Right Middle Lobe Syndrome in Sisters

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Recurrent respiratory infections began shortly after birth in two sisters who were neither atopic nor dysgammaglobulinemic. Both had extremely large amounts of mucus secretion as the cause of this condition. Such secretion could also be the initiating factor for the sinusitis and bronchiectasis of Kartagener's syndrome.

The occurrence of the right middle lobe (RML) syndrome in children is quite rare. In 1966, Dees and Spock reported a series of 30 patients over a span of ten years. In this group, only one instance of siblings is cited and these patients had dysgammaglobulinemia with IgA deficiency.

In 1967, Danielson and colleagues reported a family with four of five siblings with RML bronchiectasis—all with a strong history of being atopic, having sinusitis, but no dysgammaglobulinemia.

I present two sisters with RML syndrome who were not atopic or dysgammaglobulinemic and who had no evidence of sinusitis. The one obvious abnormality present in both was an almost unbelievable secretion of mucus from the nasopharynx. I believe these cases are a specific entity, etiologically related to Kartagener’s syndrome and not amenable to the usual forms of therapy.

Case Reports

The disease process in these children actually began shortly after birth. The older child, patient A, was born in 1957. She had very frequent respiratory infections complicated by tonsillitis and otitis media. Despite her illnesses, she grew and developed normally. At age four, she had a tonsillectomy and adenoidectomy. At age six, she had an unexplained episode of anaphylactoid purpura. The exact preceding illness was never defined. No specific allergies have ever been determined.

The younger child, patient B, was born in 1961. Her respiratory difficulty began at five days of age when she developed a left pneumothorax and pneumonia. This responded well to treatment with tetracycline, oxygen, and mist. A chest roentgenogram taken at age 14 days was normal. This child, too, had very frequent upper respiratory infections with numerous complications. Her development, however, was normal.

Both children became ill in March of 1967 exhibiting a cough that was more persistent than usual. Chest films showed RML pneumonia in both. They were treated with antibiotics and expectorants. There was some improvement but the rather severe coughing remained. Sweat chloride determinations were done in May of 1967. The values were 35 and 52 mEq/liter for patient A and B, respectively. Tuberculosis skin tests were also done at that time and the results were negative.

These children first came under my care on August 8, 1967. Results of examinations at that time were remarkably similar. Both had normal vital signs and fell within the same percentiles as far as measurements of height and weight were concerned. Both had clubbing of the nails and boggy, pale nasal mucosa with an extreme amount of mucus production. Rales and wheezes were clearly audible over the right lateral and posterior chest in each child. Both had chest roentgenograms which showed RML pneumonia.

Laboratory values obtained at that first visit were as follows:

Patient A: CBC: hemoglobin, 12.5 gm percent; hematocrit 37; white blood cell count, 13,000 with a differential of 1 eosinophil, 1 stab cell, 76 segmented cells, 2 lymphocytes, and 1 monocyte. Urinalysis: the results were normal. Throat culture grew alpha streptococci, Neisseria, and Micrococcus minima. Sputum examination revealed no acid-fast bacilli.

Patient B: CBC: hemoglobin 11.4 gm percent; hematocrit 35; white blood cell count 6,250 with a differential of 1 eosinophil, 46 segmented cells, 50 lymphocytes, and 3 monocytes. Urinalysis; the results were normal. Throat culture and sputum examinations gave the same results as those for patient A.

Treatment was started with oral penicillin V and continued for ten days. Expectorants were also used. Little or no change was noted either physically or on the roentgenograms. Bronchograms were performed on September 15, 1967. These showed RML collapse in patient A and bronchiectasis of the medial segmental bronchus of the RML in patient B. Patient B had a RML lobectomy performed on October 5, 1967. Examination of the removed lobe showed dilated bronchi and bronchioles to the periphery of the lung. It also showed the lobe to be nearly airless. Similar pathologic findings were exhibited in patient A after lobectomy was performed on October 6, 1967. Patient A had a slightly more stormy postoperative course in that she developed pneumonia and collapse of the left lower lobe. However, she recovered with the usual therapy of antibiotics, oxygen, and cough encouragement.

Both girls had a nearly complete remission of cough for several weeks but it gradually reoccurred. Their chests, however, remained clear to auscultation. Their weight, appetite, and general appearance improved markedly.

On February 22, 1968, allergy skin tests were performed on both patients. No significant reactions were noted, but because of the seriousness of the situation and reports that some patients with increased susceptibility to respiratory infections respond well to it, a vaccine consisting of the following was started: horse dust, ten assorted molds, Alternaria, B. coli, Staphylococcus aureus, H influenza and nonhemolytic Streptococcus.

Immunoglobulin (IgM, IgA and IgG) determinations on both patients’ serums were done at the Indiana University Medical Center. All were normal. Sweat chloride tests were
repeated and were normal. Sinus radiographs were done on April 28, 1968 and showed practically complete lack of sinus development in both patients.

Consultation was obtained at the Mayo Clinic in September of 1968. Sputum and gastric washing cultures were obtained there and showed no unusual findings. No additional diagnoses were obtained from this consultation.

Since then, these patients have remained generally healthy. Upper respiratory infections are very frequent but do not always require antibiotic therapy. Postural drainage is employed daily but only very small amounts of mucus are obtained. There had been no recurrence of pneumonia. The pulmonary osteoarthropathy has decreased. The massive production of eosinophil-free nasal mucus remains present, especially in patient A.

The history of the remaining members of the family is not significant as far as this type of illness is concerned. There are three male siblings, aged 12, 5, and 4. The five-year-old had had recurrent urticaria and joint swelling with some of his episodes of tonsillitis. Other than that, there is no family history of allergy or suggested immunoprotein abnormality. Both parents are well. There was no problem noted in the mother's prenatal or perinatal course with either patient.

**COMMENT**

RML disease in children may be divided into the following four categories: (1) aspiration of foreign bodies, (2) atopy or immune mechanism deficiency such as asthma or dysgammaglobulinemia, (3) congenital syndromes such as Kartagener's, and (4) idiopathic.

The predisposition of the RML to obstruction from aspiration of foreign bodies and/or mucus is well known and need not be reiterated here. However, I believe it is wise to refresh the memory concerning Culiner's theory of the etiology of the RML syndrome. He points out that the RML is nearly totally isolated from the right upper lobe, depending upon the completeness of the fissure, and completely isolated from the right lower lobe. Therefore, there is little or no collateral aeration from contiguous lobules through the pores of Kohn. This then prevents this lobe from effectively emptying its bronchi by the cough mechanism.

The relationship of atopic conditions such as asthma and RML disease are easy to understand, as are the dysgammaglobulinemic states with their marked susceptibility to respiratory infection. The congenital and idiopathic syndromes probably account for most of the cases of RML syndrome. Since these children had respiratory symptoms dating to shortly after birth and since all of the other known etiologies of such symptoms have been ruled out, one must assume that their RML syndrome is due to a congenital structural anomaly of the RML, an unusual predisposition secondary to a recognized factor, i.e., excessive mucus production, or an unknown cause. Bronchography, surgery and pathologic study of the surgical specimens reveal no structural anomaly so the final two categories must be considered. It is with this in mind that Kartagener's syndrome and its variations are reviewed.

**Kartagener's Syndrome**

There are many variations of Kartagener's syndrome. The original description, which I feel should always be closely adhered to when one chooses to use this term, dates back to 1933 when Kartagener made his first report. The essential features were bronchiectasis, situs inversus, and sinusitis. Actually, Gunther reported the same condition in 1923.

Variants of Kartagener's syndrome were reviewed in 1957 by Overholt and associates. In this article he refers to Churchill's theory that there is an altered secretory activity of the respiratory tissues which would readily explain the selectivity of the site of infection. It is in this area that these reported cases probably fall. The respiratory mucous membrane cannot be continuously or repeatedly visualized as can that of the nasopharynx, but the mucous membrane of the nasopharynx and sinuses is known to be continuous with the bronchial mucous membrane and probably secretes in a similar fashion. Even if it did not, it has been shown that the secretions from nasal sinuses will drip into the lungs, particularly when the patient is asleep. The same would be true of the nasopharynx.

Certainly these patients secrete enough mucus from the nasopharynx to account for their unusual susceptibility to respiratory infection and their chronic lung disease. As their paranasal sinuses grow and develop, these patients may exhibit the sinusitis included in Kartagener's triad. I believe that these cases support the theory of Knox and colleagues that bronchiectasis is secondary to chronic bronchitis and I would add to this that chronic bronchitis is secondary to excessive secretion of mucus in the respiratory epithelium. This would then indicate that Kartagener's syndrome does not prove that bronchiectasis is congenital, but predisposition to it is. The predisposing factor would then be the excessive production of mucus.

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Neoplasms within the Pulmonary Veins*

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Propagation of tumor thrombus from a primary or secondary pulmonary neoplasm with direct extension within the pulmonary veins into the left atrium is a rare form of cardiac metastasis. Aside from the present report, 15 previous cases have been described. Systolic cardiac murmurs were heard in three cases. Although "protective" pulmonary arterial thickening has been reported in cases of narrowing of the pulmonary veins, no such vascular changes were observed in the lungs in this case.

Propagation of tumor thrombus from neoplasms of the lung with direct extension within the pulmonary veins into the left atrium is a rare form of cardiac metastasis: 15 cases have been previously described.

**Case Report**

A 56-year-old white man had an above the knee amputation of the right leg for a pleomorphic rhabdomyosarcoma in October, 1967. Chest x-rays in May, 1968, revealed metastatic lesions of the lungs; during the subsequent ten months he was treated with a variety of chemotherapeutic agents with no response.

He complained of occasional hemoptysis in November, 1968, which progressed until February, 1969, when he was hospitalized because of the copious production of bloody sputum. Physical examination revealed bilateral crepitant rales. A split first heart sound was reported; no murmurs were heard. The patient, noted to be dyspneic throughout his six-day hospitalization, had a sudden, severe episode of dyspnea and cardiopulmonary arrest.

There was no electrocardiogram taken during the final admission. Electrocardiograms during the prior year had been normal. X-ray pictures taken on admission revealed multiple pulmonary metastases. Six days later, the cardiac silhouette was moderately enlarged with specific left atrial prominence. The bulging left auricular appendage was visible on the left heart border. A small left pleural effusion was present and the vessels in the left upper lobe were engorged (Fig 1a and b).

At autopsy the significant findings, aside from the well-healed amputation, were limited to the heart and lungs. Multiple, large, round pulmonary metastases were present bilaterally. The tumor, which filled the left lower, right lower, and part of the right upper pulmonary veins extended into the left atrium and there joined to form a nonadherent, 7 × 5 cm ovoid mass. The intra-atrial mass, while not protruding through the mitral valve, nested in its orifice (Fig 2). The right ventricle, although not hypertrophied, was dilated. Microscopically, the pleomorphic rhabdomyosarcoma showed cross-striations of an occasional oblong cells.

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FIGURE 1a (upper) and 1b (lower). Aside from metastatic tumor, x-ray films taken at a six day interval reveal enlargement of the left atrium, a small left pleural effusion, and vascular engorgement of the left upper lobe.