CASE REPORT

Malignant granular cell tumour of the mediastinum

Wee Ming SOH, Mee Ling YEONG and Kwong Pang WONG

Diagnostic Medlab, Auckland, New Zealand

Abstract

This report describes a case of malignant granular cell tumour arising in the mediastinum, detailing the investigations undertaken to reach this rare diagnosis. A 63-year-old man was referred from the Pacific Islands for investigation of a 8cm mediastinal mass extending into the left pleura and associated with pleural nodules and pleural effusion. Needle aspiration via bronchoscopy yielded insufficient material for cytological interpretation and needle biopsy showed normal respiratory epithelium. CT-guided FNA revealed scattered large polygonal to spindle cells with granular cytoplasm and indistinct borders. The needle core biopsy yielded scanty cells with abundant granular cytoplasm, oval and regular nuclei which were moderately positive for CD68, vimentin and S100 and negative for CKMNF116, CK5/6, CK7, CK20, TTF-1, chromogranin and synaptophysin. In view of the benign morphology, these cells were interpreted to be histiocytes. The incisional biopsy revealed cords and trabeculae of cells identical to the CT samples. These cells were polygonal with abundant granular cytoplasm. Some cells showed large eosinophilic cytoplasmic globules not seen in the FNA sample. The tumour was however, heterogeneous in appearance with some areas exhibiting criteria of malignancy: necrosis, vesicular nuclei with large nucleoli, high nuclear-to-cytoplasmic ratio and nuclei pleomorphism. In addition, p53 expression in 10% of tumour nuclei, a high Ki67 proliferative rate (>10%), the deep seated location and extension of the tumour into adjacent organs favoured a diagnosis of malignancy.

INTRODUCTION

Granular cell tumour are mostly benign and occur in superficial sites. Malignant granular cell tumour is a rare disease entity constituting 1-2% of granular cell tumour and occurs in deep sites. There are 2 cases registered in the New Zealand cancer registry in the 15 years between 1995 and 2009 (one each in 2003 and 2006). This report describes a case of malignant granular cell tumour arising in the mediastinum, detailing the investigations that were undertaken to reach this rare diagnosis.

CASE REPORT

History

A 63-year-old man was referred from the Pacific Islands for investigation of a 8cm mediastinal mass extending into the left pleura and associated with pleural nodules and subsequently pleural effusion (FIG. 1). A total of three invasive procedures were carried out to reach a definitive diagnosis. He was treated with radiotherapy as surgery was not suitable.

First procedure: Bronchoscopy and needle biopsy

Needle aspiration via bronchoscopy yielded insufficient material for cytological interpretation and needle biopsy showed normal respiratory epithelium.

Second procedure: CT guided fine needle aspiration of mediastinal mass

A CT guided FNA of the mediastinal mass was carried out and pleural effusion fluid was also received in the laboratory. The FNA revealed scattered large polygonal to spindle cells with granular cytoplasm and indistinct borders. (FIG. 2) The needle core biopsy yielded a scanty amount of tissue composed of cells with abundant granular cytoplasm, oval and regular nuclei. These were moderately positive for CD68 (FIG 3), vimentin and S100 (FIG. 4) and negative for CKMNF116, CK5/6, CK7, CK20, TTF-1, chromogranin and synaptophysin.

In view of the benign morphology and immunohistochemical profile in a very limited sample, these cells were interpreted to be...
FIG. 1: Computed tomography of chest (anteroposterior view)

FIG. 2: CT guided fine needle aspirate. Diff Quik x400.

FIG. 3: CT guided core biopsy. CD68 x 400

histiocytes. Pleural effusion fluid was non-contributory.

Third procedure: Mediastinoscopy and incisional biopsy

The incisional biopsy yielded abundant material. The tumour was composed of cords and trabeculae of cells identical to the CT guided FNA sample. These cells were polygonal with abundant granular cytoplasm. Some cells showed large eosinophilic cytoplasmic globules not seen in the CT guided FNA sample. The tumour was however, heterogeneous in appearance. Some areas appeared malignant (FIG. 5) while other areas lacked malignant features (FIG. 6). Four malignant morphological features observed were necrosis, vesicular nuclei with large nucleoli, high nuclear-to-cytoplasmic ratio and nuclei pleomorphism (FIG. 5). Additionally, the two other morphological features attributed to malignancy not observed were spindling of nuclei and increased mitotic activity of more than 2 per 10HPF.

The cells were more intensely immunopositive for S100 (FIG. 7). More than 10% of tumour nuclei expressed p53 protein and the Ki67 proliferative rate was high (>10%) (FIG. 8).

FIG. 4: CT guided core biopsy. S100 x 400

FIG. 5: Incisional biopsy H&E x 400. Polygonal cells with granular cytoplasm, exhibiting nuclear features of malignancy. Cytoplasmic eosinophilic globules are also seen.
The nature of the lysosomes in the cytoplasm may have contributed to the degenerative needle core biopsy. CD68 and S100 are the common immunohistochemical markers shared by histiocytes and granular cells. This further enforces that immunohistochemistry forms only a piece of the diagnostic jigsaw puzzle. A confident diagnosis was made when adequate material was obtained and showed malignant morphological features and correlations were made with the widespread nature of tumour in radiological findings and the deep site of tumour. DNA ploidy analysis has not shown correlation of chromosomal abnormality to malignancy.1

The diagnosis of malignant granular cell tumour in this case demonstrates the complementary use of histological, immunohistochemical observations in adequate material in the appropriate clinical and radiological settings. The six morphological features favouring malignant granular cell tumour are as follows. Neoplasms that meet 3 or more of these criteria are classified as malignant:
- Tumour necrosis
- High mitotic activity (>2 mitosis per ten 200x field)
- Presence of vesicular nuclei with large nucleoli
- High nuclear to cytoplasm ratio
- Nuclei pleomorphism
- Spindling of cells

Furthermore, this case fulfilled additional features in favour of malignancy, namely, (1) p53 expression more than 10%, (2) Ki67 more than 10%, and clinical and radiological findings of (1) a deep seated location and (2) tumour extension into adjacent organs.

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REFERENCE