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Ultrastructure of the May-Hegglin anomaly

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Abstract

Ultrastructural features of the leucocytes in two patients suffering from the May-Hegglin anomaly were studied using electron microscopy. In both the cases, electron dense material parallel to the long axis of the inclusions were noted. Platelet ultrastructure was normal. A review of the literature indicates that the May-Hegglin anomaly is a heterogenous condition both ultrastructurally and clinically (JPMA 47:224, 1997).

Introduction

The May-Hegglin anomaly is an autosonial dominant disorder. Morphologically. it is characterized by basophilic leucocyte inclusions, giant platelets and an associated thrombocytopcnia which is usually moderate in nature. Clinically the May-Hegglin anomaly is associated with a variable but often a mild bleeding disturbance[1]. Because the disorder is rare, it is easy to overlook the diagnosis. Nevertheless, even when the diagnosis is suspected the clinician must be careful to exclude other related but similar conditions which nevertheless are distinct from the May -Hegglin anomaly[2]. A useful investigation in this regard is to evaluate the ultrastructure of the leucocyte and the platelets by Electron microscopy. However, the information in this regard is quite limited in the literature to a few publications. This paper is a description of the ultrastructural features of the May- Hegglin anomaly in two cases seen at the University Hospital of Jacksonville in Florida USA. One of these cases has been the subject of a previous report[3]. It is hoped that this ultrastructural description will add to the literature on the subject.

Materials and Methods

Peripheral blood samples of the two patients who had the May- Hegglin anomaly diagnosed on light microscopy were prepared for ultrastructural observation. Preparation involved creating buffy coats which were fixed with Trumps fixative[4]. These were then post-fixed in 2% osmium tetroxide and embedded in a low epoxy embedding medium as reported by Spurr[5]. Semi-thin sections at 0.5 microns were cut for light microscopy and were stained with toluidine blue. Ultra-thin sections were cut on a Reichert Jung ultracut E microtome, collected on copper grids and stained with lead citrate and uranyl acetate. Finally, the sections were examined and photographed with a Zeiss 9 electron microscope.

Results

Light microscopy revealed the classical Dohic bodies in the leucocytes (Figure 1 and 2)

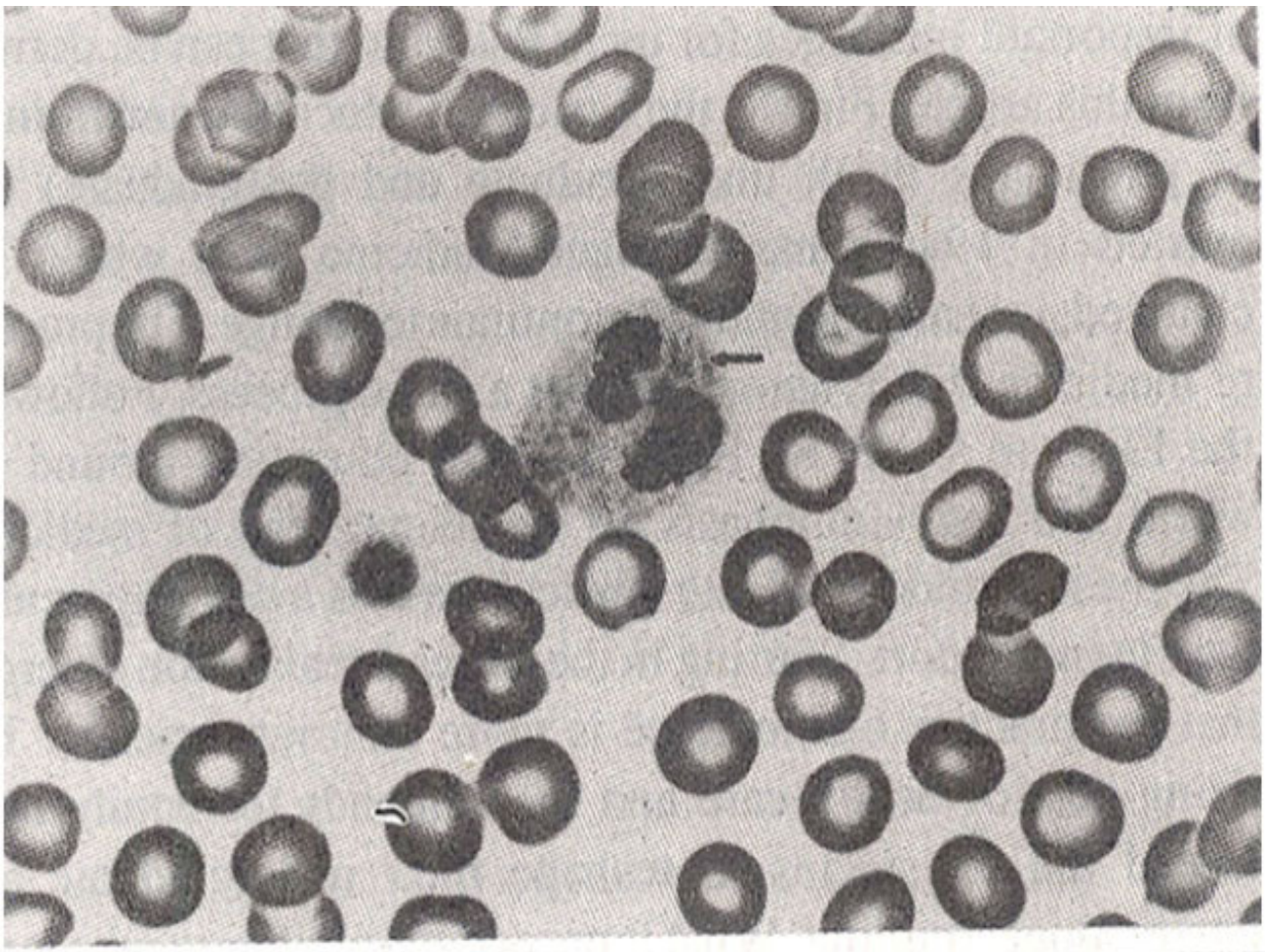

Figure 1. Wrights stain showing intracytoplasmic leucocyte inclusions and large platelets.

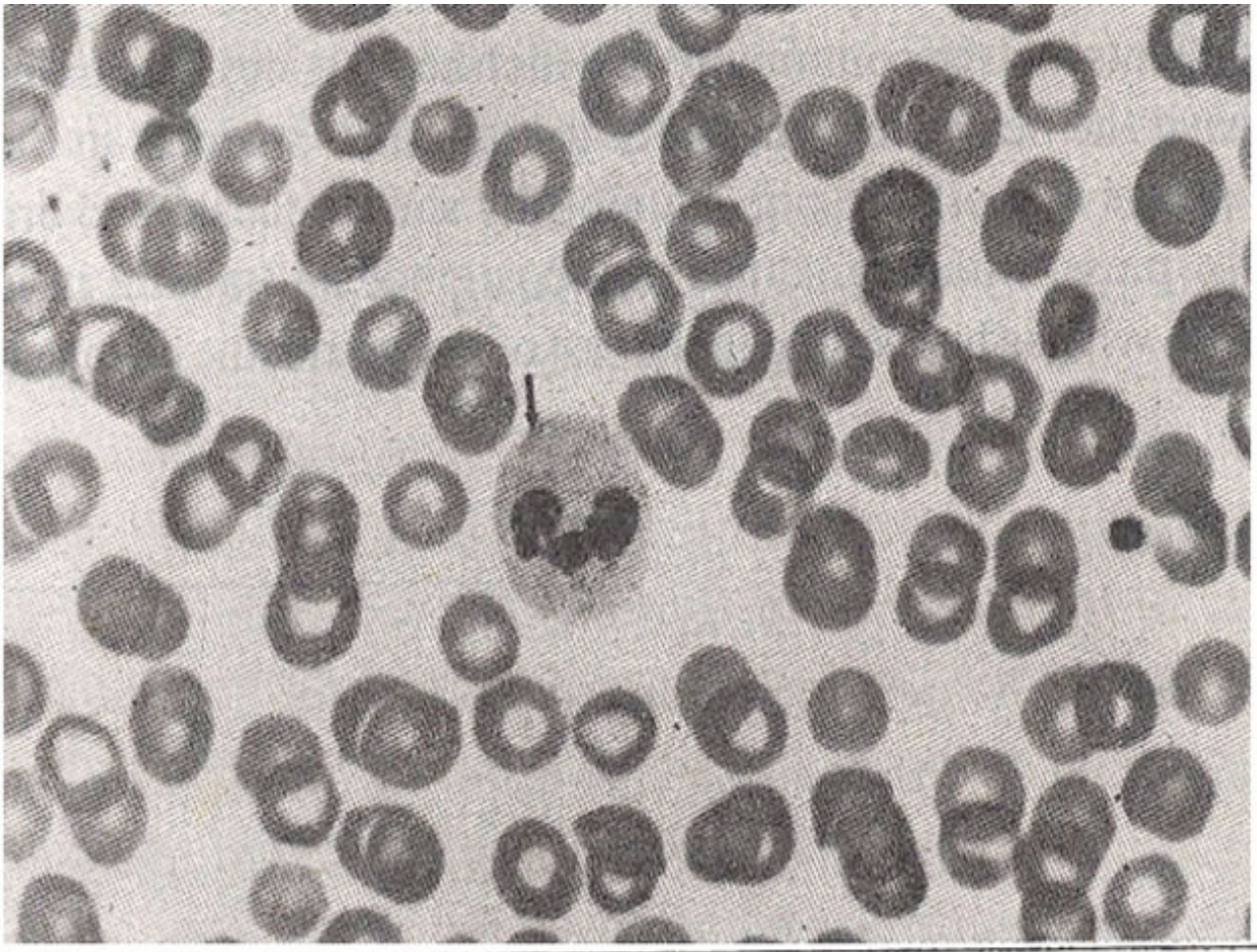

Figure 2. Wrights stain showing intracytoplasmic leucocyte inclusions and large platelets.

alongwith giant platelets in both the cases. Semi-thin sections identified similar inclusions. On ultrastntctural examination (Figure 3 and 4)

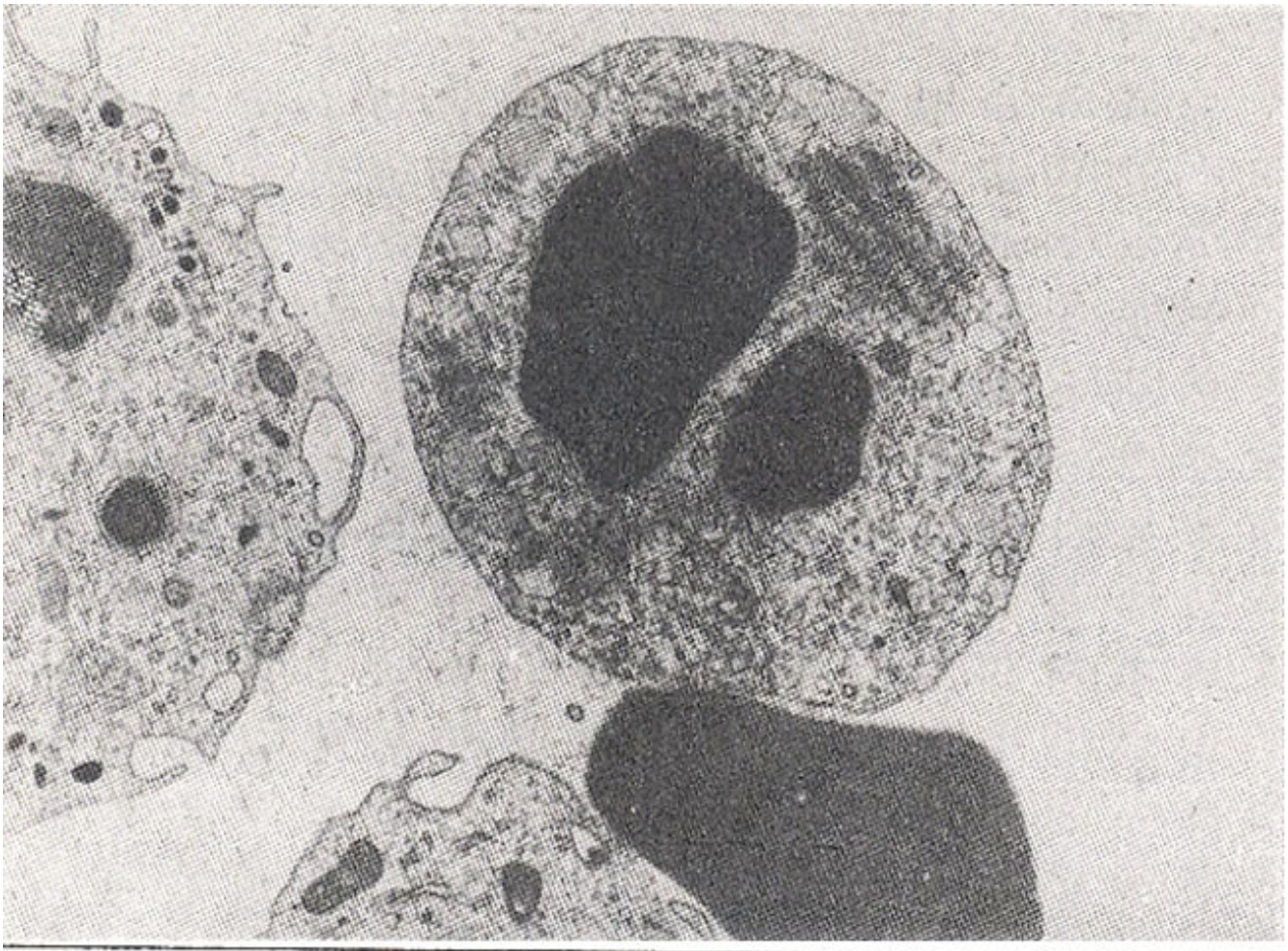

Figure 3. Electron microscopy showing the parallel bar inclusions in the leucocytes.

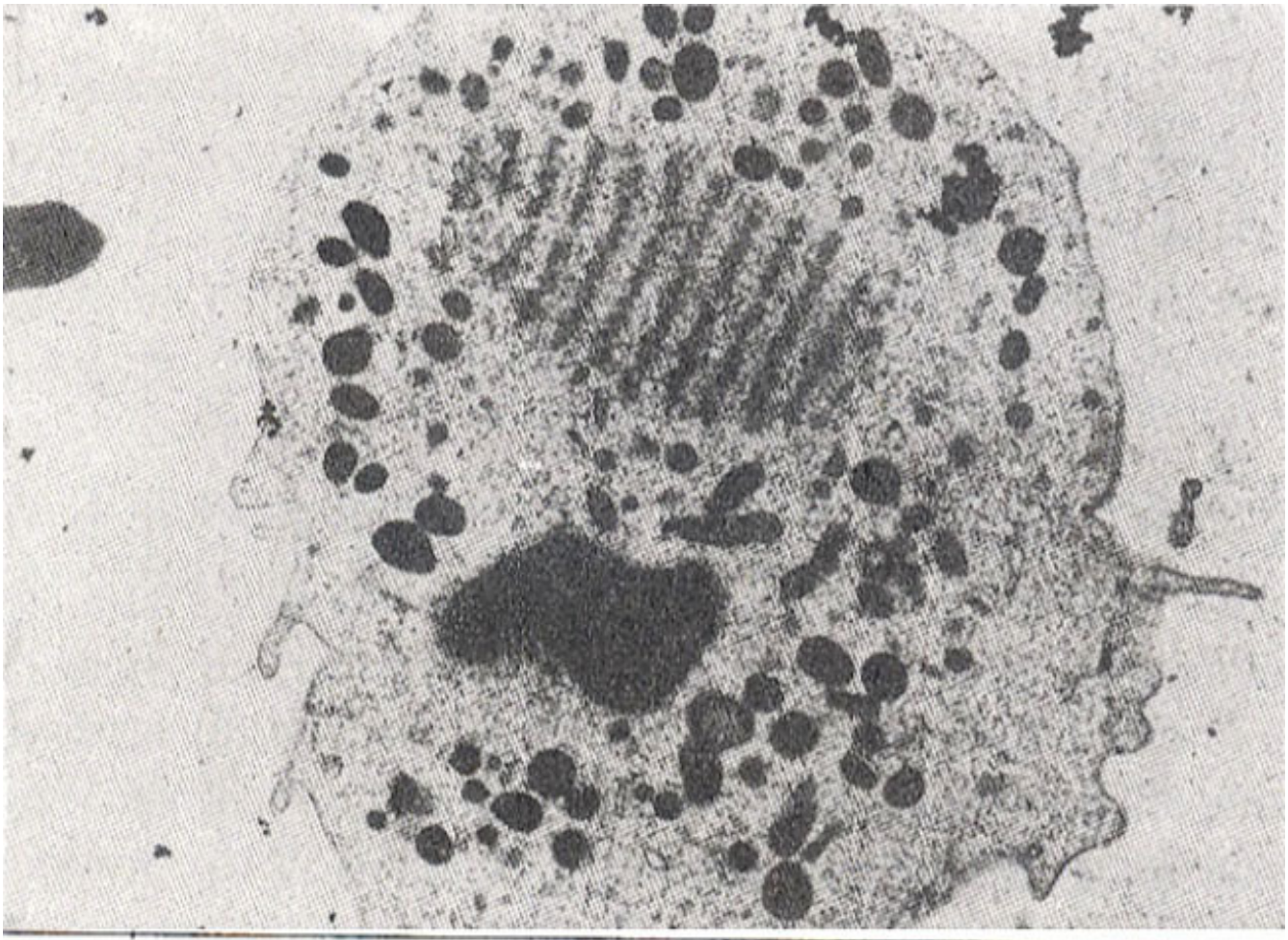

Figure 4. Electron microscopy showing the parallel bar inclusions in the leucocytes.

in both the cases, neutrophilic inclusions were 2x0.5 microns upto 2.8x1.5 microns depending on the plane of the section. The inclusions did not appear to be membrane bound and had an ovoid appearance. Bars of electron dense material parallel to each other but perpendicular to the long axis of the inclusions were noted and the bars were appmximately 100 rim wide with a periodicity of 263 nm. When the cell was examined in a different plane of section, the electron dense bars could be seen but were not as was organized. In some other plane of section the dense bars and segments of the rough endoplasrnic reticulum could be seen. Ultrastructural examination of the platelets was normal.

Discussion

The May-Hegglin anonmly belongs to a family of hereditaxy macrothmmbocytopenias[6]. This group consists of Fcchtners syndrome which has nephritis, congenital cataracts, deafness with the hematologic findings of macrothronthocytes and leucocyte inclusions[7]. The inclusion bodies consist of dispersed filaments, ribosomes and some segments of rough and smooth endoplasmic reticulum. The recently described Sebastian syndrome by Grienacher has all the hematologic hallmarks of Fechtners syndrome but none of the clinical findings e.g., nephritis and deafness[8]. There are only a few studies which have described the ultrastructural features of the May-Hegglin anomaly. By contrast many reports have stressed the clinical srctrum of this disease and its association with other entities[9-11]. In general, the reports have suggested that the platelets membrane in the May Hegglin anomaly is normal

ultrastructurally[12], but the leucocyte inclusions have distinctive characteristics. Jordan (1964)[13] and Cawley (l971)[14] were the first to describe the ultrastructuml features of the leucocyte inclusions. These, they described as parallel in 5-20 nm in diameter that ran length wise and had associated 15-20 mn granules. Certain other inclusions were also described in 1971 by Jenis[15] which were structurally somewhat different from the descriptions of Jordan and Cawley. These latter inclusions were highly organized paraczystalline array and were surreunded by endoplasmic reticulum. It was felt that the latter changes were similar to single standard depolymerised ribonucleic acid and thus implied an origin fmm the rough endoplasmic reticulum. The ultrastructural features of the two current cases of this present report resemble to some degree, the features described by Hamilton et al[16]. In their cases, a parallel bar arrangement of the leucocyte inclusions were the main features along witha slightly skewed arrangement. By contrast, inourcases the bars were pcrpendicularto the long axis of the inclusions. Recently, a report has described a case of the May-Hegglin anomaly where the inclusions had a haphazard dot like arrangement but nota spindle like appearance[17]. It is now generally agreed that the leucocyte inclusions in the May- Hegglin anomaly represent ribonucleic acid. The platelets in the May-Hegglin anomaly has generally been reported to have a normal ultrastructure. It appears then that the May-Hegglin Anomaly is more heterogenous than previously believed. This diversity appears to be a feature of both its ultrastructure and a number of recently described clinical feature[9-11].

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