Inflammatory myofibroblastic tumours of the respiratory system and the impact of the varying patterns

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ABSTRACT

Inflammatory fibroblastic tumours are very rare. They are mostly located in the respiratory system. We present three cases of patients with fibroblastic tumours. The diversity of inflammatory fibroblastic tumours in the respiratory system and the surgical considerations are discussed. Our recommendation is that treatment should include a complete resection to prevent local recurrence and malignant transformation, and follow-up review should reflect the procedure carried out, especially in terms of the anatomical location and the extent of the surgical procedure performed.

KEYWORDS

Fibroblastic – Tumour – Lung cancer

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Inflammatory fibroblastic tumours (IFT) are rare mesenchyme derived neoplasms. They are observed most frequently in the lungs although they also affect extrathoracic organs. Owing to their low incidence, knowledge regarding the aetiology and pathophysiology has been slow to progress. There is little consensus regarding the diagnostic procedures, the surgical approach, follow-up review and potential adjuvant therapy. In this paper, we present three cases of IFTs, demonstrating the variability in disease pattern that can occur in the respiratory system. We discuss the principles of diagnosing and managing this condition.

Case 1

A 41-year-old woman presented with a 12-month history of increasing dyspnoea. Chest x-ray and subsequent computed tomography (CT) revealed a tumour inferior to the vocal cords leading to a partial obstruction (Fig 1). Bronchoscopy demonstrated a fleshy tumour 2cm past the vocal cords. During the surgical procedure, the tumour was found to extend proximally, almost to the level of the cricoid cartilage. A 3cm segment of trachea was excised with reconstruction of the trachea. The patient had an uneventful postoperative recovery.

Histopathological analysis showed a myofibroblastic tumour composed of spindle cells in a storiform arrangement with elongated nuclei and moderate eosinophilic cytoplasm. The cell borders were poorly defined. There

was no obvious carcinoma and no features to suggest it was a metastatic deposit from the thyroid. There was no mitotic activity or necrosis and the tumour was lined with metaplastic squamous cell epithelium. Follow-up review has consisted of periodic bronchoscopy with no evidence of recurrence thus far.

Case 2

A 30-year-old male non-smoker presented with a 3-month history of episodic chest pain. CT showed a large left upper lobe tumour encroaching on the main pulmonary artery (Fig 2). A CT guided biopsy revealed this to be a myofibroblastic tumour. Bronchoscopy demonstrated a tumour occluding the upper lobe bronchus and extending into the bronchus of the left lower lobe. The tumour measured 5cm in diameter and was found to be originating from the left upper lobe bronchus, also occupying the subcarinal space. A left upper lobe sleeve resection was performed. The patient had an uneventful postoperative recovery.

Histopathological analysis revealed a well demarcated but non-encapsulated tumour, which was an inflammatory myofibroblastic tumour. The resection margin was tumour free and surrounding lung tissue was collapsed but otherwise unremarkable. There was a proliferation of relatively bland spindle cells and a brisk inflammatory cell infiltrate with plasma cells. Foam cells were also present. The patient is currently under follow-up review with no suggestion of recurrence.

Figure 1 Case 1: Midline sagittal computed tomography showing a tumour causing partial obstruction of the trachea approximately 2cm inferior to the vocal cords

Case 3

A 38-year-old previously fit and well man presented with a 1-month history of a cough, back pain, weight loss, night sweats and dyspnoea. CT showed multiple bilateral lung nodules (Fig 3). CT guided biopsies of the nodules did not provide a definitive diagnosis. The patient therefore underwent right-sided video assisted thoracoscopic surgery

Figure 2 Case 2: Axial computed tomography at T4, in the mediastinal window, showing the relatively well defined homogeneous left upper lobe tumour abutting the left main pulmonary artery and extending towards the anterior chest wall

Figure 3 Case 3: Axial computed tomography at T6, in the lung window, showing the bilateral pulmonary nodules. Two can be clearly seen in this slice: one anteriorly in the centre of the left upper lobe adjacent to the pericardium, and one posteriorly and in the right lower lobe, paraspinal, abutting the pleura.

(VATS) with wedge resections of lung for diagnostic purposes. Intraoperative observations confirmed normal airways but multiple lung nodules, mainly in the right upper lobe, which were associated with chest wall adhesions. The patient had an uneventful postoperative recovery.

Histopathological analysis of the excised nodules revealed well defined spindle cells showing oval nuclei with a fine chromatin pattern in the nodule. No cytological atypia was noted and there were numerous mononuclear inflammatory cells in which plasma cells predominated. Mitotic activity was negligible and the tumour cells had a storiform pattern. The features were consistent with an inflammatory myofibroblastic tumour. The patient is currently under follow-up review and remains symptomatically stable.

Discussion

IFTs are characterised by a proliferation of spindle cells associated with an inflammatory infiltrate consisting mainly of plasma cells and lymphocytes. These tumours can be classified as belonging to one of three histological patterns: organising pneumonia, fibrous histiocytic and lymphoplasmacytic types. In the majority of cases, they behave in a benign fashion. However, they do have the ability to recur if not completely resected.^{1,2} In addition, they have the potential to follow a more aggressive course as they can undergo malignant transformation.

Histopathological diagnosis can often be challenging owing to the variability in surface antigen profiles. Anaplastic lymphoma kinase (ALK) expression can be observed in IFTs in 60–90% of cases.³ ALK is also helpful in distinguishing tumours from sarcomatous proliferations. Immunohistochemistry profiles show that many other proteins are expressed in these tumours, including tenascin-C, osteopontin and fibronectin. Positivity has also been observed for actin, CD34, vimentin and desmin.

The aetiology of IFTs is still an area of controversy and speculation surrounds the causal factors. One theory is that they have a viral basis caused by the Epstein-Barr virus or human herpes virus 8. Respiratory IFTs are seen mainly in males although the true incidence is difficult to determine because of the paucity of surgical literature in this area. The incidence has been quoted as varying between 0.04% and 1% of all lung tumour resections.⁴

Surgical procedures used to remove IFTs of the respiratory system include tracheal resections, carinal resections, lobectomies, sleeve resections, bilobectomies, pneumonectomies, subsegmental resections and chest wall resections. Percutaneous biopsy to obtain the diagnosis is often inaccurate. Instead, excision biopsy is the best way to be confident about the diagnosis and also to treat this pathology.

Recurrence rates in the lung vary and it has been demonstrated that providing surgical resection is complete, surgery is curative with recurrence as low as 0–7% being observed.⁵ Conversely, incomplete excision is associated with higher rates of recurrence. Although medical therapy and radiotherapy have been described for treating IFTs, the evidence is lacking to support such an approach in isolation. With regard to adjuvant chemotherapy, there has been some promise although this requires further research.⁶

Conclusions

In this paper, we have demonstrated the diversity of IFTs in the respiratory system. The histopathological diagnosis

can be difficult owing to the varied microscopic and surface antigen profiles.

The consensus is that such tumours should be fully resected to prevent local recurrence and malignant transformation. The problem of treating multiple IFTs remains a therapeutic question if surgical resection is not possible. Adjuvant treatment should be offered although further research is required in this field.

References

1. Coffin CM, Watterson J, Priest JR, Dehner LP. Extrapulmonary inflammatory myofibroblastic tumor (inflammatory pseudotumor). A clinicopathologic and immunohistochemical study of 84 cases. *Am J Surg Pathol* 1995; **19**: 859–872.
2. Häusler M, Schaade L, Ramaekers VT *et al*. Inflammatory pseudotumors of the central nervous system: report of 3 cases and a literature review. *Hum Pathol* 2003; **34**: 253–262.
3. Freeman A, Geddes N, Munson P *et al*. Anaplastic lymphoma kinase (ALK 1) staining and molecular analysis in inflammatory myofibroblastic tumours of the bladder: a preliminary clinicopathological study of nine cases and review of the literature. *Mod Pathol* 2004; **17**: 765–771.
4. Sakurai H, Hasegawa T, Watanabe S *et al*. Inflammatory myofibroblastic tumor of the lung. *Eur J Cardiothorac Surg* 2004; **25**: 155–159.
5. Lee HJ, Kim JS, Choi YS *et al*. Treatment of inflammatory myofibroblastic tumor of the chest: the extent of resection. *Ann Thorac Surg* 2007; **84**: 221–224.
6. Dishop MK, Warner BW, Dehner LP *et al*. Successful treatment of inflammatory myofibroblastic tumor with malignant transformation by surgical resection and chemotherapy. *J Pediatr Hematol Oncol* 2003; **25**: 153–158.