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Sonographic measurement of the thymus in newborns: close association between thymus size and birth weight

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Sir: In infants, the thymus gland varies greatly in both size and shape; therefore X-ray diagnosis of absence or enlargement of the thymus is uncertain and unreliable [4]. In this study, the volume of thymus was measured in 65 full-term newborns by ultrasound. Newborns with a sign, symptom and/or laboratory finding of congenital abnormality, birth trauma, neonatal infection or metabolic disorders were excluded. The ultrasound examination was performed with a TOSBEE Sonolayer α Ultrasound Diagnostic Scanner (Toshiba Corporation Medical System Division, Tokyo, Japan) type SSA 240 A 7.5 MHz linear probe. Thymic measurements were made according to the ultrasound method described by Hesselbach et al. [3]. Pearson correlation coefficients and Student's *t*-test were used for statistical analysis, using the thymic index i.e. the largest transverse diameter (cm) × largest sagittal area (cm^2).

Table 1 shows minimum, maximum and mean values and the percentage distribution of birth weight, birth length and thymic measurements in 65 newborns (37 males and 28 females). The thymic index was normally distributed. The largest transverse diameter of the thymus in males was significantly higher than that of females (3.32 ± 0.63 versus 2.95 ± 0.7, $P = 0.027$). There was no significant difference between male and female newborns in terms of the largest sagittal area and the thymic index (4.25 ± 1.34 versus 3.91 ± 1.41, $P = 0.321$, and 14.7 ± 6.3 versus 12.1 ± 6, $P = 0.104$, respectively). Four out of six newborns with a thymic index greater than 22.4 (90th percentile of the thymic index value) were male, whereas only two out of six newborns with a thymic index of less than 4.6 (10th percentile of the thymic index value) were male. A statistically significant correlation was found between largest transverse diameter and birth weight; largest sagittal area and birth weight; thymic index and birth weight ($r = 0.276$, $P = 0.026$; $r = 0.373$, $P = 0.002$; and $r = 0.375$, $P = 0.002$, respectively). In addition, a significant correlation between the largest transverse diameter and birth length and between thymic index and birth length were also found ($r = 0.345$, $P = 0.005$ and $r = 0.262$, $P = 0.035$, respectively).

Sonographic measurement of the volume of the thymus is an alternative to radiographic determination, the latter using an uncertain and unreliable method for assessing the thymus size in infants. In post-mortem examinations after perinatal deaths, thymus weight has been found to be significantly correlated with birth weight [1]. Confirming this finding, we found that the ultrasound-estimated volume of the organ (''thymic index'') in newborns is significantly correlated with birth weight. Furthermore, it is known that the thymus is larger in males than in females during the first 2 years of life [4]. But no statistically significant difference in terms of thymus size was found between male and female newborns except in the largest transverse diameter of the organ in this study. However, most of the cases with a large thymus were male, whereas most of the cases with a small thymus were female.

In conclusion, we suggest that ultrasound examination of the thymus in newborns may be used for assessment of thymus size in various congenital diseases affecting the thymus, such as Di George syndrome, distal trisomy 14q syndrome, pediatric human immunodeficiency virus infection, ectodermal dysplasia and severe combined immunodeficiency [2, 5].

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Table 1 The mean, minimum, maximum values and percentage distributions of the birth weight, birth length and thymic measurements of 65 newborns by ultrasound examination. *Thymic index* = largest transverse diameter (cm) × largest sagittal area (cm^2)

	Mean (SD)	Min	Max	5%	10%	25%	50%	75%	90%	95%
Birth weight (g)	3497 (502)	2600	4975	2730	2830	3175	3450	3800	4170	4500
Birth length (cm)	50.2 (1.1)	47	52	48	48.5	50	50	51	51.5	51.9
Largest transverse diameter (cm)	3.16 (0.68)	1.2	4.56	1.89	2.22	2.77	3.15	3.7	4	4.16
Largest sagittal area (cm^2)	4.1 (1.37)	0.96	8	1.79	2.22	3.33	4.14	4.9	5.79	6.21
Thymic index	13.6 (6.24)	2.06	28.1	3.11	4.6	9.32	13	17.6	22.4	25.6

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First report of Guillain-Barré syndrome after rotavirus-induced gastroenteritis in a very young infant

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Sir: The Guillain-Barré syndrome (GBS) is the most common cause of acute generalised paralysis at all ages. Incidence rates are lower with decreasing age. The onset of GBS frequently follows an infectious disease [4]. Rotavirus, however, has never been described as an antecedent infection in GBS. We present a young infant with GBS after rotavirus-induced gastroenteritis.

A 20-month-old boy was admitted because of progressive weakness of the lower extremities, without other complaints. Ten days earlier he had experienced a period of fever, nausea and vomiting.

On admission, examination revealed an alert infant. Extraocular and facial muscle function was intact. In the lower extremities muscle strength was symmetrically decreased, whereas tendon reflexes were absent. Sensory functions were intact. No signs of ataxia or autonomic dysfunction were found.

Cerebral spinal fluid examination showed 10 WBC/μl, protein 0.96 g/l, glucose 3.2 mmol/l. Rotavirus was isolated from faeces. EMG revealed markedly decreased motor nerve conduction velocities (median nerve 13 m/s, peroneal nerve 15 m/s, normal 39–54 m/s).

According to the criteria of GBS [1] – progressive symmetrical motor weakness of more than one extremity, areflexia, no sensory symptoms, absence of fever at onset of neurological symptoms, elevated protein content in CSF with a relatively low WBC count and EMG signs of severe demyelinising polyneuropathy – our case fits the diagnosis of GBS [1]. Therefore intravenous immunoglobulin therapy (0.4 g/kg per day) was given for 7 days. The clinical condition gradually improved and 3 months after admission no symptoms remained.

Our patient experienced gastroenteritis before the GBS and rotavirus was isolated from faeces on admission. Epidemiological studies have demonstrated significant associations with upper respiratory or gastrointestinal illnesses before GBS onset [4]. It has been suggested that demyelinisation of peripheral nerves results from direct infection of Schwann cells by the infectious agent or from immunological mechanisms triggered by the infection [2]. Epidemiological and virological surveys of patients with GBS have failed to identify a single causative infectious agent. GBS is therefore assumed to be an immune-mediated disease that can also be triggered by non-infectious events including surgery and that responds to immunological therapy [2]. Encephalitis has been described after rotavirus-induced gastroenteritis. In these cases rotavirus was detected in the CSF [3]. We assume that in our patient GBS was mediated by rotavirus infection, which has not previously been reported.

This case report describes GBS in a very young infant after rotavirus-related gastroenteritis. Despite the low incidence of GBS in young infants, its occurrence in young floppy infants with acute illnesses should be considered, since careful monitoring and early immunoglobulin therapy is necessary. To our knowledge, this is the first report of GBS associated with preceding rotavirus infection.

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Pulmonary disease possibly caused by *Mycobacterium avium* in an HIV-negative infant

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Sir: A previously healthy 7-month-old Caucasian girl was admitted with an 8-week history of cough, wheezing and failure to thrive. She was unresponsive to oral antibiotherapy and nebulised bronchodilators. There was no known family history or contact with tuberculosis. Examination revealed generalised wheezing and a prolonged expiratory phase. Radiological investigations (chest X-ray and computerised tomography with three-dimensional reconstruction) showed mediastinal lymphadenopathy compressing the right main stem bronchus (Fig. 1) and right lower lobe atelectasis. A Mantoux test (PPD-S, 2 IU) at admission showed no induration. Extensive serological studies for viral and intracellular pathogens were negative. A rigid bronchoscopy revealed endobronchial granulation tissue obstructing 70% of the right main stem bronchus which was resected by forceps. The histopathological changes were consistent with mycobacterial infection but no acid-fast bacilli were seen. Cultures from three gastric aspirates and bronchial tissue remained negative after 2 months.

Classical antituberculous chemotherapy (rifampin, isoniazid and pyrazinamide) was begun for a presumptive diagnosis of tuberculosis, associated with a 6-week course of corticosteroids (methylprednisolone at an initial dose of 2 mg/kg daily, tapered after 2 weeks). Computed tomography after 2 weeks of treatment revealed a dramatic reduction in the size of the mediastinal adenopathy. A differential Mantoux test performed 3 months later showed no induration in response to PPD-S but 8 mm induration to avian tuberculin (PPD-A, *Mycobacterium avium* Sensitin RS 10, 0.1 μg, Statens Seruminstitut Copenhagen, Denmark).

Two months after cessation of steroid therapy, immunological studies revealed abnormal lymphocyte proliferation in response to mitogens.

A presumptive diagnosis of intrathoracic disease associated with non-tuberculous mycobacteria (NTM) was substantiated, based on clinical, radiological and histopathological findings together with the results of the differential Mantoux skin test and the lack of evidence for tuberculosis or any other aetiology. After 3 months, all antituberculous drugs were stopped and the patient remained asymptomatic. Sixteen months after her initial admission repeated differential skin tests showed 2 mm induration in response to PPD-S and 17 mm induration to PPD-A. Lymphocyte proliferative responses to the same mitogens were normal.

This case illustrates how difficult the diagnosis of intrathoracic infection due to NTM can be, and it raises some issues about its appropriate treatment.

Pulmonary disease due to NTM is very infrequent in childhood. Lincoln and Gilbert found 13 cases reported prior to 1970 [4] and a small number have been described since then. A positive diagnosis for pulmonary infection with NTM is difficult and may require invasive procedures (bronchoscopy, pulmonary or endobronchial biopsy) in an attempt to isolate the infecting organism. The American Thoracic Society recommends that the diagnostic criteria for pulmonary disease caused by NTM should include a positive culture [1]. As stated by Dore et al. [3], we suggest that differential Mantoux testing should be included especially in children because of the low yield of the culture in this age range. Differential skin testing may be very helpful in infants who are not yet sensitised to mycobacterial antigens. Studies including patients in whom the diagnosis of NTM infection (mostly adenitis) was based on a positive culture showed a very high sensitivity (> 90%) to the avian Mantoux. The greatest sensitivity is obtained with an avian cut-off point of ≥10 mm and a difference between the avian and the PPD-S reaction of at least 3 mm [2, 5]. Patients whose initial differential Mantoux tests are equivocal should be tested again several months later, especially when cultures are negative.

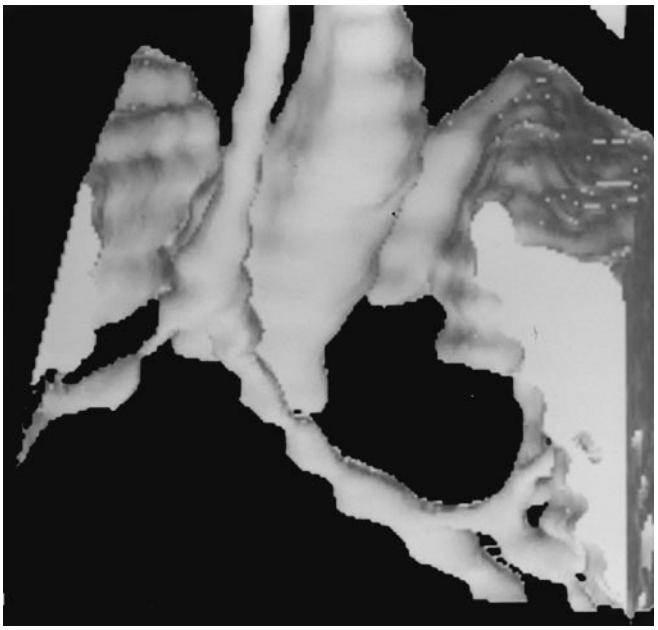

Fig. 1 Chest CT scan (three-dimensional reconstruction) showing mediastinal lymphadenopathy compressing the right main stem bronchus

All children with NTM pulmonary infection should have a full investigation of their immune system, including HIV testing. In cases of familial or intractable disease, genetic defects such as defects in the receptor for γ-interferon or interleukin-12 have been described [6]. Treatment of pulmonary infection due to NTM is not well established in paediatric patients and proposed chemotherapy regimes have included different antimycobacterial drugs, corticosteroids, intrathoracic surgery and bronchoscopic resection of endobronchial masses.

In conclusion, we believe that the use of differential skin testing should be included in the diagnostic criteria for NTM disease in children and that multicentre studies should be set up to assess the efficacy of the proposed chemotherapy regime.

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