NEWLY DISCOVERED DISORDERS ASSOCIATED WITH MEDULLARY SPONGE KIDNEY SUPPORT THE PATHOGENIC ROLE OF THE RET-GDNF AXIS

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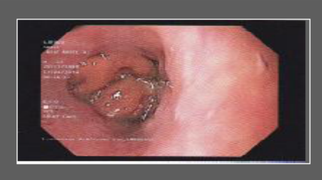
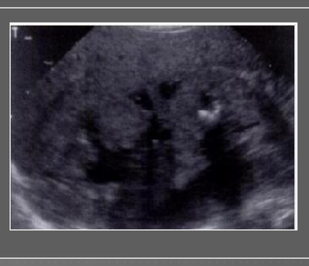
Objectives

The pathogenesis of the Medullary Sponge Kidney (MSK) is not well understood: most likely it is a congenital anomaly with delayed expression. This association with a number of urinary tract abnormalities suggests it belongs to the Congenital Anomalies of the Kidney and Urinary Tract (CAKUT) family. On the other hand its association with several developmental abnormalities of different organs suggests that there are some critical step(s) in the early mechanism of embryogenesis. The rearranged during transfection (RET) and the Glial cell line-derived neurotrophic factor (GDNF) genes have been proposed as defective in this disease and in a few families, two GDNF gene polymorphisms were discovered. Interestingly RET and GDNF have a definite role also in the development of the central nervous system, the heart, gastrointestinal system and the craniofacial skeleton. However, abnormalities in these organs have never been described in patients with MSK. Aim of this study was to look for anomalies in these organs in MSK patients.

Methods

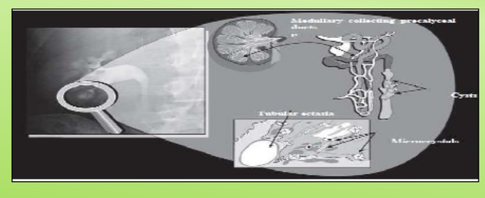
We identified, in our cohort of 143 MSK patients, several patients with previously described renal and/or urinary tract or different organs abnormalities. We specifically looked for abnormalities of the nervous system, of the heart and vessels, gastrointestinal system and of the craniofacial skeleton.
We found five patients affected by MSK associated with one or more of these alteration. They were all males, aged 18 to 50 years old. All had normal renal function (eGFR 98-148 ml/min per 1.73m^2) and normal parathyroid function.

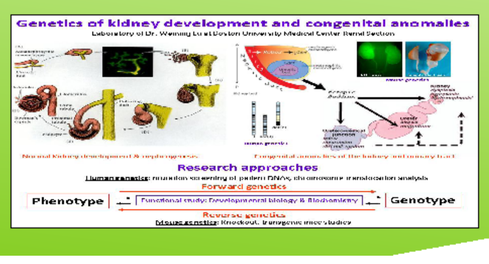
Clinical Characteristics of Patients Included in the Study

Patient	Familiarity	Organs involved	Abnormalities
B.G.	Yes for MSK	Cardiovascular	Hypertrophic cardiomiopathy, mitral valve prolapse and adipose metaplasia.
C.M.	Yes for MSK	Central Nervous System	Mental retardation and epilepsy
C.V.	Yes for NephroLithiasis	Cardiovascular and Gastrointestinal	Left-positioned vena cava and jathus hernia 
P.M.	Yes for MSK	Craniofacial skeleton	Mandibolar deviation to the left side and a concave facial profile. Absence of the incisors 
T.A.	Yes for MSK	Cardiovascular and Central Nervous System	Anomaly of the inferior vena cava (supra-hepatic veins directed into the right atrium and retro-aortic renal veins); ectasia of the celiac axis and of the spleno- portal axis. Mental retardation and epilepsy 

Conclusions

The discovery in MSK patients of abnormalities and disorders of the central nervous system, of the cardiovascular and gastrointestinal system and of the craniofacial skeleton supports the hypothesis that an of the RET-GDNF axis has a pivotal role in the MSK pathogenesis at least in a subset of patients.





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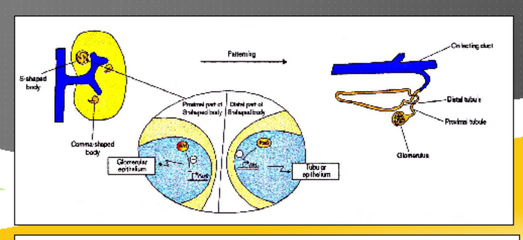

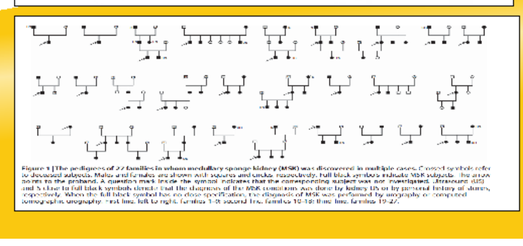

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