A rare manifestation of Neurofibromatosis type 1: A plexiform neurofibroma involving the mediastinum and lungs with endobronchial neurofibromata.

Running title: Plexiform neurofibroma involving the mediastinum.

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A rare manifestation of Neurofibromatosis type 1: A plexiform neurofibroma involving the mediastinum and lungs with endobronchial neurofibromata.

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Key words:

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Summary:

Neurofibromatosis type 1 (NF1) is a multisystem phakomatosis. The intrathoracic manifestations of NF1 are protean. We describe a rare case of a plexiform neurofibroma infiltrating the mediastinum and lungs with multiple endobronchial neurofibromata. To our knowledge, a mediastinal plexiform neurofibroma extending into the lungs on CT has not been reported.

Case Presentation:

A 24-year-old male patient with known NF1, under surveillance for an optic nerve glioma, presented with right chest wall radicular pain. CT of the thorax demonstrated a right posterior mediastinal mass, likely the cause of his symptoms. In addition, CT identified a soft tissue mass in the mediastinum encasing the carina and left main bronchus (Figure 1a and 1b) and infiltrating into the lung parenchyma along the left upper and lower lobe bronchi (Figure 1c and 1d). There were also multiple nodules present within the trachea and bronchi on both sides (Figure 2).

Bronchoscopy confirmed multiple nodules within the trachea and both main bronchi (Figure 3) of which biopsies were taken. Histopathology demonstrated myxoid stroma and bland spindle cells which were S100 positive with scattered nerve fibres on neurofilament protein (NFP) staining, consistent with neurofibromata (Figure 4). There was no evidence of malignancy.

Fine needle aspirate of the mediastinal component yielded blood-stained fluid and mixed inflammatory cells only. No malignant cells were identified. However, given the infiltrative growth pattern and biopsy proven neurofibromata within the adjacent bronchi, this was favoured to represent a plexiform neurofibroma.

Surveillance imaging has been organised to monitor for growth of the endobronchial nodules and plexiform neurofibroma, as well as to monitor for potential malignant degeneration.

Discussion:

Neurofibromatosis type 1 (NF1) is the most common phakomatosis occurring in approximately one in every 2000 births (1). It can be inherited in an autosomal dominant manner, however approximately 50% of cases occur sporadically due to a spontaneous mutation (1). NF1 involves multiple body systems with manifestations occurring in the thorax, abdomen, central nervous system, musculoskeletal system, and skin.

Many intrathoracic manifestations of NF1 are recognised, including spinal and rib abnormalities, posterior mediastinal neurofibromata, cystic lung disease, pulmonary fibrosis, and intrapulmonary neurofibromata (1). Plexiform neurofibromata are pathognomic of NF1 and in the thorax, most commonly occur adjacent to ribs and in the paravertebral region (1,2). Mediastinal plexiform neurofibromas are well described and occur in the distribution of the mediastinal nerves (2,3). Bourgouin et al.(3) described four cases of mediastinal plexiform neurofibromata which involved the entire mediastinum in three patients and the middle and posterior mediastinum in one. A mediastinal plexiform neurofibroma infiltrating along the bronchi into the lungs however has not been previously described.

Endobronchial neurofibromata in NF1 are rare (4,5). In a case report by Gillissen et al. (4), infiltration of the bronchial tree with neurofibromata was demonstrated on bronchoscopy and biopsy, however CT and MRI of the thorax were normal. In a case reported by Venugopal et al. (5), multiple nodular swellings within both main bronchi were neurofibromata on histology; additional intrapulmonary nodules were thought to represent intrapulmonary neurofibromata.

In this case, it is hypothesized that the soft tissue mass in the mediastinum and lungs is a plexiform neurofibroma given the infiltrating pattern and the presence of biopsy proven neurofibromata in the adjacent the airways. This is the first description of such an entity.

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Figure Legends:

Figure 1: Coronal (A) and axial (B-D) CT thorax demonstrating a soft tissue mass in the mediastinum encasing the carina and left main bronchus (arrows in A and B) and infiltrating into the lung parenchyma along the left upper and lower lobe bronchi (arrows in C and D).

Figure 2: Coronal (A) and sagittal (B) CT thorax demonstrates multiple nodules within the trachea (open arrow in A) and left sided bronchi (black arrows in A and B).

Figure 3: Bronchoscopy images demonstrating multiple nodules within the left main bronchus.

Figure 4: Histopathology pictures of the bronchoscopy specimens (x200 magnification) showed bland spindle cells with myxoid stroma (A). On immunohistochemistry, the cells were positive for S100 (B). Appearances are consistent with neurofibromata.

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A

B

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