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CLINICAL REPORT

Tracheal Inflammatory Myofibroblastic Tumour ALK+ as Cause of Dyspnea in a 10 Years Old Child

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Abstract
Inflammatory myofibroblastic tumours are rare lesions that could occur in airways. We report a 10 years old male who complains about dyspnea after physical exercise. Making CT and RMI images and a biopsy, we make an accurate diagnosis of an inflammatory myofibroblastic tumour ALK+. After treatment with a subtotal resection and crizotinib as adjuvant, we achieve a complete remission.

Keywords Dyspnea · neoplasms · operative procedures · chemotherapy

Introduction

An inflammatory myofibroblastic tumour (IMT) is a rare neoplasm with an intermediate malignant potential [1–4] due to the high rate of local relapses and the possibility of metastasizing [2, 4]. It mainly occurs in children and young patients and usually appears in the lower respiratory tract, abdomen and pelvis, but it's possible the development in many other areas [1, 2].

A chromosomal rearrangement involving the anaplastic lymphoma kinase receptor (ALK) gene exists in 50% of IMTs [2, 3, 5–7]. This fact implies the production of ALK fusion proteins which have potential oncogenic functions [4].

Clinical manifestations depend on the place of appearance [1, 4] being stridor, dyspnea and cough the most common symptoms in case of affectation of the trachea.

[1, 7]. A non-specific syndrome with fever and weight loss with raised inflammatory markers has been reported too [1, 4], and occurs in 15–30% of cases [4].

The optimal treatment is the complete surgical resection [2, 4, 6, 7]. Nevertheless, there are some cases where this is not possible, and chemotherapy and radiotherapy could be employed as exclusive or adjuvant treatment [2, 6].

Case Report

A 10 years old male is attended by his paediatrician due to respiratory distress and cough after intense physical exercise. Initially he starts treatment with antibiotics and anti-inflammatory therapy without achieving a complete remission of his symptoms.

A few weeks later, he goes to the emergency because of the increase of the intensity of the dyspnea. Now he has problems for breathing after making physical activity and resting. After rejecting bronchopulmonary pathology, the patient is examined by ENT.

The nasofibroscopic examination shows a subglottic stenosis over 50% of tracheal lumen (Cotton Meyer grade II) with normal activity of both cords.

A cervical CT is requested. The images show a rounded and homogeneous lesion with soft tissue density in the right wall of the trachea 9 mm over the carina. Its size is $18 \times 15 \times 12$ mm and it causes a significant stenosis of the tracheal lumen (Fig. 1A).

A cervical MRI is also requested for completing the study. The images show a hyperintense mass in T2 with enhancement with gadolinium contrast (Fig. 1B).

A biopsy is made. The lesion is composed of neoplastic myofibroblasts in a myxoid stroma with other inflammatory cells. These myofibroblasts are immunoreactive for

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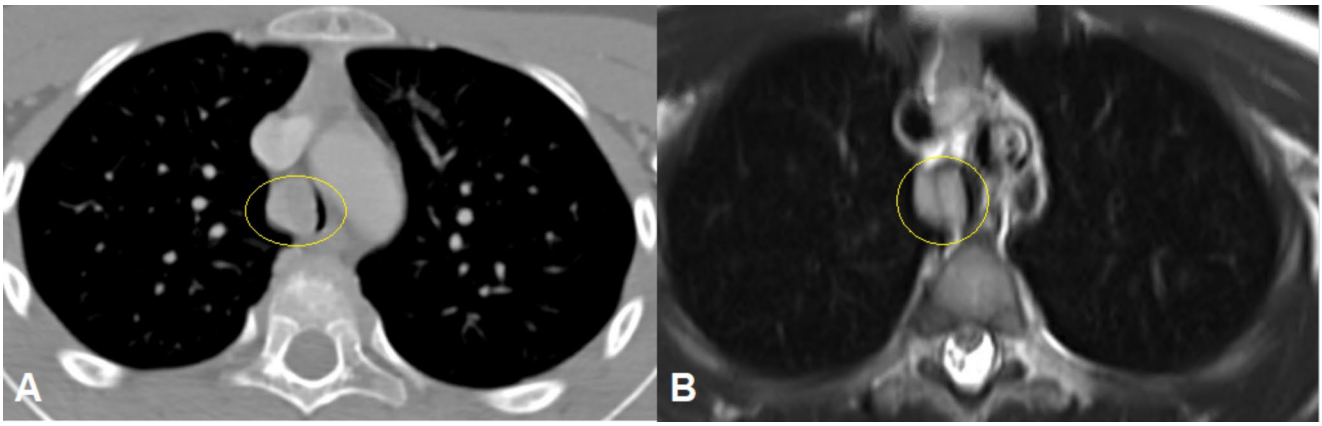

Fig. 1 CT (**A**) and T2 RMI (**B**) imagesof the lesion before starting the treatment. They show a mass with soft tissuedensity occluding more than 50% of tracheal lumen (Circle).

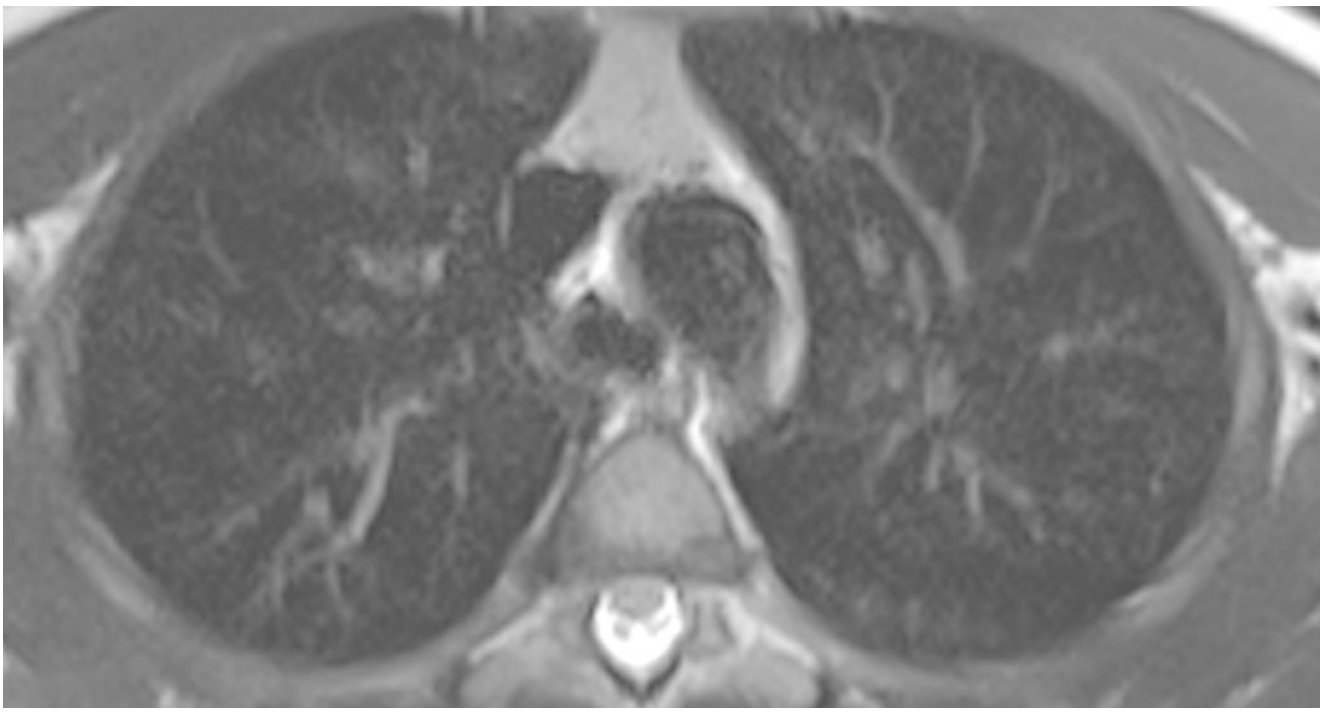

Fig. 2 T2 RMI image of the tracheal lumen two years after starting treatment and one year after finishing it

vimentin, smooth muscle actin and muscle specific actin. There is cytoplasmic immunoreactivity with anaplastic lymphoma kinase too.

We make the diagnosis of inflammatory myofibroblastic tumour ALK+.

Under general anaesthesia, a partial resection of the mass is made by microscopic translaryngeal approach, employing CO_2 laser to eliminate approximately the 90% of the mass, respecting the tracheal mucosa and the pathological tissue closest to the tracheal wall. Afterwards, he stars treatment with oral crizotinib 200 mg twice a day for 6 months.

The follow up is made with a quarterly MRI during the first year, and biannual during the second one. After two years, we offer an annual MRI if there are not new symptoms.

Nowadays, 2 years after the treatment we achieve a complete remission. There is a complete removal of the lesion in the last RMI images (Fig. 2).

Discussion

An inflammatory myofibroblastic tumour is a mesenchymal neoplasm with neoplastic myofibroblasts in a myxoid to collagenous stroma admixed with inflammatory cells [1–6, 8–11] with 150–200 new cases reported annually in

the USA [9]. It mainly affects young people [2,4–7,9-,11] and the main places of appearance is lower airway, abdomen and pelvis [3–7, 10, 11]. Local recurrences may occur after primary surgery, with a low risk of distant metastases [8]. This is the reason because of it's considered a tumour with intermediate biologic potential [1–11].

Clinical manifestations depend on the place of appearance [1, 2, 4, 10]. A non-specific syndrome with fever and weight loss with raised inflammatory markers occurs in 15–30% of cases [4, 10].

Rearrangements involving the ALK locus on chromosome 2p23 happen in 50% of IMTs [2–11]. There are many fusion partners thar serve to activate ALK [8, 9]. This fact implies the production of ALK fusion proteins which have potential oncogenic functions [4]. To differentiate ALK positive and ALK negative IMTs, cytoplasmic immunoreactivity with anaplastic lymphoma kinase must be studied, and it occurs in approximately half of cases [11].

In the past, ALK positivity was recognized as bad prognosis factor in comparation with negativity due to a higher tendency for recurrence, large size or abdominopelvic place [2, 3]. Current studies show that this is not real, because ALK negative IMTs are related with a higher rate of metastases and deaths by the tumour [10, 11]. The metastases from IMTs have a predilection for lung, brain, liver and bones [10].

The differential diagnosis is extensive and depends on the anatomic site. It includes the inflammatory pseudotumour, denditric cell neoplasm, low grade sarcomas as myxoid fibrosarcoma, sarcomatoid variant of anaplastic large cell lymphoma and nodular fasciitis [11].

For making an accurate diagnosis, the immunohistochemical studies are essential. The myofibroblastic cells are frequently immunoreactive for vimentin, smooth muscle actin, muscle specific actin, and less commonly for desmin, cytokeratin and CD68 [11]. They are no immunoreactive for S-100, CD117, CD23 and c-kit [2]. Cytoplasmic immunoreactivity with anaplastic lymphoma kinase occurs in 50% of cases [11].

The main treatment is surgical. When possible, a total resection of the lesion is curative [2, 4, 6, 7, 9]. Nevertheless, the upper airway adds an extra level of complexity because the healing process may result in stenosis as result of inflammation and scar formation [7].

There are some reported surgical techniques as the electrocautery or the KTP laser with very good results [7].

In cases where surgical treatment is not possible (cases with locally advanced neoplasm), there is multifocal or metastatic disease, or it's not possible achieving a complete resection of the lesion, radiotherapy and chemotherapy are useful tools [2–4, 9]. There are many combinations reported employing chemoterapics, but there is not a standard treatment. [9]. Crizotinib is an ALK inhibitor useful in ALK positive cases [2, 3, 6, 9]. Due to its efficacy, the U.S National Comprehensive Cancer-Network recommends the use of crizotinib as the standard of care for locally advanced or metastatic ALK positive IMT [9]. In this case, we achieve a nearly total resection, so we employ crizotinib as adjuvant treatment. Nowadays, two years after the end of treatment, this patient has no relapse.

Conclusion

Inflammatory myofibroblastic tumours are rare in upper airways. Its treatment and prognosis are different in relation with a rearrangement involving the ALK locus on chromosome 2p23. The optimal treatment is the total resection. In other cases where there is not possibility of achieving a complete resection, crizotinib could be employed as adjuvant tool in ALK + neoplasms.

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