Discussion

Persistent pulmonary hypertension in the newborn has a multiple aetiology and occurs in a variety of neonatal disorders. There is considerable evidence that thromboxane A₂ is involved in at least some forms of pulmonary hypertension.²⁻⁵ Infusion of live group B β haemolytic streptococcus, streptococcal toxin, or purified *Escherichia coli* endotoxin in animal models causes pulmonary hypertension, which is associated with high plasma thromboxane B₂ concentrations.⁵ It has also been suggested that pulmonary hypertension seen in perinatal aspiration syndrome is mediated by release of platelet thromboxane A₂ in the lungs.² Inhaled amniotic fluid may be absorbed by the lungs and cause local platelet aggregation. Thromboxane A₂ is then released from the platelets and causes pulmonary vasoconstriction.²

Our results suggest that production of platelet thromboxane A₂ is decreased in persistent pulmonary hypertension of the newborn. The lowest values were found in cases of severe meconium aspiration syndrome, but no correlations between the simultaneous blood gas values and production of platelet thromboxane B₂ were found. Although samples in the two groups were drawn from different sites, this should not influence the thromboxane B₂ results because they were expressed as nanograms per number of platelets. The high plasma thromboxane B₂ concentration in previous studies⁵⁻⁶ may originate either from the lungs or from hyper-reactive platelets, which release thromboxane B₂ excessively in vivo. If this in vivo stimulation of the release of thromboxane B₂ lasts long enough it may lead to exhaustion of the capacity of the platelets to

produce thromboxane B₂. The present in vitro data on reduced production of platelet thromboxane B₂ may support this hypothesis.

Vasoactive prostanoids and their inhibitors may be useful in the treatment of some forms of pulmonary hypertension. Selective inhibition of thromboxane A₂ formation is effective in some examples of experimental pulmonary hypertension.⁵ The biological antagonist of thromboxane A₂, prostacyclin, has been successfully used to reduce pulmonary hypertension.⁶ The response to this treatment with dilator could be enhanced if the platelet formation of the vasoconstrictive thromboxane A₂ is already diminished, as in the present cases.

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Noonan's syndrome and neurofibromatosis

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SUMMARY A child with Noonan syndrome and multiple café au lait spots, compatible in size and number with von Recklinghausen's neurofibromatosis, is presented. These features may represent a distinct genetic entity rather than the coincidence of two diseases.

Von Recklinghausen's neurofibromatosis and

Noonan's syndrome share several similar clinical findings, such as short stature, mental retardation, pubertal changes, kyphoscoliosis, and right sided congenital heart disease.^{1,2} Multiple café au lait spots are regarded as pathognomonic of von Recklinghausen's neurofibromatosis³ and have not been reported with Noonan's syndrome.² A few children have been reported recently with typical features of Noonan's syndrome and multiple café au lait spots and were diagnosed as neurofibromatosis-Noonan's

syndrome.⁴⁻⁶ We present one more case of this latter syndrome. Such cases have not been reported previously in paediatric publications.

Case report

The patient was referred to our clinic at the age of 12 years because of severe headaches. He was the fourth son of unrelated parents of Moroccan origin, both aged 47 years. The parents and the three siblings were all healthy, having normal height and weight and unremarkable physical findings. Pregnancy and delivery had been normal and birth weight had been 3500 g. Multiple cafe au lait spots were noted at birth and later were found to have increased in size and number. He sat up at the age of 9 months and walked alone at 18 months. No developmental problems were noted until he was of school age, when severe learning difficulties became apparent.

On examination, his weight was 30 kg (12th centile), height 132 cm (<3rd centile), and head

circumference 55.5 cm (75th centile). There was bilateral ptosis of the eyelids, with a downward palpebral slant and low set ears (Figure (a)). The palate was high arched and the teeth overcrowded. His hair was coarse with a low posterior hairline. The neck was short with prominent pterygium colli. He also had pectus excavatum and cubitus valgus. Physical examination of the heart yielded normal results. The testicles were in the scrotum, with a volume of 2 ml. No pubic or axillary hair was present. Scattered over the entire skin surface were more than 20 cafe au lait spots (Figure (b)), with a diameter ranging from several millimetres to 10 cm. Of these, 10 were more than 1.5 cm in diameter. No fibromata could be found. Electrocardiography and echocardiography yielded normal results. Roentgenographic survey of the skeleton failed to show any bone anomaly aside from the pectus excavatum and cubitus valgus. His bone age was 7 years. The karyotype was normal. Computed tomography of the brain, performed because of the severe headaches, did not show any disease.

Figure (a) Frontal face photograph of the child (left); (b) general appearance of the child (right).

Discussion

The present case shows some of the classical features of Noonan's syndrome—that is, short stature, pterygium colli, low set ears, ptosis, pectus excavatum, kyphoscoliosis, cubitus valgus, intellectual impairment, and delayed puberty.² The syndrome is delineated principally at the clinical level and the combination of features suggests the diagnosis. Nevertheless, the findings of numerous café au lait spots in appropriate size and number established the diagnosis of von Recklinghausen's neurofibromatosis. The coexistence of both syndromes in one patient confirmed the diagnosis of neurofibromatosis-Noonan's syndrome.⁴⁻⁶

The term neurofibromatosis-Noonan's syndrome was coined in 1985 by Opitz *et al.*, who suggested the syndrome to be a nosologically discrete, real biological entity of unknown aetiology.⁴ Although they believed neurofibromatosis-Noonan's syndrome to be fairly common,⁴ only a few such patients have been reported, and those reported had multiple café au lait spots and a phenotypic appearance appropriate for Noonan's syndrome. They seemed to have few or no Lisch nodules. Boys were more likely to have fusiform swelling of nerve strands, while girls tended to show the classical cutaneous neurofibromata. The reported cases as well as that reported by us may point toward two additional important diagnostic findings. The patients reported so far have been single cases with no familial incidence. It seems that the incidence of cardiac anomalies in these patients is low. In only one patient was there an appreciable systolic murmur; the echocardiogram, however, yielded normal results in this patient.

The aetiology of neurofibromatosis-Noonan's syndrome is not known. The possibility that both Noonan's syndrome and von Recklinghausen's neurofibromatosis occurred coincidentally in one patient is real, but most likely has a very low incidence. On the other hand, it may be suggested that these cases represent a separate genetic condition caused by a mutation at a locus that is different from either the neurofibromatosis or the Noonan's syndrome loci; alternatively, the Noonan's syndrome and neurofibromatosis loci may be close together on the same chromosome and the neurofibromatosis-Noonan's syndrome may be caused by a simultaneous mutation at both loci (probably a submicroscopic chromosome deletion). It seems that more reports of such patients are needed to learn the full extent of the clinical presentation of neurofibromatosis-Noonan's syndrome.

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Hydrops fetalis due to abnormal lymphatics

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SUMMARY A case of generalised lymphatic abnormality that presented with hydrops fetalis is described. This seems to be the first such case reported.

The reported incidence of non-immunological hydrops fetalis varies from one in 1400¹ to one in

7143.² Causes are identified in 56%³ to 85%¹ of cases, among which cardiac arrhythmia, thalassaemia, twin to twin transfusion, and congenital heart disease account for half.³ Localised lymphatic abnormalities—that is, cystic hygroma, pulmonary lymphangectasia,^{2,4} and prolonged chylous ascites²—may be causes, but there are no reports of generalised lymphatic abnormalities being associated with hydrops.