Introduction

The first case of relapsing polychondritis (RP) was reported in 1923 by Jaksch-Wartenhorst who called it 'polychondropathy', and highlighted the most common clinical features\(^1\). He described a 32-year-old male patient who presented with fever, asymmetric polyarthritis, pain, swelling and deformity of the ears and nose, as well as stenosis of the external auditory canals, which resulted in diminished hearing. Biopsy of the nasal cartilage revealed loss of cartilage matrix and a hyperplastic mucous membrane.

The estimated annual incidence rate is 3.5/million. It mostly occurs between the ages of 40 and 60 years with an average age of 47 years but cases at both extremes of life have been observed\(^2,3\). It seems to occur with similar frequency in both sexes; however, in a recent review of 66 patients, Trentham and Le found a female-to-male ratio of 3:12. Relapsing polychondritis can occur in all racial and ethnic groups, with whites predominantly being affected.

Since the initial description, more than 1,000 cases of RP have been reported adding clinical features\(^4,5\), but the involvement of the larynx is almost rare, and must be differentiated from neoplastic forms\(^6\). We here describe our case of laryngo-tracheal RP with dyspnoea and we will report a review of the literature about RP cases.

Case report

A 49 year-old female patient came to our attention in July 2007 for acute dyspnoea, transferred by the Department of Rheumatology of our
University where she had been admitted with a suspected Wegener’s granulomatosis.

Symptoms had begun in June 2004 when diffuse pain of large and small joints and a raised temperature had occurred. She had been admitted several times to medical wards and always treated with antibiotics and cortisone. The laryngeal symptoms were underestimated, but history of dysphonia was present since one year.

The only abnormal results were:
- Sedimentation rate 1°hr: 120.0 mm (2.0-20.0);
- Protein C-reactive: 8.11 mg/dl;
- Fibrinogen 536.0 mg/dl (150.0-450.0).

Increase in transaminase: SGOT 108.0 U/L (up to 31), SGPT 93.0 U/L (up to 41);
- Tests of antibodies (ANA, AMA, SMA, LKM, SMA (ACTINE), Gastric Wall Cells, Basal Membrane), of anti-neutrophyl type C citoplastic (PR3) antibodies, anti-neutrophyl type P perinuclear (MPO) antibodies and rheumatoid factor were all negative.

An ultrasound liver scan, justified by a raised level of transaminase, indicated a possible autoimmune liver pathology.

The following investigations were done: endoscopic examination with a flexible optic, which showed an overall reduction in volume of the larynx with a reduced opening (Figs. 1 and 2) which explained the dyspnoea events.

A head-neck-thorax computed tomography (CT) with contrast enhancement which showed: disappearance of the quadrangular cartilage of the septum, with saddle nose deformity (Figs. 3 and 4), and of the external ear cartilages; ongoing dissolution of the front of the thyroid shield and cricoid ring (Figs. 5 and 6); thickening of the anterior-lateral two-thirds of the tracheal wall, extending to the walls of the main bronchi.

![Fig. 1: laryngoscopic view during breathing.](image1)

![Fig. 2: laryngoscopic view during phonation.](image2)

![Fig. 3: CT scan axial plane showing disappearance of external ear cartilages.](image3)

![Fig. 4: saddle nose deformities in lateral view of profile line.](image4)

![Fig. 5-6: CT scan axial plane displaying reabsorption of thyroid shield and cricoid ring.](image5)

The patient underwent a direct laryngoscopy under general anesthesia that showed more clearly the edema of laryngeal mucosa, the cartilages were bendable on palpation with laryngoscopic instruments, and biopsies were taken from the glottal and supraglottic areas, showing the presence of chronic unspecific inflammation. At this stage the diagnosis was more clearly confirmed. Over the next few days the worsening laryngeal dyspnoea made an urgent tracheostomy necessary.
The operation demonstrated a notable reduction in the tracheal diameter and the absence of cartilaginous tracheal rings; at the same time a tracheal biopsy was taken with negative results (see Fig. 7).

![Fig. 7: CT scan axial plane showing a tracheal narrowing.](image)

The patient after one year is still under steroid treatment for RP disease. The tracheostomy was left opened because of solved completely the airways obstruction, however the laryngeal space was unmodified, also after medical treatment, probably due to cartilage destruction.

**Discussion**

The first case of RP was first reported in 1923 by Jaksch-Wartenhorst who called it ‘polychondropathy’\(^1\). The estimated annual incidence rate is 3.5/million. It mostly occurs between the ages of 40 and 60. It seems to occur with similar frequency in both sexes, though in a recent review of 66 patients, Trentham and Le found a female-to-male ratio of 3:12. Relapsing polychondritis can occur in all racial and ethnic groups, with whites being predominantly affected.

A MEDLINE search displayed that since the initial description more than 1,000 cases of RP have been reported, adding various clinical features. However, a severe laryngeal involvement was rarely described. In the review of cases reported in MEDLINE we found 95 papers after search with keywords “laryngeal relapsing polychondritis”, we excluded non-English papers, commentary without abstract and animal cases; the articles about laryngeal RP suitable for a review were only 16, because most of papers were radiological description of airways in patients with systemic RP, description of patients with idiopathic cartilage disease, and duplicate of published cases.

The cause of polychondritis is still unknown. It was first suspected by Jaksch-Wartenhorst to be of degenerative origin, but since then evidence has accumulated to suggest the role of the immune system, and it should be known as one of autoimmune manifestation or fibro-osseous tissue lesions\(^6\) in ENT patients\(^7,8\).

The onset of the disease is usually sudden and severe, with characteristic clinical signs.

Auricular chondritis is present in almost all patients. Pain, red or violaceous discoloration, swelling and tenderness may involve one or both ears. Later recurrent or persistent inflammation results in cartilage destruction. Closure of the external auditory meatus may lead to hearing impairment. In addition inflammation of the middle ear and audiovestibular structures may cause sensorineural hearing loss and vestibular dysfunction.

Joints pain is a common presenting feature and patients are frequently first seen by a rheumatologist, as in our case.

Laryngo-tracheal complications are severe manifestations of the disease and predict a poor prognosis. The larynx and trachea are most frequently affected. Mortality from respiratory complications, mainly infections and tracheal collapse, has been reported to be between 10 and 50%\(^2,3,9\).

Nasal chondritis is seen in nearly 50% of the patients. Cardiovascular involvement occurs in 24% to 52% of patients. Renal disease is rare and may occur independently from an associated connective tissue disease (e.g. SLE)\(^10\). Dermatological manifestations, though frequent, are non-specific and cannot be defined as characteristic of RP\(^11\). Neurological disease, such as cranial myopathy, is particularly uncommon\(^12\).

The diagnosis of RP is relatively easy, based on characteristic clinical manifestations. Sometimes the diagnosis of RP can be overlooked due to its low incidence and atypical initial symptoms. There is often a delay in diagnosis with the initial presentation misdiagnosed as infection. Trentham et al. reported a mean delay of 2.9 years from the first visit to a doctor until diagnosis\(^2\). The delay was longer than one year for 68% of patients and one-third of patients attended five or more physicians before RP was diagnosed.

Diagnostic criteria were first described by McAdam et al. in 19763 and were summarized in Table I. Biopsy of involved auricular or other cartilage can confirm the diagnosis but biopsy may not be necessary in the presence of a typical clinical presentation. Three of six criteria need to be present.

More liberal diagnostic criteria were introduced by Damiani and Levine in 1979\(^13\), requiring only one of three criteria (Table II). A third set of diagnostic criteria were introduced by Michet et al. in 1986\(^14\) (Table III).
Only one of two criteria is needed and the criteria overlap with the prior proposed criteria sets. There has not been a consistent use of one set of diagnostic criteria over another. There are no specific or reliable markers for diagnosis of RP. In addition there are no reliable markers to determine disease activity. Tests generally demonstrate changes consistent with acute or chronic inflammation, such as elevated erythrocyte sedimentation rate (ESR), and C-reactive protein, normochromic/normocytic anaemia. Tests for rheumatoid factor, antinuclear antibodies or anti-neutrophil cytoplasmic antibodies (ANCA) are negative unless other coexisting autoimmune disease is present. Serum antibodies to type II collagen have been found in 20-50% of patients, a frequency that is too low for the presence of this antibody to be a useful diagnostic marker\(^{15,16}\).

Useful investigations, according to the case, are: conventional radiographs, computed tomography, three-dimensional or spiral magnetic resonance imaging, laryngoscopy, endobronchial ultrasonography, scintigraphy, pulmonary function tests, echocardiography\(^{3,10,17-21}\). Many imaging techniques have been used for evaluation and monitoring of patients with relapsing polychondritis. Chest radiography can detect tracheal and main bronchial narrowing\(^{22}\). Nuclear medicine may play a role in the initial work-up because bone scintigraphy has been shown to be helpful in suggesting the diagnosis in a handful of case reports\(^{23}\).

### Table I: Diagnostic Criteria for Relapsing Polychondritis by McAdam et al.\(^{4}\).

1. Recurrent chondritis of both auricles
2. Chondritis of nasal cartilages
3. Chondritis of the respiratory tract involving laryngeal and/or tracheal cartilages
4. Nonerosive inflammatory polyarthritis
5. Inflammation of ocular structures including conjunctivitis, keratitis, scleritis/episcleritis and uveitis
6. Choclear or vestibular damage manifest by neurosensory hearing loss, tinnitus and vertigo
7. Cartilage biopsy confirmation of a compatible histologic picture

### Table II: Diagnostic Criteria for Relapsing Polychondritis by Damiani and Levine\(^{11}\).

1. Inflammatory episodes involving at least two of three sites: auricular, nasal or laryngotraheal cartilage
2. One of those sites and two other manifestations, including ocular inflammation (conjunctivitis, keratitis, episcleritis, uveitis), hearing loss, vestibular dysfunction or seronegative inflammatory arthritis

### Table III: Diagnostic Criteria for Relapsing Polychondritis by Michet et al.\(^{12}\).

1. At least three of McAdam’s criteria, then no histological confirmation needed.
2. One or more of McAdam’s signs with histological confirmation.
3. Chondritis in two or more separate anatomical locations with response to steroids and/or dapsone.

### Table IV: Management of laryngeal RP: tracheotomy, although rarely, may be required in case of acute dyspnoea.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Cases</th>
<th>Surgical Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee, C C(^5)</td>
<td>2006</td>
<td>1</td>
<td>Tracheotomy</td>
</tr>
<tr>
<td>Heman-Ackah, Y (^25)</td>
<td>2005</td>
<td>1</td>
<td>Laryngoplasty</td>
</tr>
<tr>
<td>Sato, M(^6)</td>
<td>2010</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>Karaman, E(^7)</td>
<td>2010</td>
<td>3</td>
<td>Laryngoplasty (3)</td>
</tr>
<tr>
<td>Chang, S J(^8)</td>
<td>2005</td>
<td>1</td>
<td>Tracheotomy</td>
</tr>
<tr>
<td>Eliashar, R(^9)</td>
<td>2005</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>Kim, C M(^10)</td>
<td>2003</td>
<td>1</td>
<td>Tracheotomy</td>
</tr>
<tr>
<td>Narozny, W(^11)</td>
<td>2001</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>Spraggs, P D(^12)</td>
<td>1997</td>
<td>4</td>
<td>Tracheotomy (2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Laryngoplasty (1)</td>
</tr>
<tr>
<td>Port, J L(^13)</td>
<td>1993</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>Gaffney, R J(^14)</td>
<td>1992</td>
<td>1</td>
<td>None</td>
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<tr>
<td>Casselman, J W(^15)</td>
<td>1988</td>
<td>1</td>
<td>None</td>
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<tr>
<td>Dahlqvist, A(^16)</td>
<td>1983</td>
<td>1</td>
<td>Tracheotomy</td>
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<tr>
<td>Damiani, J M(^17)</td>
<td>1979</td>
<td>4</td>
<td>Tracheotomy (2)</td>
</tr>
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<td></td>
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<td></td>
<td>None (2)</td>
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<tr>
<td>Daly, J F(^18)</td>
<td>1966</td>
<td>1</td>
<td>Not available</td>
</tr>
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lower airways. Typical CT findings of relapsing polychondritis include subglottic stenosis, tracheobronchial luminal narrowing, densely calcified and thickened tracheal cartilage, peripheral bronchial narrowing and bronchiectasis, calcifications of the pinnae, and nasal cartilage collapse\(^{(10)}\).

There are no specific tests for diagnosis, which is principally clinical. Biopsy of perichondrial tissue from ear cartilage may confirm the diagnosis, though nasal and tracheal biopsies rarely provide characteristic findings. In fact when the clinical picture strongly suggests polychondritis, a biopsy, in our opinion, is superfluous.

Relapsing polychondritis generally shows an intermittent but progressive course. Sites of involvement, the severity of inflammation, inner organ manifestations and response to therapy are unpredictable.

The life expectancy of patients with RP is reduced. Common causes of death are respiratory or cardiovascular complications, secondary infections, renal failure or systemic vasculitis. The nature of airway problems is diverse, with tracheomalacia being the most common; airway intervention is frequently required and in experienced hands results in symptom improvement\(^{(24)}\). Acute airway obstruction intractable with medical therapy may require tracheostomy, and patients with laryngo-tracheal collapse could be managed with stent positioning or laryngoplasty\(^{(25)}\). Tracheostomy has been recommended for patients with localized subglottic involvement\(^{(26)}\).

The tracheotomy should be opened very attentively, because of the possible damage of the cartilage rings, which are affected by the chronic inflammation. This emergency procedure may represent the only lifesaving treatment in case of acute dyspnoea as showed in several reports\(^{(12,10,12,24,27)}\) and in our case as well (Table IV). Tracheotomy could compromise other successive treatments, such as laryngotracheal reconstruction, which may be performed after medical therapy\(^{(4)}\). However, it carries a serious risk by inducing fatal airway obstruction because the small glottis resulting from cartilaginous destruction may make intubation difficult during anesthesia\(^{(5)}\). The role of surgery is mainly the management of the acute respiratory distress.

As well as in other disorders of unknown aetiology, the treatment of RP is only symptomatic. Corticosteroids are the mainstay of treatment to date; they decrease the frequency, duration and severity of flares.

In 1992 Gaffney et al. reported a case of relapsing polychondritis of the larynx and upper trachea managed with the use of nebulized racemic ephedrine, to reduce the airway edema, which characterizes acute exacerbations of the disease\(^{(28)}\).

In patients who are unresponsive to or are intolerant of steroids, or where the high steroid dose contends with other agents, immunosuppressive drugs may be useful. Because of there is no standard medical therapy for RP an individual approach is necessary.

### Conclusion

As can be seen the diagnosis of RP today remains very difficult, when those cases presenting with typical clinical characteristics are excluded. The delay in diagnosis of our patient was considerable and had severe consequences. The literature states that delay in diagnosis is now estimated to be about 2.9 years and that patients are seen by several doctors, sometimes as many as five, before a diagnosis is made. The case of our patient coincides with these figures exactly. Perhaps an ENT examination would have hastened the diagnosis when the obvious laryngo-tracheal involvement is considered. The present clinical picture should be kept in mind during examination of a dyspnoeic patient. A tracheotomy may represent an emergency procedure that may be required in RP patients.

### References


Corresponding Author:
FRANCESCO LORUSSO
Via Isidoro La Lumia n 80
90139 Palermo (Italy)