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Neuroendocrine tumours of gut wall incidence, presentation, diagnosis and management.

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Abstract

Neuro endo crine tumors commonly affect the gastro intestinal tract. The neuro endo crine tumors arise from the diffuse system of neuro endo crine cells. It is seen that patients with GI neuro endo crine tumors exhibits the following mani festations; abdominal pain, diarrhea / constipation, rashes, intestinal bleeding, scale like skin sores, mental confusion, nausea / vomiting, weight loss, jaundice, fatigue, etc. The present prospective study was conducted in Department of General and Minimal Access Surgery in collaboration with Department of Pathology to study the incidence, presentation, diagnosis and management of neuro endo crine tumors of gut wall. Patients having diagnosed with NETs of gut wall and admitted in various departments of SKIMS were studied after obtaining the informed consent for entire clinical profile, presentation and treatment modalities applied. It was observed that majority (57%) of the subjects were females as compared males 43 %, and the mean age of presentation was 56.2 years with arrange of 51 – 60 years. Out of 44 cases, 32 cases got operated and 12 were on non-operative management. 23 subjects don't have chemo / radio therapy, whereas 5 subjects were on Neo adjuvant radiotherapy, 7 subjects were on Neo adjuvant Che motherapy, 20 were on Adjuvant Che motherapy and 2 were on Adjuvant radio therapy. The present study concluded that Immuno his to chemistry study with chromogran in A and other anti-bodies like CK and CD56 can prove to be very beneficial in tumours having a conflict of patho logical diagnosis between micros copically similar looking tumours like Neuro endo crinal tumours and poorly differentiated adeno carcinomas and tumours having focal neuro endo crine differentiation.

Keywords: Cancer, GIT carcinoma, Neuro endo crine Tumors, Pattern and Gut wall.

Introduction

Neuro endo crine tumours commonly affect the gastro intestinal tract and it accounts for 1.2%–1.5% of all gastrointestinal neoplasms, with an incidence of 1.6–2.0 new cases per 100,000 persons per year.[1]

There are many different types of endocrine cells in the gastrointestinal tract which can give rise to various neuroendocrine tumours that differ considerably from the more commonly seen tumors.[2]

The neuro endocrine tumours arises from the diffuse system of neuroendocrine cells.[3] These are heterogenous group of benign or malignant tumors with various morphologies.[4]

It is seen that patients with GI neuro endo crine tumours exhibits the following manifestations; abdominal pain, diarrhoea / constipation, rashes, intestinal bleeding, scale like skin sores, mental confusion, nausea / vomiting, weight loss, jaundice, fatigue, etc.[5]

Immuno his to chemical staining has played an important role in the diagnosis of neuro endo crine tumours. The CT-scans, MRIs, sono graphy (ultra sound), and endoscopy (including endo scopic ultra sound) are commonly used for mor pho logical imaging.[6,7]

Treatment and prognosis depend on the grade and stage of the tumour. Current treatment modalities include endoscopic resection, surgery, somatostatin analog therapy, Peptide receptor radiolig and therapy, Che motherapy, liver targeted therapy (radio frequency ablation, bland embo lization and Che Mo embolization) and sympto matic treatment.

Thus, the present study was conducted to study the incidence, presentation, diagnosis and management of neuroendocrine tumours of gut wall.

Aims and Objectives

The present study aimed to:

1. Find the incidence of neuroendocrinal tumours among the gut wall tumours in our operative /hospital set up and in Kashmiri population.
2. See the presentation and incidence of a particular symptom in the study group.
3. See the distribution of NETs in the gut wall in the study group.
4. Study the expression of various tumour markers in the study group. This part was dealt in the Department of Pathology.
5. See the effect of treatment modalities on tumour course and quality of life of patient.

Material and methods

This prospective study was conducted in Department of General and Minimal Access Surgery in collaboration with Department of Pathology after taking the permission from institutional ethical committee over a period of 3 years from Jan 2019 to Dec 2021.

Patients having diagnosed with NETs of gut wall and admitted in various departments of SKIMS were studied after obtaining the informed consent for entire clinical profile, presentation and treatment modalities applied.

A detailed history was collected and physical / local examination was done. Special emphasis on EGD, colono scopy, sigmoido scopy and the biopsies obtained were sent for HPE.

Specimens removed at the time of surgery were subjected to gross and HPE in Dept of Pathology, SKIMS under proper conditions. Thereafter the blocks which were characteristic of NETs or had a diagnostic

dilemma between NETs and poorly differentiated carcino mas were taken for immuno his to chemistry including chromogran in A, CD56, CK and Ki 67. On HPE/ follow up.

patients case was discussed with medical and radiation oncologist for neoadjuvant and adjuvant chemotherapy. The patients were being followed in OPD and telephonically for their quality of life and symptoms. The data was analyzed through suitable statistical techniques and inference was drawn accordingly.

Patients having been missed in prospective study/series were retrospectively followed through their biopsy reports in the Dept. of Pathology and subsequently their records were obtained.

The patients` records were obtained through MRD section and RCC Centre of skims located in State Cancer Institute.

Observations and results

In the present study majority (57%) of the subjects were females as compared males 43 %, and the mean age of presentation was 56.2 years witharangeof51-60years.Out of 44 cases, 32 cases got operated and 12 were on non-operative management.

23 subjects don't have chemo / radio therapy, whereas 5 subjects were on Neo adjuvant radio therapy, 7 subjects were on Neo adjuvant Che motherapy, 20 were on Adjuvant Che motherapy and 2 were on Adjuvant radio therapy.

Table 1: Total no. of neuroendocrinal tumours as proven by biopsy

Year	Total cases
2019	14
2020	07
2021	23
Total	44

Table 2: Total number of gut wall tumours as governed by their location registered in RCC (regional cancer Centre) of SKIMS

Site of cancers	Total no. of cases
Esophagus	848
GE junction	477
Stomach	946
GIST	57
Duodenum	19
Jejunum	7
Ileum	13
Appendix	9
Colon	543
Rectosigmoid	50
Rectum	394
Anal	14
Total	3377

The reported incidence of NETs among all neoplasms of gut in our hospital from Jan 2019 to Dec 2021 was 1.3% and the incidence of NETs among Kashmiri population during the same period was 1.9 per million.

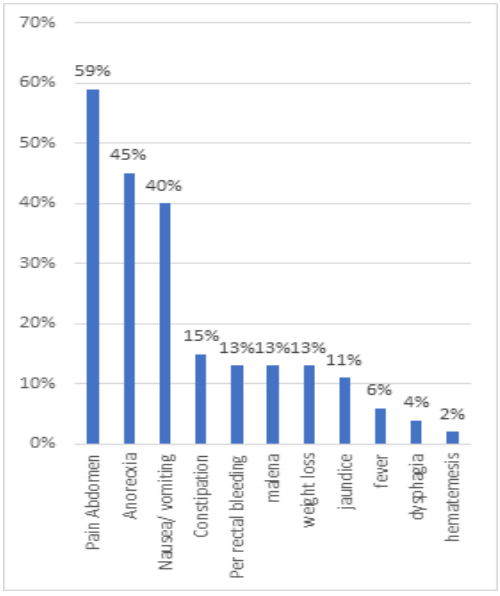

Figure 1: Distribution of symptoms

Figure 1, represents that the common symptom was abdominal pain (59%), followed by anorexia (45%), nausea / vomiting (40%), constipation (15%), per rectal bleeding, Malena and weight loss (13% each respectively), jaundice (11%), fever (6%), dysphagia (4%) and hematemesis (2%).

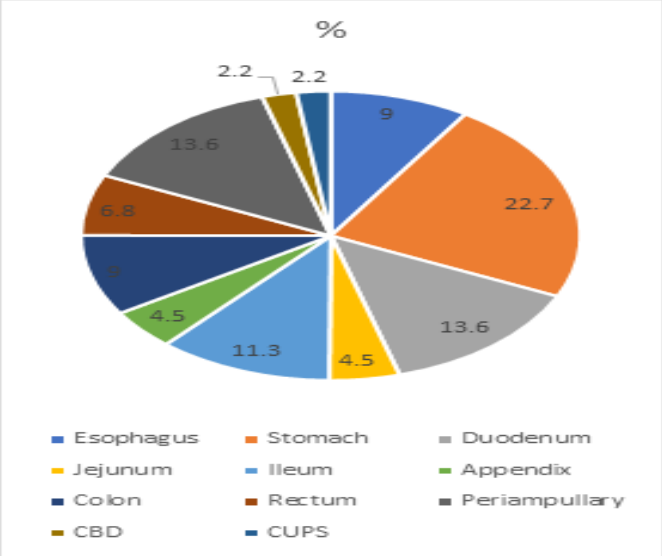

Figure 2: Distribution by site

It was reported that the maximum number of cases were reported from stomach followed by small intestine combined as shown in figure 2.

Table 3: Distribution by differentiation

Differentiation	No. of cases	%
Well	31	70
Moderately	8	18
Poor	5	12

It was observed that the majority of tumours were well differentiated tumours as depicted in table 3.

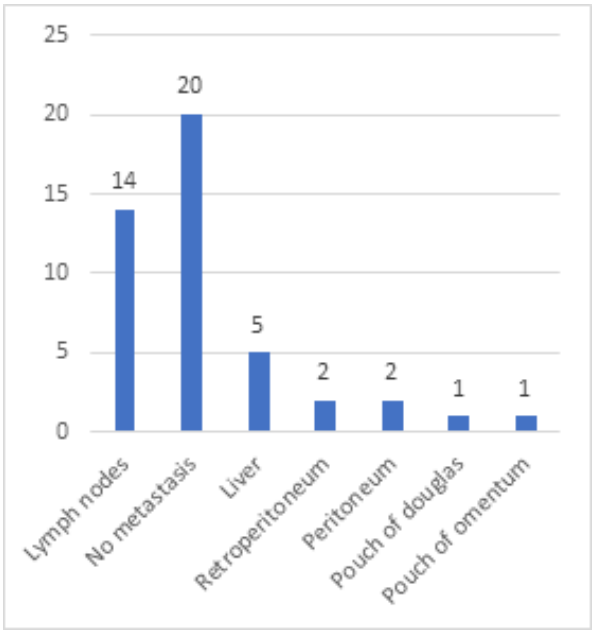

Figure 3: Site of metastasis

Figure 3, shows that 14 subjects had metastasis in lymph nodes, followed by liver (n=5), retroperitoneum and peritoneum (n=2 respectively), pouch of Douglas and omentum (n=1 respectively) and no metastasis was observed in 20 subjects.

Table 4: Distribution by immuno his to chemistry

IHC marker	+Ve Cases (n)	+Ve % (Sensitivit)	-Ve (n)
Chromogranin A	31	70	13
CK	32	72	12
CD56	19	43	25
Ki67	31	70	13

Table 4 represents that out of the 44 cases, 31 cases had positive Chromogranin A and Ki 67 with sensitivity of 70%.

Table 5: ECOG Score

ECOG score	No of patients
0	24
1	9
2	6
Not known	5

In our study the maximum patients (n=24) had 0 ECOG score followed by 1 ECOG score (n=9), 2ECOG score (6) and among 5 subjects score was not known.

Discussion

The data and findings of the present study were discussed with previously available literature.

A total of 44 cases and incidence was calculated as 1.9 per million. Our results are comparable to Lawrence et al 2010 where they found the incidence of tumour being 3.6 in USA population.[8] Ellis et al 2010 found the incidence of tumour being 1.3 in UK.[9]

We observed in our study group the youngest age recorded was 20 years and uppermost age was 77 years. The maximum incidence of NETs was in age group 51 – 60 years. The mean age of presentation was 56.2 years. Our results are comparable to Para medina etal where they found that mean age of presentation was 60.2 years.[10] Deidi etal found that mean age of presentation was 62 years.[11]

We reported 19 males and 25 females who accounted for 43% and 57% respectively with male to female ratio being 1:1.3. our results are comparable to Dasari A etal who found that 47% of the study group was males as compared to 53% of the female study group.[12]Ellis etal also found female preponderance.[9]

We found that pain abdomen, vomiting and features of intestinal obstruction were common clinical features. Cives M etal found the same clinical mani festations being common[13]Mastracci L etal also found same symptoms being prevalent in gut tumours. [14]

Our study showed that the stomach and small intestine combined were the predominant sites. Ellis etal also found the same distribution in their study in UK.[9]Cives etal also found the same type of distribution among their own group.[13]Nederle MB also found the same observation in their study.[15]

In our study majority of patients were from well differentiated group. It was in accordance with Kloppel G etal[16] who had the same distribution between well and poorly differentiated tumours. Modlin IM etal also found the same results. [17] Sor bye H also found the same result.[18]

The largest no of metastasis was to lymph nodes followed by liver. Modlin etal also found the same result.[17]Dasari etal also found same observations in his study.[12]

The chromogranin A had the sensitivity in about 70% and Ki 67 in least number of patients in our study. Our results are in accordance with Bajetta E etal who recorded sensitivity of 67%.[19]Eunsung Jun etal also found same observations for the tumour markers for large tumours.[20]

We found that 32 out of 44 patients were operated and majority of patients received Adjuvant chemotherapy with some patients receiving neoadjuvant Che Mo radio therapy in metastatic cases. This strategy was found to have better survival in study conducted by Ducreux M etal. [21] Uri I etal also found the same survival benefits in patients undergoing debulking surgery with adjuvant chemotherapy. [22]

Many patients were doing well after their surgery with marked symptomatic relief in majority of patients. In some patients there were recurrences following surgery too. Felix J etal had found the heterogeneity in quality of life in patients undergoing surgery along with chemo therapy. [23]

Basuroy R etal also studied the quality of life following multiple treatment modalities in neuro endo crinal tumours of stomach and pancreas.[24]

Conclusion

The present study concluded that Immunohistochemistry study with chromogranin A and other antibodies like CK and CD56 can prove to be very beneficial in tumours having a conflict of patho logical diagnosis between micros copically similar looking tumours like Neuro endo crinal tumours and poorly differentiated adeno carcino mas and tumours having focal neuro endo crine differentiation. Therefore, immuno his to chemistry is the confirmation of NETs and index for their grade.

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