The DLE patients were diagnosed as described earlier (4). The biopsies were randomly selected from among the 10 cases presented earlier (5). The LP patients all had lichen planus of the reticular type and the LEUK patients had homogeneous leukoplakia. Both groups fulfilled the WHO criteria (7). The patients designated DLE?, LP? had oral lesions which clinically as well as histopathologically had features common to DLE and LP, but a definite diagnosis could not be made. Skin lesions were absent in these patients.

Biopsies from all patients had at the same time been submitted for direct immunofluorescence (IF) study (16). The biopsies were processed for electron microscopy as previously described (5). From each biopsy two tissue blocks (termed A and B) were chosen and from each block

Table 1. *Patient data*

| Diagnosis | *N* | Sex | Age in years, range |
|---|---|---|---|
| DLE | 5 | 4 F, 1 M | 31–40 |
| LP | 5 | 3 F, 2 M | 38–81 |
| LEUK | 5 | 4 F, 1 M | 29–74 |
| DLE?, LP? | 3 | 2 F, 1 M | 27–69 |

Table II. *Occurrence of cytoplasmic tubular structures (CTS) in vascular endothelium in oral lesions*

*P*-Values refer to differences between the group of DLE biopsies and the other groups, respectively. $^{**}P<0.01$

| | No. of biopsies examined | No. of biopsies positive for CTS |
|---|---|---|
| Discoid lupus erythematosus (DLE) | 5 | 5 |
| Lichen planus (LP) | 5 | 0** |
| Leukoplakia (LEUK) | 5 | 0** |
| DLE?, LP? | 3 | 1 |

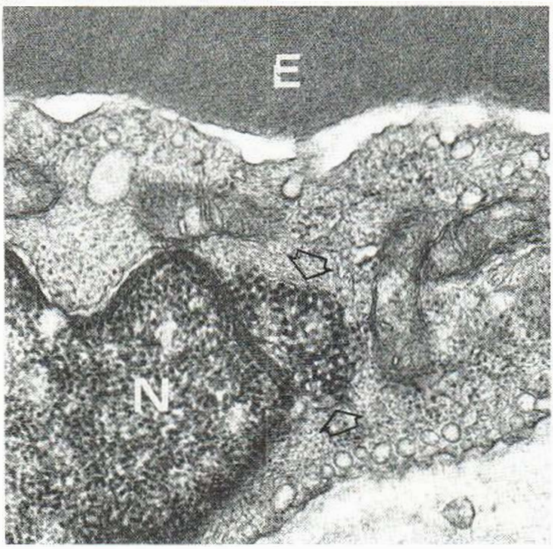


*Fig. 1.* Cytoplasmic tubular structures (*arrows*) in endothelial cell of oral lesion of DLE. Nucleus (*N*). Erythrocyte in capillary lumen (*E*). ×27 500.

one section was chosen at random. All sections were numbered randomly from 1–36 and evaluated in this sequence without knowledge of the clinical diagnosis corresponding to each section. The sections were screened systematically at 3000 × magnification for transverse or oblique sectioned capillary vessels not exceeding 30 μm in diameter. Five consecutive vessels were examined at 16 700 × magnification (44 000× with oculars) for presence of CTS in endothelial cells. The number of endothelial cell cross sections was recorded and each vessel was photographed. The time needed for screening each biopsy section was recorded. The prevalence of CTS-positive biopsies of DLE were compared with the other groups of patients by using Fisher's exact test. *P*-values (two-tail) below 0.05 were regarded as significant.

## RESULTS

The CTS were observed in the endothelial cells as aggregates of tubular structures with a diameter of approximately 20 nm (Fig. 1). They often occurred within membrane-limited cisternae connected to profiles of the rough endoplasmic reticulum or the perinuclear space.

All DLE biopsies showed presence of CTS in endothelial cells. Further, one biopsy of DLE?, LP? showed CTS, whereas CTS could not be demonstrated in biopsies of LP or LEUK, as seen in Table II. The distribution of CTS-positive vessels in the two sections from each biopsy of DLE is seen in Table III. The frequency of CTS-positive vessels showed a minor intralesional variation (variation between section A and B). The frequency of CTS-positive cell sections in each biopsy of DLE ranged from 12 % to 37 % (mean 27 %).

The time needed for sceening each biopsy (two sections) was 79 min on average for DLE and 65 min for the other groups.

Direct IF staining of the DLE lesions revealed

Table III. *Distribution of cytoplasmic tubular structures (CTS) in five biopsies of oral lesions of DLE and one biopsy of DLE? LP?*

Case no. in parentheses refers to case no. in previous study (5)

| Diagnosis And case no. | No. of vessels positive for CTS: Section A $n=5$ | Section B $n=5$ | Total $n=10$ | No. of CTS-positive cell sections/no. of examined cell sections | |
|---|---|---|---|---|---|
| DLE 1 (4) | 4 | 3 | 7 | 13/49 | (27 %) |
| DLE 2 (5) | 5 | 3 | 8 | 18/60 | (30 %) |
| DLE 3 (6) | 5 | 4 | 9 | 17/46 | (37 %) |
| DLE 4 (7) | 5 | 4 | 9 | 18/59 | (31 %) |
| DLE 5 (10) | 2 | 2 | 4 | 6/49 | (12 %) |
| DLE?, LP? | 2 | 2 | 4 | 7/40 | (18 %) |

deposits of immunoglobulins in 3 out of the 5 DLE (cases 1, 2 and 5), whereas all biopsies from the other groups showed no deposits. These results have been included in another study (6).

## DISCUSSION

The present study has shown that presence of CTS in vascular endothelium is a consistent finding in oral lesions of DLE, using a standardized examination procedure. CTS occur significantly more frequently in oral lesions of DLE than in LP or LEUK. The occurrence of CTS in DLE was not related to age of oral lesions or previous topical or general treatment, as discussed earlier (5). In DLE of the skin, CTS occurs more frequently in active lesions than in inactive ones (3). The present DLE lesions were all clinically active, i.e. showing central erythema with white spots and a border zone of irradiating white striae. It remains for further studies to show if the frequency of CTS in oral discoid lesions is related to clinical activity. The time required, 65 min on average for the non-DLE biopsies compared with 79 min for the DLE biopsies, can be attributed to difficulties in identifying the capillaries in the DLE due to the intense inflammatory infiltrate. The time needed for screening each capillary was fairly uniform in the various biopsies.

The diagnosis of oral lesions of DLE is usually based on clinical and histopathologic examination. In clinically and histologically atypical cases, direct IF staining for demonstration of deposits of immunoglobulins is often of value (6). However, the 3 DLE?, LP? were negative on IF-staining. The one DLE?, LP? patient showing CTS had increased DNA-antibody in serum and positive antinuclear factor indicating that this patient may possibly develop SLE later on. The two DLE biopsies in this study, which were negative on IF-staining (cases 3 and 4) both showed CTS.

To conclude, CTS occur in endothelial cells of active lesions of oral DLE, a CTS-positive biopsy can be identified by using a reasonable time and CTS seem to be absent from oral lesions of LP and LEUK, which are the most important differential diagnoses for oral DLE. Although clinical, histopathological and direct IF examination are the primary diagnostic procedures, the demonstration of CTS by using electron microscopy may be a helpful auxiliary diagnostic procedure in oral lesions of DLE.

## ACKNOWLEDGEMENTS

The technical assistance of Miss G. Bomholt is gratefully acknowledged. This investigation was supported by grant no. 512-5151 from the Danish Medical Research Council.

## REFERENCES

1. Eady, R. A. J. & Odland, G. F.: Intracndothelial tubular aggregates in experimental wounds. Br J Dermatol *93:* 165, 1975.
2. Grimley, P. M. & Schaff, Z.: Significance of tubuloreticular inclusions in the pathobiology of human diseases. Pathobiol Annu 6: 221, 1976.
3. Hashimoto, K. & Thompson, D. F.: Discoid lupus erythematosus. Electron microscopic studies of paramyxovirus-like structures. Arch Dermatol *101:* 565, 1970.
4. Schiødt, M., Halberg, P. & Hentzer, B.: A clinical study of 32 patients with oral discoid lupus erythematosus. Int J Oral Surg *7:* 85, 1978.
5. Schiødt, M. & Andersen, L.: Ultrastructural features of oral discoid lupus erythematosus. Acta Dermatovener (Stockholm) *60:* 99, 1980.
6. Schiødt, M., Holmstrup, P., Dabelsteen, E. & Ullman, S.: Deposits of immunoglobulins, complement and fibrinogen in oral lupus erythematosus, lichen planus and leukoplakia. Oral Surg. In press 1981.
7. W. H. O. Collaborating centre for oral precancerous lesions: Definition of leukoplakia and related lesions: An aid to studies on oral precancer. Oral Surg *46:* 518, 1978.

# Drug-induced Bullous Dermatosis with Linear IgA Deposits along the Basement Membrane

T. Ø. Gabrielsen, F. Stærfelt and P. O. Thune

*Department of Dermatology, Ullevål Hospital, Oslo, Norway*

Received February 13, 1981

*Abstract.* A 63-year-old woman presented with a drug-induced (diclophenac) bullous dermatosis. Direct immunofluorescence showed linear deposition of IgA along the basal membrane in both lesional and perilesional skin.

*Key words:* Drug-induced eruption; Linear IgA bullous dermatosis; Diclophenac