

Microcephaly, retinal dysplasia, pedal edema, mental retardation, and short stature

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ABSTRACT

Microcephaly, retinal dysplasia, pedal edema syndrome is a rare syndrome and possibly under diagnosed. We could find less than 25 cases reported in the literature. Patients were initially categorized as having either microcephaly and lymphedema or microcephaly and chorioretinal dysplasia. The existence of the 3 criteria in the same patients is reported. Other features such as mental retardation and short stature were noticed in other patients. In the Pediatric Department of the Armed Forces Hospital Southern Region, Kingdom of Saudi Arabia, we report a case with all clinical manifestations described in the above-related syndromes. The girl has microcephaly, retinal dysplasia, pedal edema, short stature, mental retardation, and some other dysmorphic features. The parents are not relatives, but both have retinal dysplastic changes. This report documents the existence of all different features reported in the literature in one patient, suggesting that different clinical features of reported patients are possibly the variable expression of the same syndrome.

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The consistent association of chorioretinopathy in microcephalic patients reported by McKusick,¹ indicated the existence of an entity distinct from simple microcephaly.¹ Abdel-Salam et al² stated that 40 cases of microcephaly with chorioretinal dysplasia had been reported.² Microcephaly-lymphedema was first reported by Leung³ in a 4-generation Chinese family with 5 affected members, and 2 instances of male to male transition, supporting autosomal dominant inheritance.³ Although microcephaly-lymphedema and microcephaly-chorioretinopathy have been considered 2 separate autosomal dominant entities, Feingold and Bartoshesky⁴ as well as Angle⁵ reported 2 unrelated sporadic cases with microcephaly, lymphedema, and chorioretinal dysplasia.^{4,5} Frys et al⁶ reported another sporadic case with microcephaly, pedal lymphedema, and chorioretinal dysplasia with

retinal folds.⁶ He described the finding of a small terminal 13q34 deletion.⁶ In addition to the autosomal dominant inheritance, few reports of autosomal recessive microcephaly-chorioretinal dysplasia were described,^{7,8} as well as a case of autosomal recessive microcephaly-lymphedema.⁹ We report on a child who has all of the above mentioned clinical features.

Case Report. A 3-year-old girl, known to have developmental delay and microcephaly presented with a 2-week history of poor feeding, vomiting, and on and off fever. She developed right-sided facial convulsions with circumoral cyanosis but no loss of consciousness. During pregnancy, the mother had no problems and the delivery was spontaneous vaginal at term. The girl was admitted to the neonatal intensive care unit because of the remarkable microcephaly.

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Her parents are not relatives and have no major illnesses. They have another 2-year-old apparently healthy daughter. On admission, she was severely dehydrated, febrile, and desaturated in room air. Her body parameters revealed weight, height, and head circumference below the 3rd centile. She had bifrontal narrowing, prominent glabella, puffy eyes, mild epicanthal folds, short nose, and smooth lips (**Figure 1**), mild retrognathia, big ears, small teeth, and high arched palate. Her fingers were short with tapering distal ends. She had shortening of the fourth toe, bilateral pedal edema, medial deviation of the forefeet and pes-planus with fine feet creases (**Figure 2**). Her chest and cardiovascular examinations were unremarkable, and she had no organomegaly. She was fully conscious with truncal hypotonia and hyperreflexia. She had global developmental delay, compatible with a 6-month chronological age. Her

blood workup revealed normal blood count, blood gas, electrolytes apart from hypernatremia, and normal lactate and ammonia. Blood culture grew no organisms. Her chromosomal analysis revealed 46 xx pattern with no structural aberrations. She was treated for hypernatremic dehydration and focal seizures. Magnetic resonance imaging of the brain detected dural sinus thrombosis. There was moderate brain atrophy. Metabolic workup was unremarkable. Ophthalmology consultation revealed retinal dysplastic changes. Both parents are healthy and normal looking with no apparent dysmorphic features. Mother's weight is on the 50th percentile with height and head circumference on the 25th percentile. Father's weight and height are on the 25th percentile with head circumference between the 10th and 25th percentile. Both parents were found to have bilateral retinal changes. The parents could not remember whether there are family members with dysmorphic features, in particular short stature or microcephaly. The diagnosis of lymphedema, microcephaly, and chorioretinopathy syndrome was raised. She was treated accordingly and maintained on carbamazepine. She was discharged in good condition. On follow up visits, she had no convulsions or focal signs.

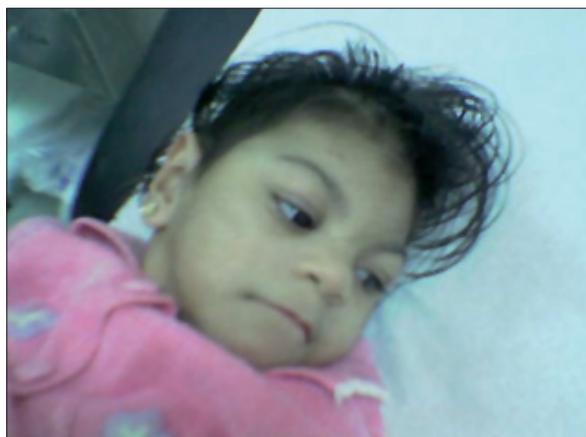


Figure 1 - The girl has bifrontal narrowing, prominent glabella, puffy eyes, mild epicanthal folds, short nose, and smooth lips.



Figure 2 - Shortening of the fourth toe, pedal edema, and medial deviation of the forefeet.

Discussion. The description of a syndrome encompassing microcephaly and chorioretinal dysplasia was first mentioned by McKusick.¹ Leung³ described 5 individuals with microcephaly and pedal edema in a 4-generation family and ascribed it to be a dominantly inherited syndrome.³ Since then, reports of variable clinical manifestations that seemed to be of the same entity but of variable expression were reported.

In 1992, Feingold and Bartoshesky⁴ described 2 unrelated patients with microcephaly, chorioretinal dysplasia and lymphedema.⁴ Sadler and Robinson¹⁰ described a family with an apparent autosomal dominant form of microcephaly, chorioretinal dysplasia, and mental retardation.¹⁰ Mental retardation was not consistently mentioned by others.^{3,10} Strenge and Froster¹¹ reported a family with microcephaly-lymphedema syndrome and short stature as an additional manifestation.¹¹ The family history of the reported boy suggested autosomal dominant inheritance but x-linked inheritance could not be excluded.¹¹ It was postulated that there may be 3 distinct entities: microcephaly and chorioretinal dysplasia; microcephaly and lymphedema; and microcephaly, lymphedema and chorioretinal dysplasia.⁴ The question whether these are truly distinct entities or just variable expressions of the same condition was raised many times.^{4-6,10-12} Our case favors the possibility that

these are a group of heterogenous entities accounting for the different manifestations and for the different forms of inheritance in some families. In fact, our patient has all the clinical manifestations mentioned in previously reported cases. She has microcephaly, pedal lymphedema, retinal dysplasia, short stature, mental retardation and the aforementioned other dysmorphic features. The inheritance in our case is likely to be autosomal dominant with variable expression. The parents are not related, and both have bilateral retinal changes while the other daughter is apparently normal. The possibility of autosomal recessive inheritance cannot be completely excluded.

We hope that the existence of all abnormal features mentioned in those related syndromes, in our patient, helps answer the question that has been raised for a long time.

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