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Primary ciliary dyskinesia in adults

Dyskinésie ciliaire primitive chez l'adulte

English / French

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KEYWORDS
Primary ciliary dyskinesia;
Kartagener's syndrome;
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Sinusitis

Summary
Introduction. — Primary ciliary dyskinesia is an autosomal recessive genetic disorder leading to structural and/or functional abnormalities of motor cilia. Impaired mucociliary clearance is responsible for the development of a multi-organ disease, which particularly affects the upper and lower airways.
State of the art. — In adults, primary ciliary dyskinesia is mainly characterized by bronchiectasis and chronic ear and sinus disorders. *Situs inversus* is found in half of patients and fertility disorders are commonly associated. Diagnosis is based on specialized tests: reduced level of nasal nitric oxide concentrations is suggestive of primary ciliary dyskinesia, but only a nasal or bronchial biopsy/brushing with analysis of beat pattern by videomicroscopy and/or analysis of cilia morphology by electronic microscopy can confirm the diagnosis. However, the diagnosis is difficult to achieve due to the limited access to these specialized tests and to difficulties in interpreting them. Genetic tests are under development and may provide new diagnostic tools. Treatment is symptomatic, based on airway clearance techniques (e.g., physiotherapy) and systemic and/or inhaled antibiotics. Prognosis is related to the severity of the respiratory impairment, which can be moderate or severe.
Perspectives and conclusions. — Diagnosis and management of primary ciliary dyskinesia remain poorly defined and should be supported by specialized centers to standardize the diagnosis, improve the treatment and promote research.

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MOTS CLÉS
Dyskinésie ciliaire primitive ;
Syndrome de Kartagener ;
Monoxyde d'azote nasal ;
Dilatation des bronches ;
Sinusite

Résumé
Introduction. — La dyskinésie ciliaire primitive est une maladie génétique autosomique récessive, à l'origine d'anomalies structurales et fonctionnelles des cils moteurs. Les altérations de la clairance mucociliaire sont responsables d'une atteinte multi-organes prédominant sur les voies aériennes supérieures et inférieures.
État des connaissances. — L'atteinte clinique est marquée chez l'adulte par des dilatations des bronches et une atteinte oto-sinusienne chronique. Un *situs inversus* est présent dans la moitié des cas et les troubles de la fertilité sont fréquents. Le diagnostic repose sur des tests spécialisés : un effondrement du monoxyde d'azote nasal est évocateur mais seuls un prélèvement de l'épithélium nasal ou bronchique pour une étude du battement ciliaire et une analyse en microscopie électronique permettent un diagnostic de certitude. Des tests génétiques sont en développement et pourraient favoriser le diagnostic dans les prochaines années. Le traitement est symptomatique, fondé sur la kinésithérapie respiratoire et l'antibiothérapie par voie systémique et/ou inhalée. Le pronostic est lié à l'atteinte respiratoire qui peut être modérée ou sévère.
Perspectives et conclusions. — La prise en charge de la dyskinésie ciliaire primitive reste mal codifiée et doit s'appuyer sur des centres spécialisés afin d'améliorer le diagnostic et les traitements, et de promouvoir la recherche.

English version

Introduction

Primary ciliary dyskinesia (PCD) is an autosomal recessive genetic disorder. It is characterized by structural and/or functional abnormalities of the motor cilia that mainly affect the surface of respiratory epithelial cells. The first cases of PCD have been reported by Siewert in 1904 then by Kartagener in 1933. The first 3 signs described were the presence of a *situs inversus*, bronchiectasis and chronic rhinosinusitis. A link between Kartagener's syndrome and ciliary immobility found in airway ciliated cells has only been established in the 1970s [1]. However, the *situs inversus* is only present in 50% of patients with PCD and its absence does not allow ruling out the diagnosis. PCD is a rare and underdiagnosed disease whose treatment is poorly defined. The size of reported series is most often small and they mainly include pediatric cohorts [2—4]. The largest cohort of adults with PCD only included 47 patients [5].

The objectives of the present review article are:

- to describe the main clinical situations of the diagnosis of PCD faced by pulmonologists;
- to describe the main tests required for the differential and positive diagnosis of PCD;
- to explain the benefit for the patients to be followed in a specialized center.

Epidemiology

The estimated prevalence of PCD in the general population is 1/15,000, corresponding to approximately 5000 patients in France [4]. These figures, extrapolated from the prevalence of *situs inversus*, are inaccurate because the diagnosis of PCD requires performing specialized tests without which the underdiagnosis remains high. In the absence of National French registry, it is difficult to know the number of patients diagnosed and followed.

The diagnosis of PCD is often performed within the first 10 years of life [6,7] but this diagnosis can be made at any age; 5—30% of PCD are diagnosed in adulthood [3,8], sometimes after the age of 70 years [9]. The diagnosis is often delayed compared to the onset of the symptoms, even in the presence of a *situs inversus*, because of the unawareness of this disease, of the multiplicity of clinical presentations and the relative complexity of diagnostic tests [10]. The presence of a *situs inversus* and management in a specialized center are factors associated with an earlier diagnosis [4], which presumably improves patient's prognosis.

- The prevalence of primary ciliary dyskinesia in the general population is 1/15,000, corresponding from to approximately 5000 patients in France but this disease is underdiagnosed.
- Primary ciliary dyskinesia may be diagnosed at any age and its diagnosis is often delayed compared to the onset of the symptoms.

Pathophysiology

PCD belongs to the group of ciliary diseases or ciliopathies [11]. Cilia are highly conserved structures in the phylogenesis and they are found in many organs. There are different kinds of cilia, including:

- non-motor cilia (e.g., sensory cilia found in the retina, but also those found in the bile ducts or renal tubules);
- motor cilia, including:
  - embryonic nodal cilia, which enable cell motility during embryogenesis and play important roles in organ lateralization,
  - motor cilia with multiplanar rotation that are found in particular on ciliated cells of the airway epithelium.