Asteroid bodies and autophagy

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Published in:
Journal of Cutaneous Pathology

DOI:
10.1111/cup.14483

Publication date:
2023

Received: 22 February 2023 | Revised: 22 May 2023 | Accepted: 31 May 2023

DOI: 10.1111/cup.14483

JOURNAL OF CUTANEOUS PATHOLOGY WILEY

BRIEF COMMUNICATION

Asteroid bodies and autophagy

Asteroid bodies are star-shaped inclusions in the cytoplasm of multinucleated giant cells. Asteroid bodies are not pathognomonic for a single disease, as these structures may be encountered in various granulomatous inflammatory conditions, including sarcoidosis, foreign body-type granulomas, and mycotic granulomas.

In hematoxylin and eosin-stained light-microscopic preparations, asteroid bodies are strongly eosinophilic and surrounded by a halo of small clear vacuoles, as shown in Figures 1–3. Their bright red color reflects a high protein content, whereas the halo of clear vacuoles likely represents an artifact due to dissolved lipid material.

In the past, asteroid bodies have intrigued several researchers and electron microscopy has been applied to unravel the composition and pathogenesis of this most peculiar microscopic phenomenon. About 40 years ago, it was discovered that the shape of asteroid bodies in Langhans-type giant cells is determined by the structure of the cytosphere, an ordered central subcellular structure consisting of a pool of centrioles, radiating microtubules, and radially arranged Golgi networks.[1] In the 1990s, other investigators observed that the halo of clear vacuoles around the asteroid body contains loosely arranged myelin membranes, possibly representing excessive remnants of cellular membranes formed after the fusion of activated histiocytes.[2]

Notably, these seminal electron microscopic studies of asteroid bodies may point towards a possible role of autophagy in the formation of asteroid bodies. Herein, it is hypothesized that these structures contain aggregates of misfolded proteins and damaged organelles transported along a microtubular network and delivered to lysosomes in an organizing center close to the Golgi complex. In this pilot immunohistochemical study, evidence is provided that asteroid bodies contain both the autophagy receptor p62 (also known as SQSTM1) and the autophagosome marker LC3.

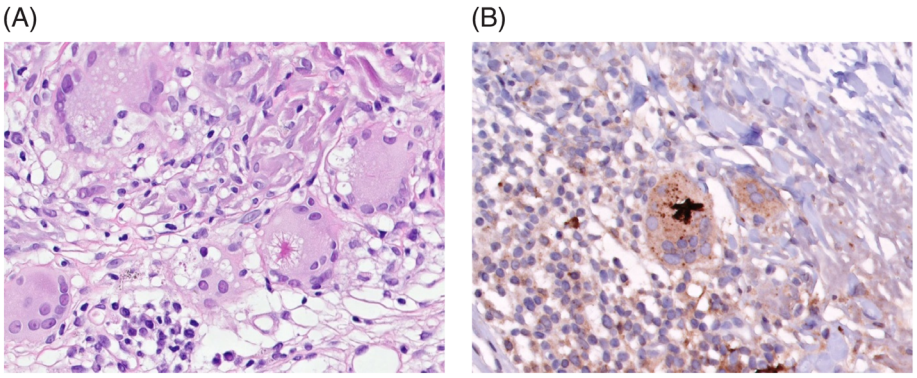

FIGURE 1 (A) An annular elastolytic granuloma of the skin with a Langhans-type giant cell harboring an asteroid body. The asteroid body is strongly eosinophilic, and its spokes are surrounded by clear vacuoles (×200, H&E). (B) The asteroid body contains p62 protein by immunohistochemistry (×200, IHC-p62).

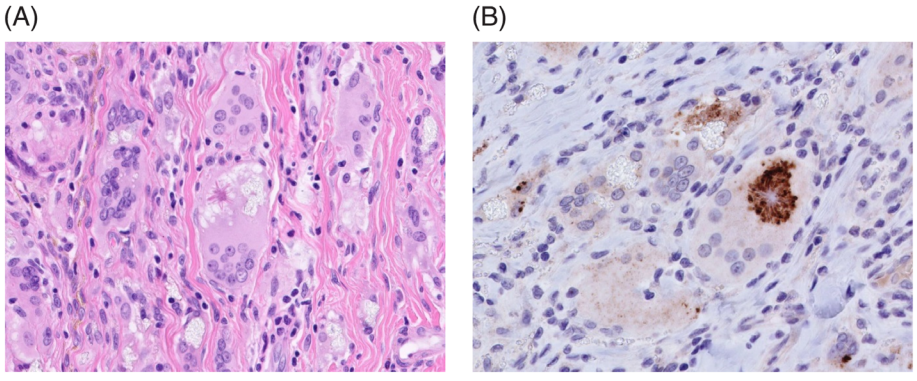

FIGURE 2 (A) A silicone foreign body-type granuloma showing a multinucleated giant cell with intracytoplasmic silicone material and a typical asteroid body (×200, H&E). (B) The asteroid body is surrounded by autophagic aggregates staining positive for LC3 by immunohistochemistry (×200, IHC-LC3).

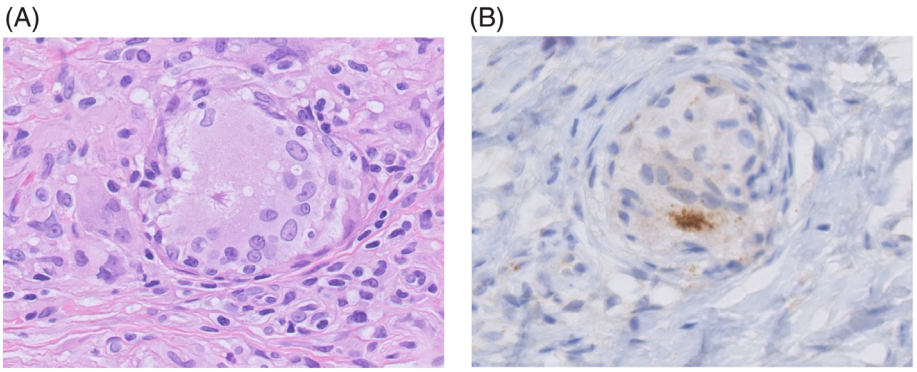

FIGURE 3 (A) A case of cutaneous sarcoidosis showing a multinucleated Langhans-type giant cell with a typical asteroid body (×400, H&E). (B) The asteroid body in cutaneous sarcoidosis is surrounded by autophagic aggregates staining positive for LC3 by immunohistochemistry (×400, IHC-LC3).

For technical details of immunohistochemistry (IHC) please see the study by Te Rijdt et al.[3] At the molecular level, the interaction of LC3 with p62 facilitates the fusion of autophagosomes with lysosomes during the degradation of protein aggregates or cell organelles. Notably, LC3-positive granules become larger in cells where autophagosome formation is abrogated.[4]

The first case concerns an annular elastolytic granuloma, a rare granulomatous skin disease of unknown etiology and pathogenesis, in which degraded elastic fibers are phagocytized by histiocytes and multinucleated giant cells. In this case, easily discerned asteroid bodies (Figure 1A) contained both p62 (Figure 1B) and granular deposits of LC3. The second case represents a foreign body-type granulomatous disease, in which granulomas had formed around abundant silicone material that had leaked from an elbow prosthesis into surrounding soft tissue (particle disease). In this case, many asteroid bodies were seen in the cytoplasm of multinucleated giant cells that had ingested the silicone rubber (Figure 2A). Here, asteroid bodies also contained both p62 and particularly large granules with LC3 (Figure 2B). Third, Figure 3 represents two different cases of cutaneous sarcoidosis, a disease in which Langhans-type giant cells with characteristic asteroid bodies usually are rare (Figure 3A). As in the other granulomatous inflammatory disorders presented herein, the asteroid body was surrounded by LC3-positive material (Figure 3B).

In conclusion, ultrastructural studies published many decades ago have shown that the stellate shape of asteroid bodies is determined by the radial arrangement of a microtubular network around the so-called cytosphere. In this pilot study, IHC staining for the autophagy markers LC3 and p62 indicated that autophagy may play a role in the morphological appearance of asteroid bodies. For instance, it is conceivable that the dynamics of autophagy contribute to the bright red color of aggregated proteins around asteroid cores in hematoxylin and eosin-stained light-microscopic preparations. Moreover, given the remarkably large size of LC3-containing granules found in foreign body-type granulomas, it seems likely that autophagy may become impaired during a rapid cellular turnover when mononuclear histiocytes fuse into multinucleated giant cells.

DATA AVAILABILITY STATEMENT

I have no problem concerning data sharing, including the complete text and all three figures.

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