Kartagener's Syndrome*

R. Drew Miller, M.D., F.C.C.P., and Matthew B. Divetie, M.D., F.C.C.P.

Clinical observations of 19 patients with Kartagener's syndrome seen during the past 25 years support the concept of congenital functional or anatomic defects in the mucociliary epithelium and its supporting structures. The case of a woman with this syndrome, who is alive at the age of 72 years, is detailed to suggest that, with reasonable medical supervision, the syndrome is compatible with a full life span.

Siewert reported the first definite case of bronchiectasis associated with situs inversus in 1904, but it was Kartagener's detailed study of 11 cases that implicated a common pathogenic predisposition and led to the association of that author's name with the syndrome. Because of the high incidence of sinusitis in these cases, the more exclusive criterion of Kartagener's triad often has been used. Because sinusitis is common in otherwise normal subjects with bronchiectasis, it is not surprising that the triad usually is present in patients with this combination of congenital maldevelopment and bronchiectasis in which disease of the nasal sinuses forms the least distinctive feature. Bronchiectasis occurs in as many as 25 percent of patients with situs inversus and probably in less than 0.5 percent of the general patient population. On this basis, it seems likely that some combination of immunologic or structural defects exists from birth, although their exact nature is not yet certain.

The purpose of this study was to add to the first report from this institution by A. M. Olsen, who described 14 patients with this syndrome in 1943. Subsequently, Mayo and Rice, writing on abdominal surgical challenges of situs inversus, mentioned 17 patients, of whom 14 were described in Olsen's original report. In addition, we would like to call attention to the case of a 72-year-old woman, who is to our knowledge the oldest survivor with the triad.

*From the Mayo Clinic and Mayo Foundation, Rochester, Minnesota. Reprint requests: Section of Publications, Mayo Clinic, Rochester, Minnesota 55901

Material and Results

One hundred and six patients with complete or partial situs inversus were seen at the Mayo Clinic during the past 27 years since Olsen's report covering the preantibiotic era. Nineteen of these fulfilled the criteria of Kartagener's triad, and their clinical characteristics are summarized in the Table. Situs inversus was documented by physical examination, thoracic roentgenograms, and electrocardiographic characteristics. Bronchiectasis was documented by a history of chronic production of purulent sputum and roentgenographically by accepted criteria. In most cases, additional confirmation was obtained at bronchoscopy by the presence of purulent secretions or bronchitis or by typical bronchographic changes. Because at our institution we obtain bronchograms on potential surgical candidates only, bronchoscopy was not done on patients who had extensive bilateral disease or other conditions that precluded curative pulmonary resection. Roentgenographic evidence of sinusitis was absent in two patients, but each had a history of recurrent nasal symptoms. In some cases, roentgenographic studies of the gastrointestinal tract confirmed that the transposed gastric bubble and hepatic shadow were due to complete situs inversus of the gastrointestinal tract.

The average age of the 19 patients with the triad was 26 years, whereas of the remaining 87 it was 28 years. In the total group of 106 patients, the ages ranged from a few months to 72 years, and the sex distribution was equal. Significant cardiovascular abnormalities were conspicuously absent in those with the triad, whereas there were 28 instances of cyanotic or other significant defects among the 87 patients in whom bronchiectasis was absent. Only six patients had bronchiectasis that was sufficiently localized to allow effective resection when symptoms warranted surgical intervention. Several patients underwent sinus or ear surgery. In the remainder, antibiotic therapy was used intermittently to control recurrent infection.

Our 19 cases of Kartagener's syndrome added to the 14 described by Olsen and the additional three mentioned incidentally by Mayo and Rice bring the total from the Mayo Clinic to 36, or about 10 percent of the number reported in
the world literature. These 19 cases are gleaned from 106 cases of situs inversus seen during a period when 1.3 million patients were examined at our institution. This gives an incidence in a selected population of about 1 in 12,000, which is similar to the 1 in 8,000 noted in a mass roentgenographic survey of a Norwegian population. The incidence of Kartagener's syndrome at our institution among persons with visceral transposition was 18 percent, similar to that reported by Olsen in the preantibiotic era. In the Mayo Clinic population, the incidence of Kartagener's syndrome from these figures is 1 in 68,000.

**REPORT OF THE CASE OF OUR OLDEST PATIENT**

A farmer's wife was first seen at the Mayo Clinic on September 6, 1967, when she was 88 years old. Her presenting complaint was aching in both legs. The aching was associated with stiffness, was worse on arising, and spread to involve her arms and shoulders. At times, physical activity aggravated the leg pain, suggesting intermittent claudication. Inventory of systems revealed that the patient had a productive cough all of her adult life. She sometimes coughed one-half cup of yellowish green sputum daily. Over the previous five years, she had noted wheezing upon recumbency and exertion.

Physical examination revealed coarse rales and wheezing, most severe over both lung bases posteriorly. She had a low-grade basilar ejection murmur at the left sternal border, and an area of cardiac dullness was in the mirror-image position on the right. The liver edge was just palpable along the left costal margin, and gastric-bubble resonance was noted on percussion over the lower right anterior rib margin. There was muscle tenderness in the deltoid and calf areas, and muscle testing showed moderate degrees of weakness of the deltoids, biceps, iliopsoas, hamstrings, and glutei.

Significant hematologic findings were a blood hemoglobin level of 10 gm per 100 ml, erythrocyte sedimentation rate of 105 mm in 1 hour (Westergren), low serum albumin level of 2.0 gm/100 ml, and a high borderline γ-globulin value of 1.62 gm/100 ml. Thoracic roentgenograms confirmed situs inversus and showed increased bilateral basilar markings characteristic of bronchiectasis (Fig 1). Roentgenograms of the paranasal sinuses showed pansinusitis. Roentgenograms of the stomach and colon confirmed situs inversus totalis. The usual leads of the electrocardiogram indicated situs inversus (Fig 2), and the precordial leads showed reversion to the right (Fig 3). In a muscle biopsy and temporal artery biopsy, there were changes consistent with polyarteritis nodosa. Cortisone was administered orally, 100 mg, four times daily. The dose was reduced in one week to 50 mg four times daily, with amelioration of muscle aching and weakness.

Thirteen months later, the patient was hospitalized because of hemoptysis. Steroid medication had been discontinued within two months after her previous examination. Results of physical examination were similar to those of the previous visit, except that there was no muscle weakness or vascular tenderness. Antibiotic therapy (based on data from sputum cultures), inhalation of heated mist, increased fluids by mouth, chest physical therapy, and postural drainage changed sputum color from green to white and reduced the daily volume from 6 ounces to 1 ounce. The patient returned on several additional occasions because of complete heart block and biventricular failure with moderate dependent edema. A temporary transvenous pacemaker improved ventricular efficiency, and a permanent pacemaker was then implanted. A long-term program of monthly use of ampicillin or a similar broad-spectrum antibiotic for a six- to ten-day period controlled sputum production adequately. The main basis for the periodic examinations was the evaluation of the cardiac pacemaker.

The hemoglobin level had increased to an average of 12 gm/100 ml, and the sedimentation rate varied between 57 and 67 mm in 1 hour (Westergren). The values for IgA, IgM, and IgG were 3.15, 3.55, and 17.5 mg/100 ml, respectively; the IgM and IgG levels were above the normal range for our laboratory. One year later, the IgG level was normal but that of the IgM remained high at 4.7 mg/100 ml. At no time was immune globulin deficiency detected, and at the age of 72 years, she continues to be reasonably active.

**COMMENT**

The bronchiectasis of Kartagener's syndrome is morphologically indistinguishable from that seen in children as a result of severe respiratory infections. However, the true incidence of bronchiectasis in the general population is difficult to determine because its clinical features are frequently indistinguishable from those of bronchitis, which is usually a concomitant feature. Approximately 20 percent of patients with situs inversus have bronchiectasis and sinusitis, a much higher frequency than the estimates available for sinopulmonary disease in the general population, which has been estimated to be less than 0.5 percent. Such a frequency of association has lent support to the belief that the cause and relationship of bronchiectasis to situs inversus are congenital.

Isolated dextrocardia is almost always associated with other cardiac anomalies, which are often serious. When accompanied by situs inversus, serious cardiac malformations are less common, but

![Figure 1. Posteroanterior thoracic roentgenogram showing situs inversus and increased basal markings characteristic of bronchiectasis.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21543/)
these and anomalies of skeleton, spleen, and other viscera have been described. Sinus involvement in Kartagener's triad is the least distinctive sign of the syndrome and has included absence or hyperplasia of one or more sinuses, polyposis, or simple infections. However, sinusitis is frequently found with bronchiectasis in patients who have no visceral maldevelopment, and its presence suggests widespread infection of the respiratory tract. Kartagener's triad is not characterized by hemodynamically significant heart disease, and the sinopulmonary suppurative disease (which is its symptomatic feature) is similar to that of simple sinusitis and bronchiectasis in otherwise normal patients. The patients in our series had a pattern similar to that described by others, which classically is that of repeated respiratory infections since early childhood, recurrent pneumonias, otitis media with its complications, cough of a variously productive nature, hemoptyis of variable occurrence and degree, and eventually respiratory and cardiac failure. The use of antibiotics has greatly reduced the severity and incidence of these infectious problems and has lessened the need for surgery. Only six of the patients in our series required operation, a proportion similar to that reported by Logan and coworkers.

Because of the geographic distribution of the patient population at our institution, sibling studies and prolonged investigations were not possible for this particular study. However, others have studied various aspects of this interesting association of abnormalities. Olsen agreed with the opinion of the time that inherited defects of the respiratory tract predisposed to bronchiectasis and sinusitis in patients with situs inversus. The complete syndrome has a high familial incidence, appearing only in one generation, and multiple siblings may have various combinations of its components, which do not appear in their children. It has been noted in monozygotic twins but, as in our series, shows no particular sexual predilection. These features
and the high incidence of consanguinity among the apparently normal parents of affected children support the contention that the genetic abnormality is carried as an autosomal recessive. Phenotypic variations have been described and are probably due to a single genetic abnormality.

Bronchiectasis is principally a pediatric problem, and in about half of the affected persons, the onset of respiratory symptoms can be traced to before the age of three years. In an adult population, the time of childhood onset is more difficult to determine, but seven of our patients were less than ten years old. In five of these, respiratory symptoms were present within the first three years of life. Infection and atelectasis are believed responsible for the bronchial dilatation, which is cylindric at first but, as the disease worsens, changes to the more destructive saccular type. Deficiencies of bronchial supporting structures, the production of abnormal secretions as occurs in mucoviscidosis, and ineffective mucociliary clearance mechanisms have been considered singly or in combination as possible pathogenetic factors. Mucoid impaction accompanying bronchiolitis in infancy or childhood is believed to be the cause of bronchiectasis in the Swyer-James or MacLeod syndrome and also could be responsible for the suppurative pulmonary disease either in its simple form or when it is associated with situs inversus. Mechanical obstruction of main bronchi by a malrotated heart in Kartagener's syndrome has been considered, but supporting evidence is lacking. The association of nasal polypsis has raised the possibility of hypersensitivity to environmental antigens in patients with the triad, and one of our patients had a history compatible with allergic bronchopulmonary and sinus diseases. Generally, however, the accumulated information does not support a mechanism of this kind.

Recurrent infections of the respiratory tract and nasopharyngeal cavities have directed attention to deficiencies of immunologic defense mechanisms.
Table 1—Clinical Characteristics of 19 Patients with Kartagener's Triad

<table>
<thead>
<tr>
<th>Sex</th>
<th>First Examined</th>
<th>Last Examined</th>
<th>Major Symptom</th>
<th>Pulmonary Surgical Treatment</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>38</td>
<td>—</td>
<td>Cough, recurrent infection</td>
<td>—</td>
<td>No current sinusitis clinically</td>
</tr>
<tr>
<td>M</td>
<td>52</td>
<td>—</td>
<td>Dyspnea, occasional hemoptysis</td>
<td>—</td>
<td>No current sinusitis clinically</td>
</tr>
<tr>
<td>M</td>
<td>26</td>
<td>27</td>
<td>Cough, green sputum</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>34</td>
<td>—</td>
<td>Cough, green sputum, purulent nasal discharge</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>5</td>
<td>7</td>
<td>Cough since age one yr</td>
<td>Lobectomy (rt lower lobe at age five yr)</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>8</td>
<td>—</td>
<td>Productive cough since birth</td>
<td>—</td>
<td>Nasal polypoid hyperplasia</td>
</tr>
<tr>
<td>F</td>
<td>17</td>
<td>—</td>
<td>Productive cough, dyspnea</td>
<td>Lobectomy (lt lower and middle lobes)</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>5/12</td>
<td>18</td>
<td>Hay fever, asthma, cough</td>
<td>—</td>
<td>Thoracic transposition only, hay fever and asthma, Lt aortic arch</td>
</tr>
<tr>
<td>M</td>
<td>56</td>
<td>—</td>
<td>Cough, yellow sputum</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>2</td>
<td>—</td>
<td>Cough, wheeze, recurrent pneumonia</td>
<td>—</td>
<td>Thoracic transposition only</td>
</tr>
<tr>
<td>F</td>
<td>25</td>
<td>25</td>
<td>Cough, foul sputum</td>
<td>—</td>
<td>Antral windows</td>
</tr>
<tr>
<td>M</td>
<td>62</td>
<td>—</td>
<td>Cough, foul sputum</td>
<td>Lobectomy (lt lower and middle lobes)</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>2</td>
<td>20</td>
<td>Cough, sputum</td>
<td>—</td>
<td>Antral windows, thoracolumbar scoliosis</td>
</tr>
<tr>
<td>M</td>
<td>8</td>
<td>18</td>
<td>Cough, recurrent infection</td>
<td>—</td>
<td>Thoracic transposition only, stomach bubble on Lt</td>
</tr>
<tr>
<td>M</td>
<td>22</td>
<td>—</td>
<td>Cough, sputum</td>
<td>Lobectomy (rt lower lobe)</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>27</td>
<td>—</td>
<td>Cough, sputum, nasal discharge</td>
<td>Previous lobectomy (lt lobe)</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>7</td>
<td>13</td>
<td>Cough, sputum</td>
<td>Lobectomy (rt lower lobe)</td>
<td>Submucous resection</td>
</tr>
<tr>
<td>F</td>
<td>33</td>
<td>—</td>
<td>Cough, sputum, nasal stuffiness</td>
<td>—</td>
<td>Complete allergy skin tests</td>
</tr>
<tr>
<td>F</td>
<td>68</td>
<td>72</td>
<td>Leg aching, cough, dyspnea</td>
<td>—</td>
<td>Complete heart block, congestive failure, pacemaker</td>
</tr>
</tbody>
</table>

The ataxia-telangiectasia syndrome is transmitted as an autosomal recessive. It is characterized by conjunctival telangiectasia and cerebellar ataxia and is complicated by recurrent sinopulmonary infection. IgA forms the major part of antibodies in external secretions and protects specific areas from infection. IgA has been found to be deficient, both in the serum and in the parotid saliva of patients with this neurologic disorder. However, a deficiency was not found in the saliva of five patients with Kartagener's syndrome reported by Holmes and associates. Deficiency of this immunoglobulin is found in apparently healthy subjects, but the influence of a delay in its appearance in external secretions, as occurs normally in the neonatal period, is of potential importance in the genesis of bronchiectasis, both alone and in association with Kartagener's triad. Holmes and associates also noted transient deficiency of IgG in early life in two instances. There was no deficit of immunoglobulins in the elderly patient in our series.

The possibility that cell-mediated immunity might be abnormal in Kartagener's syndrome, with resulting disturbances in delayed hypersensitivity, also has been considered. However, the thymic and lymphatic tissues have a normal appearance, and an appropriate cutaneous response develops to standard antigenic challenge by purified protein derivative, mumps antigen, and Candida albicans. These features distinguish patients with the triad from those with ataxia-telangiectasia, Swiss-type agammaglobulinemia, or the Wiscott-Aldrich syndrome, in all of which recurrent infections are characteristic features. The significance of systemic vasculitis in our 72-year-old patient is uncertain and probably should be regarded as coincidental. Certainly, bronchiectasis is not a recognized feature of diffuse vasculitis of this type or of such connective tissue disorders as systemic lupus erythematosus, in which a disordered immunomechanism exists.

A study of the 19 patients with Kartagener's syndrome in our series has not yielded a specific clue as to the pathogenesis of the various elements of the triad or their coincidental development. In spite of an increased breadth of knowledge from which to speculate, there has been no incisive penetration of the depth of our understanding since the original descriptions were written. However, the...
occurrence of the triad in a 72-year-old woman indicates that, with reasonable medical supervision, it is compatible with a full life span.

ACKNOWLEDGMENT: We feel highly privileged to participate in the A. M. Olsen Festschrift, for he has been to us a teacher and still, as our colleague, remains a teacher. His medical interests continue as broad in scope as they extend in various areas in depth. He has studied and written on both the esoteric and the importantly commonplace. It is to the former of these areas that we wish to contribute in this issue.

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