

## Short reports

### Tadpole shaped structures in a further patient with granulomatous lung disease

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In the hope of finding electron microscopic evidence of transmissible agents in sarcoid granulomas, Wang *et al*<sup>1</sup> scrutinised biopsy material from nine patients with features compatible with this diagnosis. They identified "tadpole shaped" structures in the granulomas of four of their nine patients. Although the nature of these bodies is unknown, their identification in sarcoid granulomas is potentially of great importance in understanding the aetiology of this disease; but so far there have been no confirmatory reports from other laboratories. In particular, we did not encounter such bodies in a recent study of the ultrastructure of cells from lung lavage fluid and lung tissue granulomas from 35 patients with sarcoidosis.<sup>2</sup> We have, however, encountered tadpole shaped structures in a further patient with granulomatous lung disease.

#### Case report

A 43 year old Italian waiter, resident in Britain for 21 years, was admitted to another hospital with severe left sided chest pain. Exertional dyspnoea had been developing gradually for two months. Treatment with diuretics had no effect. Chest radiographs showed nodular opacities in both lower zones and possible paratracheal lymphadenopathy. The heart was not enlarged. He underwent a transbronchial lung biopsy. Histological examination of the material was thought to show fibrosed alveolar walls. A diagnosis of fibrosing alveolitis was made and he was treated with prednisolone 60 mg daily for one month, with rapid symptomatic and radiological improvement. He was referred to the Brompton Hospital for advice regarding prognosis. Review of the biopsy material showed a little fibrous tissue but nothing specific. Review of his radiographs showed probable hilar prominence as well as nodular opacities in the lungs. Lung function tests showed normal lung volumes, mild airflow obstruction and a diminished transfer factor (TLCO) but a normal KCO. The serum IgM concentration was slightly raised (205 IU/ml; normal range 58-197) and C1 binding immune complexes, consisting of IgM, IgG, and C1Q, were present. Serum angiotensin converting enzyme activity was 53 nmol/ml/min (normal range 16-52); other laboratory tests were non-contributory. He underwent bronchoalveolar lavage and a further transbronchial lung biopsy. The lavage fluid showed increased numbers of neutrophils (50%) and lymphocytes (15%). Most of the lung biopsy material was processed to paraffin.

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Accepted 24 January 1984

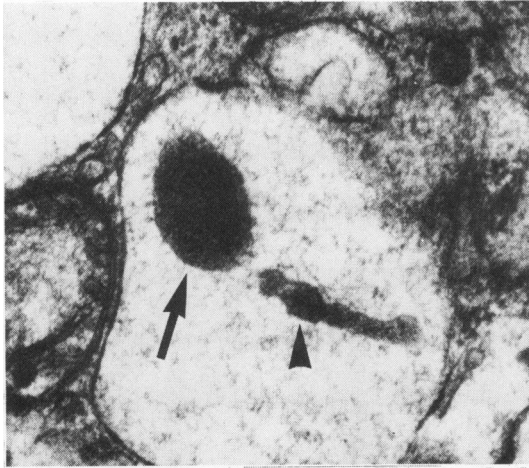
This showed mild interstitial chronic inflammation and fibrosis, with a solitary Langhans' giant cell. The remainder of the biopsy material was submitted for electron microscopy. Semi-thin sections of this tissue showed two poorly formed non-necrotising epithelioid cell granulomas. Transmission electron microscopy confirmed the epithelioid cell transformation of macrophages, showing numerous membrane bound vesicles and mitochondria, with occasional rough endoplasmic reticulum but no lysosomes. The vesicles contained the usual slightly electron dense, finely granular material<sup>2</sup> and also occasional tadpole shaped structures, as described by Wang *et al*<sup>1</sup> (figs). The latter were rod shaped with knob like bulbous dilatations and larger terminal "heads," both of which contained electron dense material. The size and shape of the heads varied but they were generally round to ovoid and measured 400 × 250 nm. The full extent of the tails could not be assessed in our thin sections but they measured up to 600 nm in length, were about 50 nm in width, and were often beaded. The bulbous dilatations measured 100 nm in diameter. Dr Nai-San Wang confirmed that the tadpole shaped structures were indeed the same as those in his cases.

#### Discussion

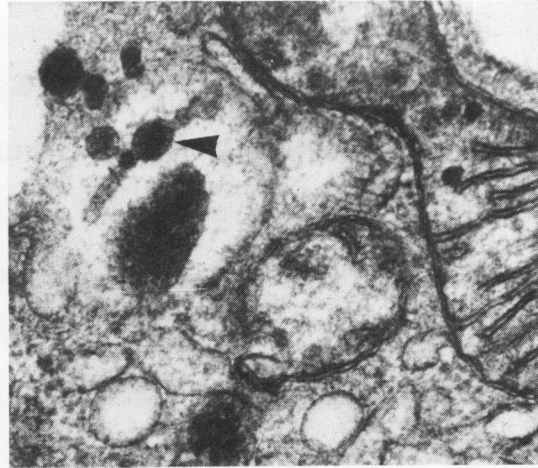
While this case shows several features compatible with sarcoidosis, the diagnosis is not conclusive. For this reason we have preferred to reserve judgment and use the less committed terminology of granulomatous lung disease.

The purpose of this report is merely to record the identification of Wang's tadpole shaped structures within a pulmonary granuloma in another laboratory and, moreover, one in another continent (the original report coming from Montreal). At present we do not know what these structures represent. The possibility that they are an infective agent is an exciting one that requires further consideration, but they appear too big for viruses and too small for bacteria and we are advised that they do not resemble mycobacteriophage, mycoplasmas, spiroplasmas, or any other recognised microbiological agent. The possibility that they are infective agents therefore appears rather remote. If, however, these structures do represent infective agents, it remains conjectural whether they are causative or commensal.

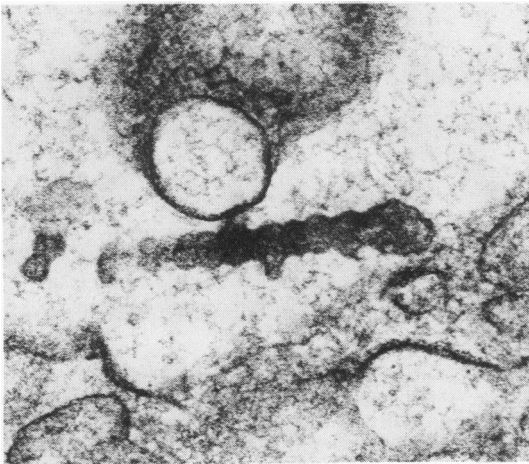
We are grateful to Drs DS Ellis, J Grange, JS Porterfield, DIH Simpson, and D Taylor-Robinson for examining our electron micrographs and advising on the possibility that the tadpole shaped structures represent infective agents. We are also grateful to Dr Brian Kirby for referring the patient to us.



A



B



C

*Electron micrographs of "tadpole shaped" structures within cell vesicles, illustrating electron dense heads (arrow) and beaded tails with bulbous dilatations (arrowheads). (A and B:  $\times 49\,400$ ; C:  $\times 66\,700$ .)*

#### References

<sup>1</sup> Wang N-S, Schraufnager DE, Sampson MG. The tadpole-shaped structures in human non-necrotising granulomas. *Am Rev Respir Dis* 1981;**123**:560-4.

<sup>2</sup> Danel C, Dewar A, Corrin B, Turner-Warwick M, Chretien J. Ultrastructural changes in bronchoalveolar lavage cells in sarcoidosis and comparison with the tissue granuloma. *Am J Pathol* 1983;**112**:7-17.