EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 8
Issue: 9
540-542
Year: 2021

A CASE REPORT ON MULTIPLE ENDOCRINE NEOPLASIA TYPE 2B

Reshma Ramesan[1], Rajalekshmi K.[1], Dr. Manju Rosy Jose[2]

[1,2]Sixth Year Pharm D. Student, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom, Neyyattinkara, Trivandrum, Kerala, India.
[3]Clinical Pharmacist, Department of Oncology, Believers Church Medical College Hospital, Thiruvalla, Pathanamthitta, Kerala, India.

***Corresponding Author: Reshma Ramesan**
Sixth Year Pharm D. Student, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom, Neyyattinkara, Trivandrum, Kerala, India.

Article Received on 24/06/2021 **Article Revised on 15/07/2021** **Article Accepted on 05/08/2021**

ABSTRACT
In this study, the location of suitable areas for urban forest construction has been investigated. Geographic Information System (GIS) and multi-criteria decision analysis (MCDA) were used for this purpose. Based on the opinions of experts and past research, three main criteria were selected: ecological, access to urban services and socio– political terms. Also, sub-criteria were selected for each criterion and the desired spatial layers were prepared. Network analysis (ANP) method was used to categorize each criterion. For this purpose, the relevant questionnaire was prepared and after consulting experts, the weight of each criterion was calculated. The raster layers corresponding to each layer were prepared by fuzzy normalization method and the weight of each layer was applied in the corresponding layer. Then the layers were overlapped using the weighted linear combination (WLC) method and suitable areas for urban forest construction were selected. After locating, 8 areas were selected as proposed areas. Then 7 templates were selected and prioritized to categorize them. Then, based on the TOPSIS model, 8 options were prioritized and its map was presented.

KEYWORDS: Urban Forest, Green Space, Locating, Yazd, ANP, GIS.

INTRODUCTION

Multiple endocrine neoplasia type 2 (MEN2) is an inherited disorder characterized by the development of medullary thyroid cancer (MTC), parathyroid tumors and pheochromocytoma. MEN2 results from germline mutations in the RET proto-oncogene and is transmitted in an autosomal dominant fashion. There are two MEN2 syndromes: MEN2A and MEN2B.[1]

Each of the two major types of multiple endocrine neoplasia affects an estimated 1 in 30,000 people.[1] Among the subtypes of multiple endocrine neoplasia type 2, type 2A is the mostcommon form, followed by familial medullary thyroid cancer. Type 2B is relatively uncommon, accounting for about 5 percent of all cases of multiple endocrine neoplasia and reported in approximately 1000 families worldwide in 2001.[2]

The MEN2A syndrome is further classified on the basis of the presence of associated conditions. Classical MEN2A is characterized by MTC, pheochromocytoma, and primary hyperparathyroidism. Three additional variants are MEN2A with cutaneous lichen amyloidosis (CLA), MEN2A with Hirschsprung disease (HSCR), and familial medullary thyroid cancer (FMTC), which is diagnosed when the patient has a RET germ line pathogenic variant and MTC but no family history of pheochromocytoma or hyperparathyroidism.[3]

MEN2B is less common than MEN2A, accounting for 5% of MEN2 cases. It is characterized by more aggressive MTC (occurring in 100% of cases), pheochromocytoma (50%), mucosal neuromas (95%-98%) and intestinal ganglion neuromas (40%). Hyperparathyroidism is absent. In addition, nearly all patients have a distinct marfanoid habitus.[1]

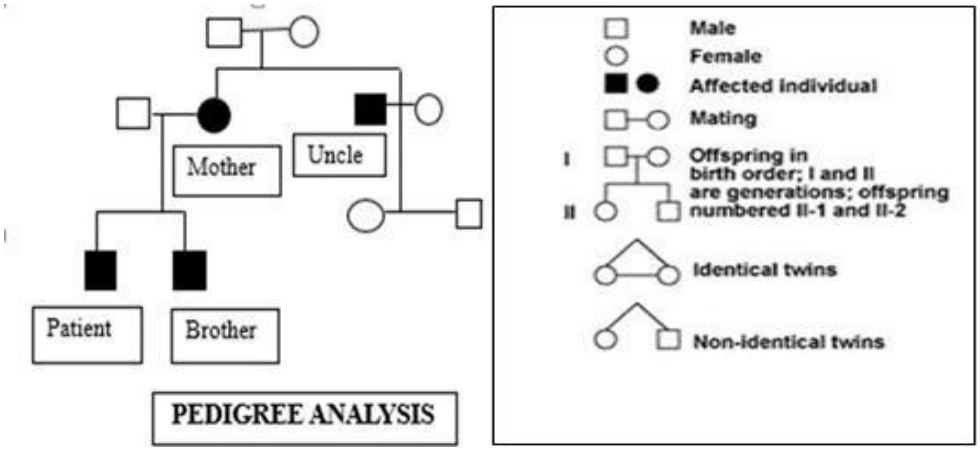
Multiple endocrine neoplasia type 2B (MEN2B) is caused by certain genetic changes (mutations or pathogenic variants) in the RET gene. This gene provides instructions to the body to make a protein that helps regulate the growth and division of cells of the endocrine system. This protein is supposed to tell the body when it is appropriate to allow the cells of the endocrine system to divide. When there is a pathogenic variant in the RET gene, the cells of the endocrine system are able to grow and divide out of control. This causes the signs and symptoms of MEN2B, as wellas the increased risk for the development of tumors.

CASE REPORT

A 34 year old male was presented to the Endocrinology

department with intractable diarrhea, altered bowel habits and generalized weakness for about 3 months with bowel opening 5-6 times daily. He also had history of weight loss of about 3kg. He appeared to have Marfanoid habitus. He had undergone Thyroidectomy in 2006 in view of thyroid disorder and was on T.Eltroxin 150mcg. He also has a strong family history of thyroid disorder. Apparently, his mother, elder brother and maternal grandfather had undergone thyroid surgery. Also his uncle had a historyof thyroid disease for which details was not available.

He developed chronic diarrhoea and was evaluated for it in 2018. As routine tests and medications failed to control diarrhoea, he was seen by gastroenterology. Initially, his colonoscopy and biopsy was done which was normal. Then his CECT chest+ abdomen was done. CECT chest showed bilateral apical fibrosis, mediastinum revealed small pre-carcinal volumes and right hilar subcarinal lymph nodes. Also CECT abdomen showed features of enlarged liver studded with multiple heterogenic lesions of variable size, fatty hepatomegaly, splenic lesion, bilateral adrenal lesions, spinal lesion. His report's impression was features of metastatic deposits in liver, spleen and bilateral adrenals. His USG was done repeatedly and showed no obvious collection or ascites, thin pleural effusion with basal lung atelectasis as a reactionary change.



Pedigree Analysis of the Patient.

Laboratory investigation

- ✓ Total count- 12000 cells/mcL
- ✓ Neutrophils- 80 %
- ✓ Eosinophils- 2%
- ✓ Lymphocyte- 17%
- ✓ Hemoglobin- 14.70g/dL
- ✓ RBC count- 5.37million
- ✓ T3- 111.6 nm/L
- ✓ T4- 7.44 nm/L
- ✓ TSH- 32.2 m-IU/L

He was referred for USG guided liver biopsy and the investigation was done. He was presented with right sided abdominal pain and right shoulder pain post procedure. His USG abdomen showed features of multiple SOL in liver. His biochemistry revealed elevated Calcitonin,carcino-embryonic antigen and elevated Meta-nephrines. He was found to have Metastatic lesions in liver, spleen and bones. Subsequent CT scan also showed metastatic deposits in the liver, spleen, adrenals and the bony skeleton, and this was confirmed to be Metastatic Medullary Thyroid Carcinoma on biopsy`. ECG changes include tall T wave, V2, V3, V4 and V5. His genetic analysisrevealed (C.1853 G>Cp. C6185) mutation on the exon 10 of the RET gene and family screening revealed that his child also carried the same mutation. Thus confirmed the diagnosis of MEN 2B and bilateral pheochromocytoma with post bilateral cortical sparing adrenalectomy on steroid replacement. Adrenal lesions were bilateral Pheochromocytomas (PCC).

Radiological Investigations

- ✓ CT scan-Small volume pre-carcinal /right lesions, sub-centimetric lymph nodes.
- ✓ Liver- Enlarged multiple lesions 0.5 to 5cm
- ✓ Liver- Enlarged multiple lesions 0.5 to 5cm
- ✓ Spleen- Multiple heterogenous enlarged lesions of size 0.2 to 1.9cm
- ✓ Right adrenal gland-3.6*3.3*5.4cm lesion
- ✓ Left adrenal gland-4*4.4*4.3cm lesions in the lateral limits Mesenteric haziness of multiple small volume mesenteric and parasitic nodes
- ✓ Lytic lesion in the bone with spine, ribs and sternum
- ✓ Increased calcitonin and metanephrine levels

He was referred to another center for peptide receptor radiotherapy (PRRT). He underwent bilateral cortical sparing adrenalectomy and later received MIBG therapy twice, to which he responded well. He was due for third but could not go due to the current situation related to the pandemic.

DISCUSSION

Inherited medullary thyroid carcinoma is known to occur in three settings: MEN 2A, MEN 2B and familial medullary thyroid carcinoma (FMTC). Among the causes of inherited MTC, MEN 2B is the least common

occurring in less than 5% of cases. It is also the earliest to present and has the worst prognosis with an average life expectancy of 30 years. Hence current guidelines recommend DNA analysis of the proband and the kindred for RET proto-oncogene mutations. All individuals harbouring the RET gene mutation require prophylactic thyroidectomy, while the timing of surgery is dictated by the specific mutation present.

In 50% of patients with MEN 2B, pheochromocytoma may be asymptomatic. Failure to recognise concurrent pheochromocytoma can lead to intraoperative hypertensive crisis in a patient operated for medullary thyroid carcinoma. Thus all patients with medullary carcinoma of thyroid require biochemical screening for pheochromocytoma.

Our patient had marfanoid habitus and his biochemistry revealed elevated Calcitonin, Carcino Embryonic Antigen and elevated metanephrines. Genetic analysis revealed (c.1853 G>C;p C618S) mutation on the exon 10 of the RET gene.

The final goal of further elucidating the natural history and pathogenesis of MEN2-related tumors should be the chance to offer patients with RET germline mutations an optimal cancer prevention (e.g. codon specific recommendations for prophylactic thyroidectomy) and treatment program.[6-8]

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