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Tracheomegaly in Brachmann-de Lange syndrome

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Abstract Brachmann-de Lange syndrome is a well-described congenital disorder. Skeletal anomalies and respiratory infections are its hallmarks. To the known imaging signs, the authors add tracheomegaly, which has not been reported so far.

Introduction

Brachmann-de Lange syndrome (B-dL) is a well-documented congenital disorder affecting various body systems [1–4]. Multiple skeletal anomalies [1–5] and recurrent respiratory infections, most probably related to gastroesophageal dysfunction, have been reported [5, 6].

Review of the chest radiograms of two patients with B-dL who have had respiratory difficulties since birth revealed the presence of tracheomegaly. For a third patient, no radiograms were available but a written description of the trachea was at hand. The involvement of the trachea in B-dL has not been previously described in the literature.

Materials and methods

Three patients, all male, presented at our department at the ages of 7 years, 5 years, and 4 days (patients A, B, and C, respectively). The patients had been diagnosed at 2 years, 5 months, and day 2, respectively, as having B-dL. Patients B and C died of severe pulmonary complications, while patient A is doing well after undergoing a Nissen fundoplication. The gastrointestinal manifestations of patients A and B have been previously published [6]; their major clinical and radiographic findings are summarized in Table 1. Patient C is presented in detail later on.

Chest X-ray films were obtained in the recumbent or upright position, according to the age and cooperation of the patient. Conventional or high-KV radiograms, employing standard focus-film distance and exposure, were used. The magnification factor was negligible (0.07–0.09). The transverse diameter of the trachea was measured at its cervical and intrathoracic sections in the anteroposterior or posteroanterior and lateral projections. Tracheomegaly was determined based on the normal values of the tracheal dimensions reported by Griscom [7], Griscom and Wohl [8], Menu and Lallemand [9], and Torkammani-Rezay and Ball (unpublished data, 1988).

In patients A and B recurrent chest radiograms were performed because of upper airway infections diagnosed as tracheobronchitis and/or pneumonia (Figs. 1, 2a). Patient B also underwent coronal computed tomography (CT) of the trachea and major bronchi (Fig. 2b). In patient C, a radiogram was done immediately after intubation, and repeated radiograms were made after extubation.

Patient C is presented in detail, as no radiograms or pathological material was available and the information was retrieved from the written clinical and autopsy records. This patient was born at 34 weeks of gestation by cesarean section to a multipara Jewish-Ashkenazic woman. Body weight was 1100 g. Apgar score at birth was 0, and assisted ventilation was started immediately. At 5 min the Apgar score was 6 and at 10 min it was 8. The patient was extubated after 8 h. Physical examination disclosed unequal lung aeration. Echocardiography revealed persistent fetal circulation and an atrial septal defect.

After the baby was stabilized, repeated physical examinations revealed bushy eyebrows meeting at midline, long curly eyelashes, low-set frontal hairline, depressed nose bridge, prominent philtrum, low-set ears, micrognathia, and webbed neck; also noted were proximal implantation of the thumbs, clinodactyly of the 2nd, 3rd, and 5th fingers, and a single transverse palmar crease.

Table 1 Major clinical and radiographic findings[a]

	Patient A	Patient B
Physical findings:		
Head	Microcephaly	Microcephaly
Hairline	Low-set	Low-set
Eyelashes	Long and curly	Long and curved
Eyebrows	Bushy, wide and synophrys	Bushy and synophrys
Mouth	–	Cleft palate
Ears	–	Purulent discharge
Lungs	Rales and bronchial breathing	Bronchial breathing; bilateral pneumonia
Heart	–	Systolic murmur
Elbows	Supination and extension limitation	Limitation of supination, pronation, and extension
Hand	Broad; short thumb, proximally implanted	Broad; clubbing of fingers; proximal thumb insertion
Hirsutism	Marked	Generalized
Radiographic findings:		
Chest	Bilateral pneumonia; wide trachea	Bilateral pneumonia; wide trachea; cardiomegaly
Hands	Hypoplastic first metacarpal bone and small first finger	Hypoplastic first metacarpal bone and small first finger
Elbows	Hypoplasia of the radial head and posterior luxation	Hypoplasia of radial head and dorsal subluxation
Follow-up:		
Recurrent aspiration pneumonia	+	+
Gastroesophageal reflux	+	+
Nissen fundoplication	+	+
Outcome:	Doing well	Died

[a] Patient C is described in detail in the text

There was supination-pronation limitation, together with extension-flexion hindrance at the elbows.

Repeated chest radiograms after extubation demonstrated an enlarged heart with mildly hyperinflated oligemic lung fields. A strikingly wide trachea was noted. Thirteen pairs of ribs were counted.

On day 4 cyanosis developed, accompanied by a severe drop in blood pressure. The baby died during resuscitation. Major findings at autopsy were as follows: The immediate cause of death was severe aspiration pneumonia of gastric content and bilateral pulmonary interstitial emphysema. There were multiple hematomas in the adrenal glands, right testis, and subpleural and subcapsular of the liver. Other macroscopic findings included hypoplasia of the corpus callosum, an unusually wide trachea for a newborn, hypoplasia of both kidneys, undescended testes, and hypoplasia of the penis with hypospadias. All other physical findings described above were confirmed. The final clinicopathological diagnosis was Brachmann-de Lange syndrome.

Results

The phenotypic appearance of the three patients, together with the skeletal radiographic findings and the pulmonary complications, are consistent with B-dL [1–5]. The pertinent findings related to the respiratory tract were as follows: A wide tracheal lumen was identified in all three cases. The tracheomegaly uniformly involved the whole length of the trachea. In patient A the wide lumen extended into the right main bronchus, whereas in patient B the wide lumen extended into the major bronchi (Fig. 2 a).

In patient A the transverse diameter of the cervical and intrathoracic trachea measured 13 mm (Fig. 1); the right main bronchus was wide. In patient B the transverse diameter of the cervical trachea measured 13 mm and its intrathoracic section 12 mm (Fig. 2 a); on coronal CT the intrathoracic section of the trachea measured 12.5 mm (Fig. 2 b). The bronchial lumen on both sides was wide, and the right main bronchus appeared even wider than the intrathoracic section of the trachea. For patient C no numerical measurements were available; however, the autopsy protocol stated: "An unusually wide trachea for a newborn infant." Thus, a wide tracheal lumen is the common denominator in all these cases.

In patient B a cleft palate was identified (not mentioned so far in B-dL), which was repaired at the age of 2 years. In patient C, 13 pairs of ribs were identified [5].

Discussion

Brachmann-de Lange syndrome is characterized by low birth weight (patient C) and failure to thrive. The facial appearance is striking, with low-set irregular hairline, eyebrows that meet at the midline, a long upper lip, and a small mandible [1, 2, 4, 5]. The radiologic features are mandatory to confirm the diagnosis [1–5].

In the patients presented above, the diagnosis of B-dL was made on the basis of the phenotypic appearance, physical examination, and radiographic results.

Radiographically, these children demonstrate microcephaly and brachycephaly and, on cranial CT, cerebral atrophy with ventricular dilatation. In patient B, cerebral atrophy was present on a brain CT. In patient C, hypoplasia of the corpus callosum was found (as well as anomalies of the genitourinary tract). The more obvious findings in B-dL are located in the upper extremities, including a hypoplastic, tapered, posteriorly subluxated proximal radius and hypoplasia of the first metacarpal bone. These findings were identified in the present patients. Flexion contractures are frequently observed at the elbows and knees, with supination-pronation difficulties at the upper extremities (patient C) [1–5, 10]. The thorax has a round inlet with a wide upper rib cage, a short ster-

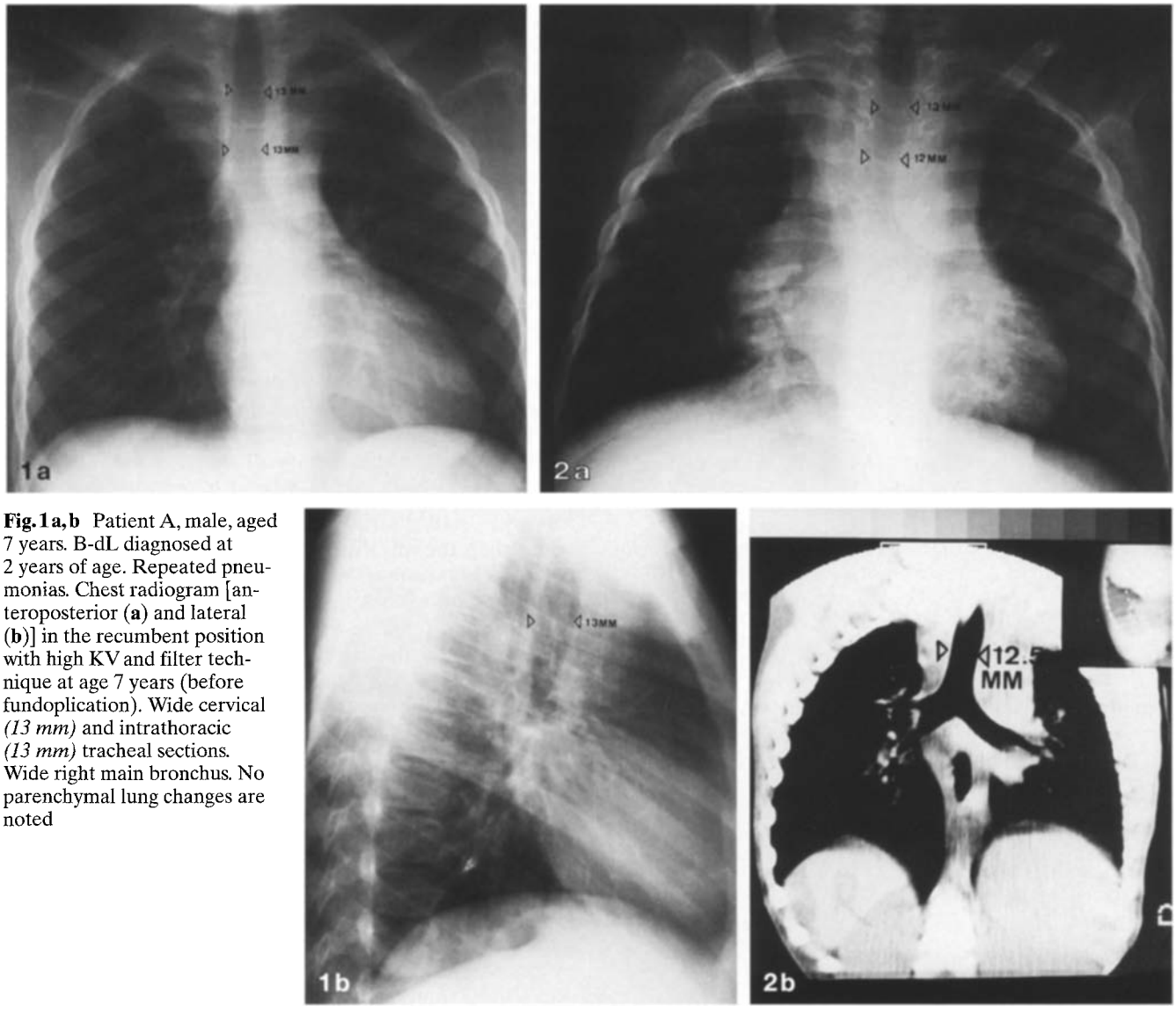

Fig. 1a, b Patient A, male, aged 7 years. B-dL diagnosed at 2 years of age. Repeated pneumonias. Chest radiogram [anteroposterior (**a**) and lateral (**b**)] in the recumbent position with high KV and filter technique at age 7 years (before fundoplication). Wide cervical *(13 mm)* and intrathoracic *(13 mm)* tracheal sections. Wide right main bronchus. No parenchymal lung changes are noted

Fig. 2a, b Patient B, male, aged 5 years. Recurrent pulmonary infections since birth. B-dL diagnosed at age of 5 months. Died at 5 years of age of a superimposed adenovirus pneumonia. The family refused permission for autopsy. **a** Chest radiogram (anteroposterior projection) in recumbent position, high KV and filter technique, at the age of 4 years and 6 months. Wide extrathoracic *(13 mm)* and intrathoracic *(12 mm)* tracheal lumen and major bronchi. Increased bronchial markings in both lower lung fields. Enlarged right heart. **b** Coronal CT of the trachea at 5 years of age. Wide tracheal *(12.5 mm)* and bronchial lumen. The right main bronchus is wider than the intrathoracic section of the trachea

num, and advanced development of the sternal ossification centers, in contrast to the retarded skeletal maturation. The ribs have a horizontal pitch [4, 5].

The normal tracheal transverse diameter between the ages of 5 and 7 years has been estimated by Menu and Lallemand [9] to range from 7 to 11 mm and by Griscom and Wohl [8] to average 9.3 mm. In patients A and B, the transverse diameter was increased, and this finding is strengthened by applying the standard deviations of Griscom and Wohl [8].

The first inclination is to attribute the tracheomegaly in B-dL to the gastroesophageal reflux and the aspiration pneumonia, leading to changes in the tracheal wall. However, in the children presented here, the wide trachea was already present a few days (patient C) or months (patient B) after birth. Thus, the repeated aspirations could not have been the major cause of the tracheomegaly. Every pediatric radiologist is familiar with severe cases of gastric reflux and aspiration, but tracheomegaly is usually absent. It is not likely that the cleft palate in patient B, which was repaired at the age of 2 years, or the short period of assisted ventilation in patient C was the cause of

the tracheomegaly [11]. The widening of the trachea in B-dL affects the whole length of the tube, in contrast to other disorders where there is only segmental dilatation [11, 12] which regresses after medical or surgical treatment. Moreover, the dilatation on B-dL appears to be present very early in life (patients B and C) and increases with age (in patient A, the tracheomegaly has persisted during follow-up and is progressing).

Because of the small number of children in the present series, and in order to consolidate this observation, the authors reviewed the chest radiograms published in other papers [1, 2, 4, 5]. However, a consistent observation could not be determined from the reproductions, although the figures in the papers of Lee and Kenny [1] and Kurlander and DeMyer [2] are suggestive of tracheomegaly. In conclusion, in the setting of a child with dysmorphic facies and recurrent lung infections, the finding of tracheomegaly suggests the diagnosis of Brachmann-de Lange syndrome.

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