

# Mutation of RET gene causes multiple endocrine neoplasia type 2B in an Adolescent: report of one case and literature review

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## Background:

The occurrence of multiple endocrine neoplasia type 2B (MEN2B) in Asians is very rare. In particular, cases with intractable constipation as the main clinical manifestation are even rarer. Atypical clinical manifestations are likely to lead to diagnostic delay. In this report, we described a case of delayed diagnosis of MEN2B, whose first clinical manifestation was intractable constipation.

## Case presentation

A female teenager had suffered intractable constipation since her infancy. Because the results of colonoscopy and biopsy in local hospitals did not confirm her as congenital megacolon, the girl had been followed up at a local clinic for a long time. The diagnosis was not confirmed until the thyroid masses were found in pediatric department, Shanghai Ruijin Hospital when she was 12 years old. On the examination, her weight was 26.8kg (<-2SD), height was 136cm (<-2SD) and had a BMI of 14.49kg/m<sup>2</sup> at that moment, which was in the 10th percentile for her age. Her external genitalia and breasts were in Tanner stage I, and had no pubic hair. Therefore, she has not undergone puberty yet. Her blood pressure was 100/64mmHg. The physical examination also revealed there were multiple painless, firm nodules on her gingival, tongue and buccal mucosa, which were considered as mucosal neuromas (Fig. 1A, B). Her thyroid was enlarged and multiple hard nodules could be palpable on the surface of thyroid. There were no palpable mass in her abdomen. Results of laboratory tests and Image findings were shown in following figures and table. After our detailed evaluation, she had suffered with Hirschsprung disease (HD), growth retardation, medullary thyroid carcinoma (MTC) and mucosal neuroma due to a mutation in RET gene (c.2753T>C, p.M918T). Thus the diagnosis of MEN 2B was confirmed. Afterwards, the girl underwent several surgeries (radical thyroidectomy and cervical lymph node dissection in Feb. 2016, mediastinal tumor resection and thyroid cancer enlargement radical surgery in Sept. 2016 and colectomy in Oct. 2017) and was followed up to date.

## Conclusion

MEN2B has atypical clinical symptoms at the early stage. refractory constipation may be the only clinical manifestation that lasts for several years. Therefore, we recommend that patients with severe constipation due to HD should receive early screening and gene sequencing to determine the cause of the disease in order to improve survival.

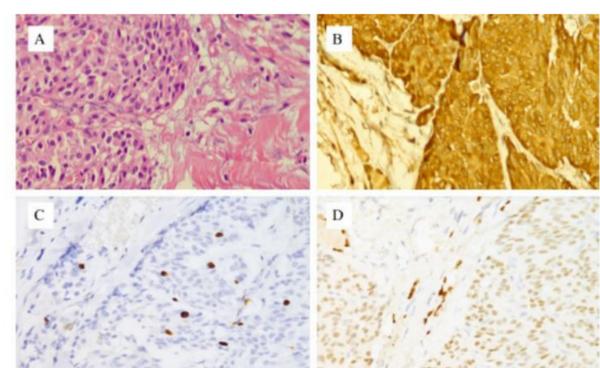
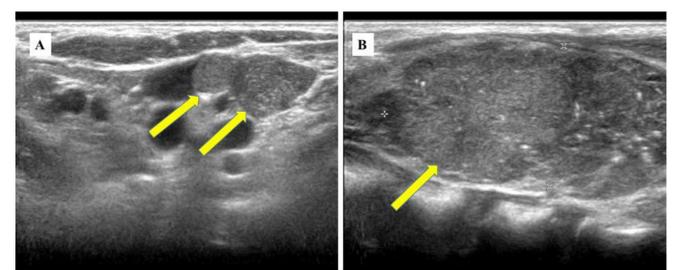
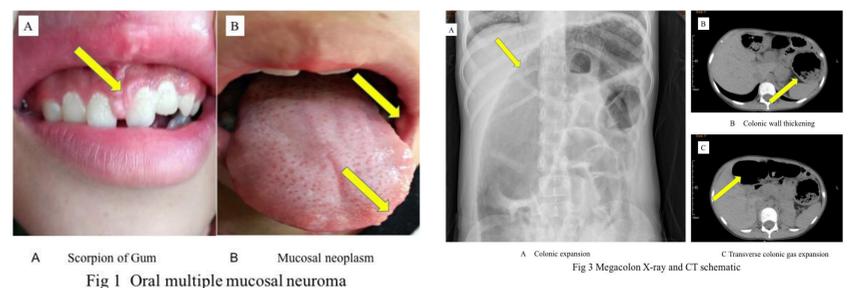


Fig4 : A: Pathological electron microscopy of thyroid biopsy (HE staining, 40 × 10), showing the arrangement of spindle-shaped medullary carcinoma cells, amyloid deposition under HE; B, C, D are immunohistochemical photomicrographs (DAB) Staining, 40 × 10 suggest Calcitonin (+), Ki67 (+), TTF-1 (+).

Fig4 Thyroid tissue biopsy pathology of patient

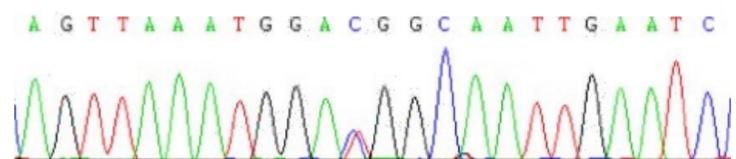


Fig 5 Patient RET gene mutation site sequencing map (c.T2753C, p.M918T)

Table Results of Laboratory Tests Before Surgery and During Follow-up

Index	Unit	Feb-16	Mar-16	Apr-16	Jul-16	Sep-16	Apr-17	Nov-18	Reference
CT	(pg/ml)	>1187↑	850.80↑	1072.07↑	973.39↑	442.47↑	519↑	>2000↑	<10
TSH	(uIU/ml)	3.09	0.201↓	0.014↓	0.827	2.53	0.018↓	0.013↓	0.35-4.94
FT3	(pmol/l)	5.24	6.92↑	5.56	4.52	4.1	2.07↓	4.33	2.63-5.70
FT4	(pmol/l)	13.85	24.25↑	22.68↑	14.64	13.71	15.29	18.41	9.01-19.04
PTH	(pg/ml)	75.5↑	114.9↑	-	-	67.8	-	-	15.0-68.3
CEA	(ng/ml)	655.4↑	164.9↑	44.55↑	34.28↑	19.03↑	16.39↑	46.45↑	<5.00
AFP	(ng/ml)	2.92	-	-	-	-	3.11	-	0-8.78
Ca	(mol/l)	2.29	2.18	2.39	2.33	2.21	1.75↓	-	2.00-2.75
P	(mol/l)	1.62↑	1.69↑	1.49	1.74↑	1.81↑	1.36	-	0.80-1.60
E	(pg/ml)	57.4	-	-	-	-	28.9	-	14-90
NE	(pg/ml)	94.4	-	-	-	-	43.5	-	19-121