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## PRELIMINARY REPORT

## ULTRASTRUCTURE OF MAST CELLS IN THE IRIS OF CASES OF BEHÇET'S DISEASE

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Behçet (1937) first identified as a distinct entity a disease presenting the three cardinal symptoms of iridocyclitis with hypopyon, aphthous lesions in the mouth and ulceration of the genitalia, and suggested that the disease might be caused by a virus. For the past two decades cases of Behçet's disease in Japan have gradually increased and now the prevention and cure of this disease has become of great concern. However, the etiology of the disease has not yet been clarified, although a few pertinent hypotheses have been presented, namely, autoimmunity, slow virus infection, bacterial infection and post-infectious hypersensitivity. In investigations on this disease we first examined whether a virus could be considered as a causative agent and then studied the cytopathology of the disease. On electron microscopic examination of the irises of patients with Behçet's disease we observed several cytopathological changes. Among these, the morphology of mast cell granules was the most striking and this preliminary report describes their morphology.

Twelve samples of iris were obtained, 11 by iridectomy from 10 patients with Behçet's

disease and the other from an enucleated eyeball of another patient. All the samples were immersed in 2% glutaraldehyde immediately after excision. After overnight fixation they were thoroughly washed, postfixed with 1% osmium tetroxide for 1 hr, dehydrated and embedded in epoxy resin. As controls two samples of iris, one from a patient with senile cataract and the other from a patient suspected of having iritis tuberculosa, were treated in the same way. Ultrathin sections were examined with a Hitachi 11 B electron microscope.

Fig. 1 illustrates granules in the cytoplasm of a mast cell found in the iris of the patient suspected of having iritis tuberculosa. These granules were round or oval in shape with somewhat irregular outlines and ranged in diameter from 0.3 to 0.6  $\mu$ , most being 0.5 to 0.6  $\mu$ . The round granule in the center of the picture consists of lamellar structures and fine particulate material while the other granules consist of groups of lamellae, some in the form of scrolls (arrow). The scroll structures seem to be cross sections of the lamellar and cylindrical entities. Granules consisting of lamellar structures are very common in human mast

cells and are perhaps the most differentiated and mature of the granules in the latter cells (Hibbs, Burch and Phillips, 1960; Hibbs, Phillips and Burch, 1960; Iwamoto and Smelser, 1965; Horiki, 1967; Bessis, 1973).

In 7 of the 12 samples from cases of Behçet's disease mast cells could be detected and their granules were morphologically quite peculiar (Fig. 2, 3) and different from those illustrated in Fig. 1. Some granules (single short arrows in Fig. 2, 3) consist of electron dense strands, while others (single long arrow in Fig. 2) are filled with particulate materials of similar or slightly lower density and still others are demarcated by an ill-defined limiting membrane and contain loosely packed less electron dense particles (double arrow in Fig. 3). Parallel

membranous structures rather resembling the lamellar structures in Fig. 1 are seen in Fig. 3. However, typical lamellar structures were rarely seen in the samples from cases of Behçet's disease.

The peculiar morphology of mast cell granules described above was seen in all 7 samples in which mast cells were observed. In one sample morphological changes of mast cells were extremely pronounced and the cytoplasm appeared vacuolated (picture not presented here).

There are three possible explanations of the peculiar morphology of mast cell granules in Behçet's disease. First, degranulation may occur in these mast cells. Our observations resemble the ultrastructural alterations seen in

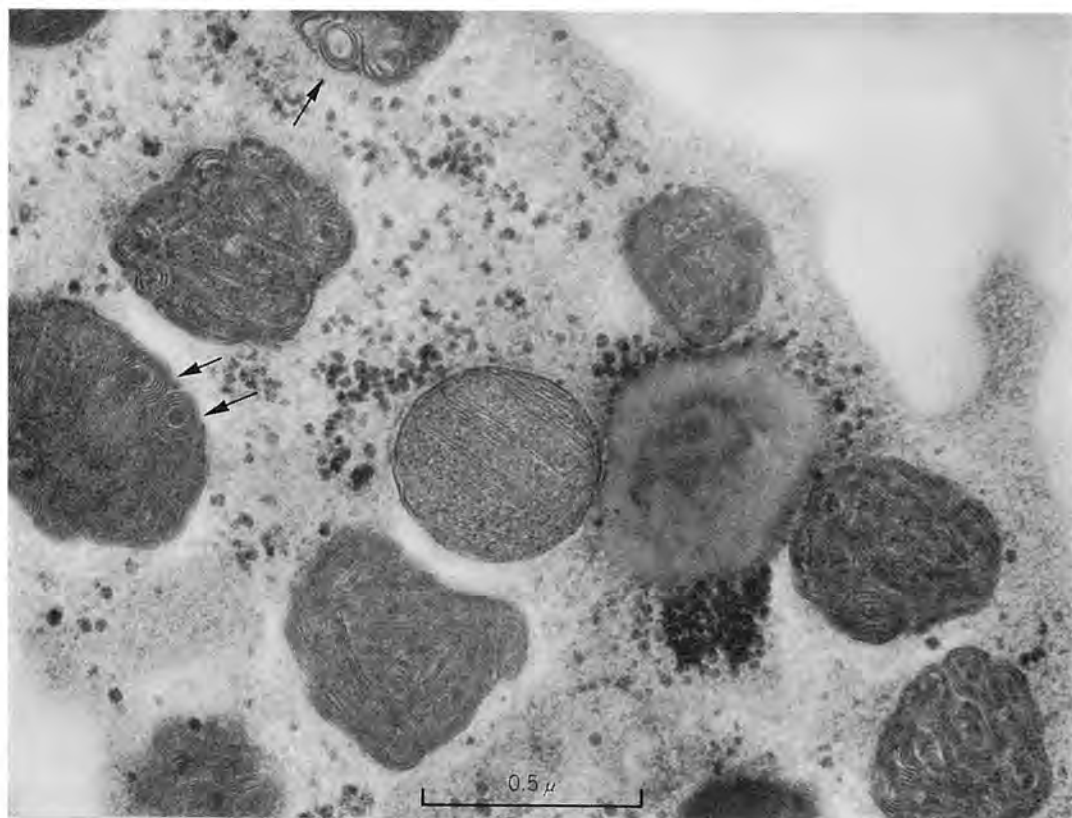


FIGURE 1. Granules in the cytoplasm of a mast cell from the iris of a patient suspected of having iritis tuberculosa. The round granule seen in the center of the picture consists of lamellar components and fine particulate material. The other granules consist of groups of lamellae, some of which are seen in the form of scrolls, as indicated by arrows.

guinea pig mast cells exhibiting this phenomenon during anaphylaxis (Taichman, 1971). As described above, we observed pronounced cytopathological changes of mast cell granules, apparently accompanied by vacuolation of the cells in one specimen. Morphologically these granules were similar to some of those reported by Orfanos and Stüttgen (1962), who made time-sequence electron microscopic observations on human skin materials in cases of mastocytosis after treatment with the histamine-liberator, compound 48/80. Morphological changes induced by this chemical in mast cells of rodents have also been reported by Bloom and Haegermark (1965) and several other investigators.

A second possibility is, as suggested by

Hatai (personal communication, 1973) that the mast cells observed in the irises of cases of this disease may be immature cells and so differentiation of their granules may still be incomplete. It should be noted in connection with this that Ishibashi (1973) distinguished several morphological groups of granules in the mast cells in the lymph nodes of rats and discussed their developmental stages.

The third possibility is a combination of the above two possibilities. Namely degranulation may start before maturation of mast cell granules is complete.

At present it is difficult to decide which possibility is most plausible. Further electron microscopic observations on the tissues of Behçet's disease are in progress and detailed

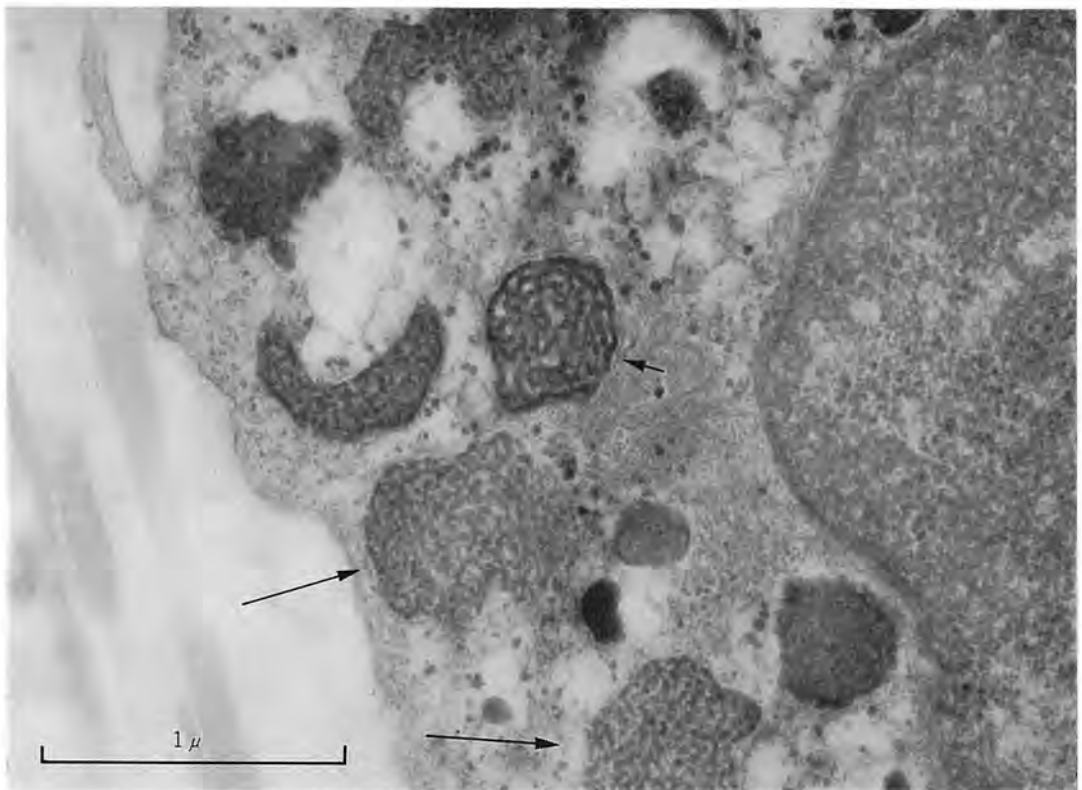


FIGURE 2. Granules in the cytoplasm of a mast cell found in the iris of a case of Behçet's disease. The granule indicated by a short arrow has an electron-dense stranded structure and the two granules indicated by long arrows are filled with particulate material.

studies will be published elsewhere.

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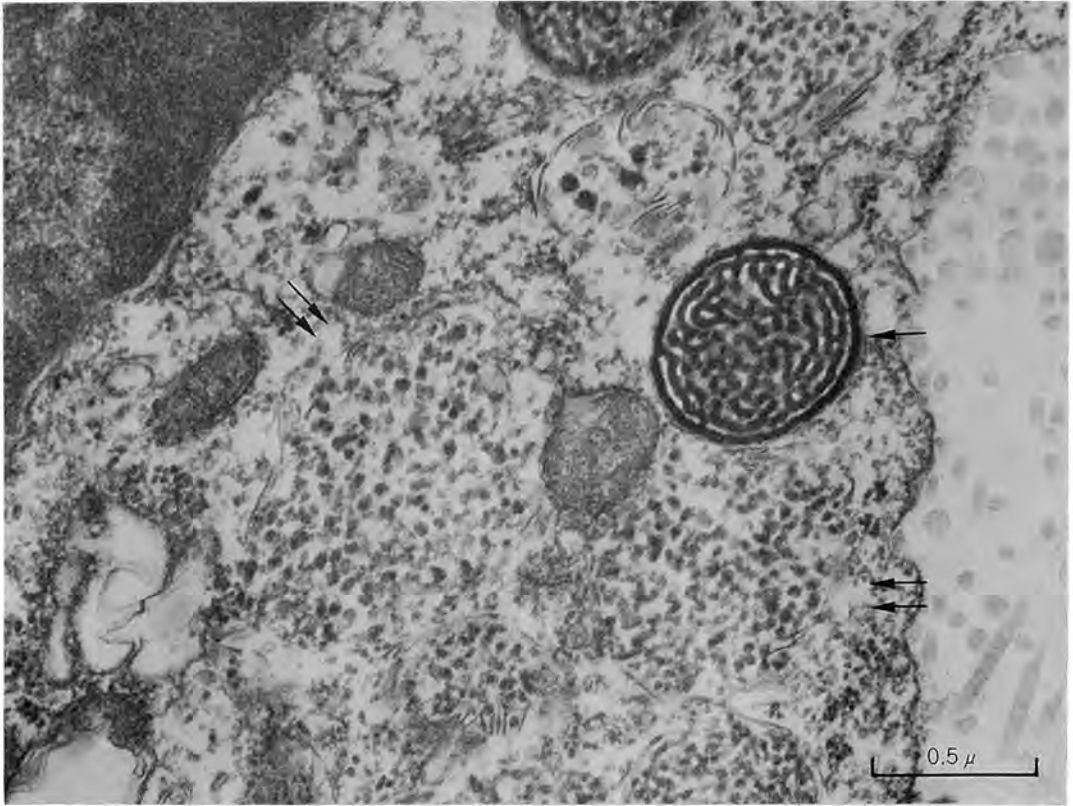


FIGURE 3. Part of the cytoplasm of a mast cell from the iris of a case of Behçet's disease. The granule indicated by a short arrow has an electron dense stranded structure. The two granules indicated by double arrows consist of loosely packed particles.

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