International Journal of Research in Medical Sciences
Sreedharan S et al. Int J Res Med Sci. 2015 Sep;3(9):2499-2502
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20150662

Case Report

Diffuse intestinal ganglioneuromatosis with coexisting gastrointestinal stromal tumour - gastrointestinal manifestations of neurofibromatosis: an unusual case report

Sily Sreedharan[1]*, Vineeth Rao[2], Malini Thomas[3]

[1]Assistant Professor, Department of Pathology, Malabar Medical College, Modakkalur, Calicut, Kerala, India
[2]Assistant Professor, Department of Surgery, Malabar Medical College, Modakkalur, Calicut Kerala, India
[3]Senior Consultant Pathologist, Calicut Pathology Centre, Calicut, Kerala, India

Received: 13 July 2015
Accepted: 11 August 2015

***Correspondence:**
Dr. Sily Sreedharan,
E-mail: sily.vinod@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Gastrointestinal involvement in neurofibromatosis occurs in four major forms: true neurogenic neoplasm; neoplasm arising from interstitial cells of cajal; endocrine tumours & vasculopathy. In our case, a known case of familial neurofibromatosis showed diffuse colonic ganglioneuromatosis & coexisting very low risk gastrointestinal stromal tumour (GIST) in jejunum. For one of its rare associations we are presenting this case.

Keywords: Gastrointestinal, Ganglioneuromatosis, Gastrointestinal stromal tumour, Neurofibromatosis

INTRODUCTION

Gastrointestinal manifestations of neurofibromatosis usually arise in mid-life or later with appearance of cutaneous manifestations of the disease. The frequency varies from 5-25%.[1] Gastrointestinal manifestations of neurofibromatosis include: true neurogenic neoplasm; neoplasm arising from interstitial cells of cajal; endocrine tumours & vasculopathy.[2] We are reporting the first case with coexisting diffuse colonic ganglioneuromatosis & GIST in a neurofibromatosis patient.

CASE REPORT

We present a case of 50 year old female, a known case of neurofibromatosis, who presented with vague dull aching lower abdominal pain of 2 years. duration, not relieved by medication. Local examination revealed a vague mass in the right iliac fossa. General examination revealed multiple neurofibromas all over the body. Routine examination revealed normocytic normochromic anaemia. Radiological investigations included CT Abdomen which revealed multiple neurofibromas in the entire colon. She gives family history of neurofibromatosis. She was advised to undergo colectomy.

Histopathological examination

Gross: Right hemi colectomy specimen measuring 42 cm. Colonic wall appeared thickened. On cutting open showed diffuse colonic wall thickening (Figure 1) and nodules of varying size ranging from 0.5 cm to 1.5 cm. Cut section of all the nodules were whitish glistening. A separate glistening nodule was also identified at the mesocolon measuring 5 cm in diameter. A separate Jejunal nodule was received measuring 4x3 cm. Cut section of which was whitish firm (Figure 2).

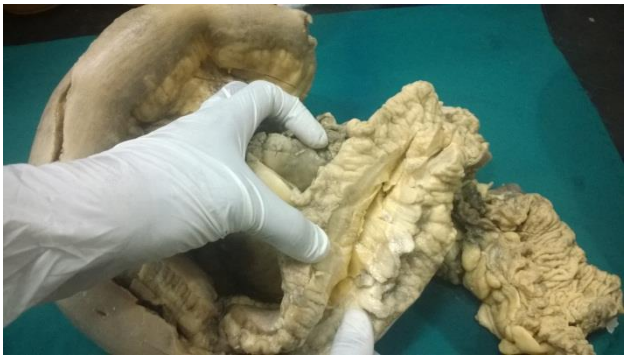

Figure 1: Colonic wall thickening ITH nodularity of mucosa.

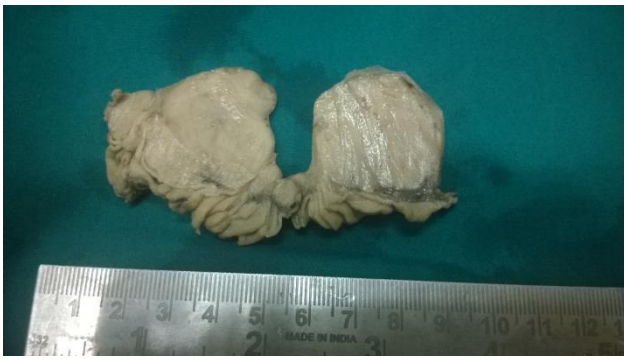

Figure 2: Grey white well circumscribed jejunal nodule.

Microscopy: Colonic wall showed a diffuse lesion composed of proliferated spindle cells with tapering nucleus& scanty cytoplasm arranged diffusely in the sub mucosa (Figure 3) with thickened blood vessels. Some areas showed ganglion cells admixed with nerve fibres (Figure 4). The lesion was involving the entire colon. Section from mesocolon showed similar lesion. No mitosis, atypia noted. Jejunal nodule showed a benign neoplasm composed of benign spindle cells with moderate eosinophilic cytoplasm, plump nucleus arranged as fascicles (Figure 5). Skeinoid fibres noted in between the spindle cells (Figure 6). No ganglion cells seen. No mitosis, atypia noted.

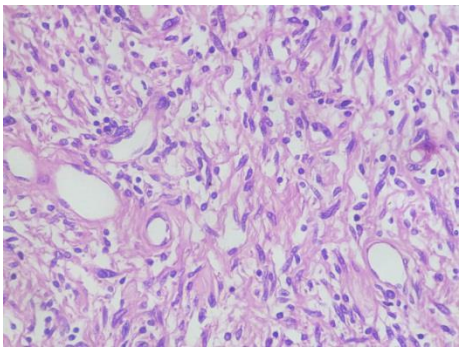

Figure 3: High power showing uniform spindle cells with moderate eosinophilic cytoplasm, dispersed uniformly.

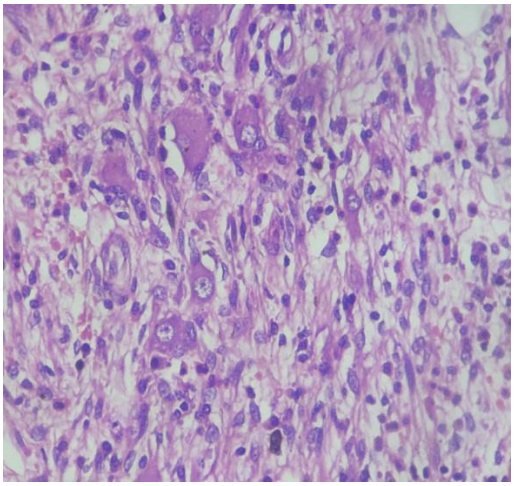

Figure 4: Ganglion cells scattered between the spindle cells.

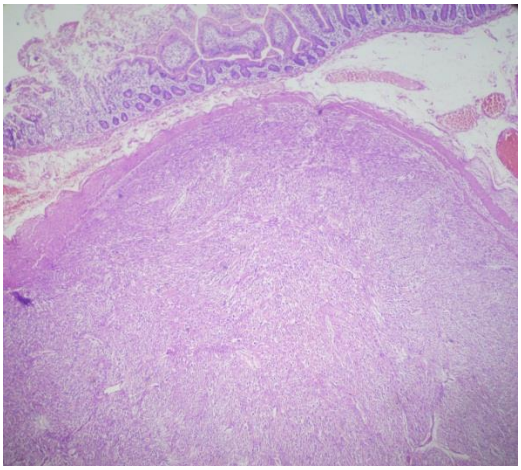

Figure 5: Jejunal nodule low power view.

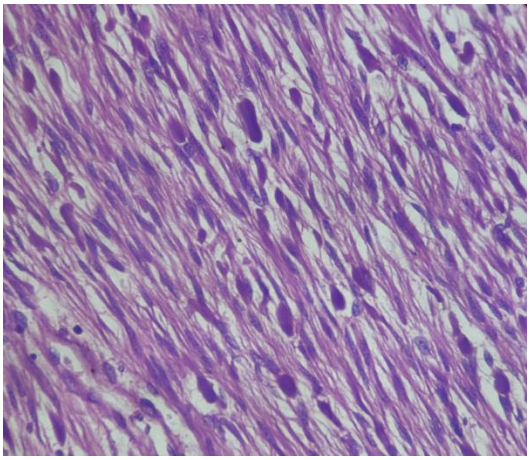

Figure 6: High power showing skeinoid fibers.

Immunohistochemistry showed colonic lesion with S-100 positive & c-kit (CD117) negative (Figure 7 and 8). Jejunal nodule was c-kit (cd117) positive & S-100 negative (Figure 9 and 10).

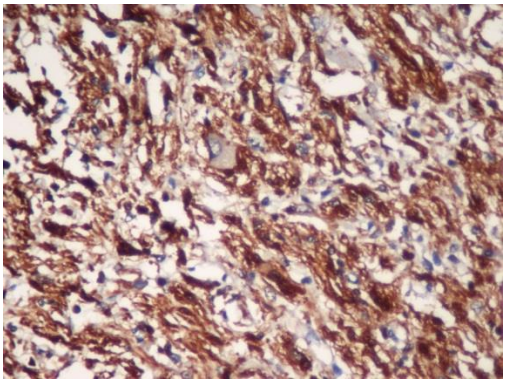

Figure 7: S-100 in colonic lesion.

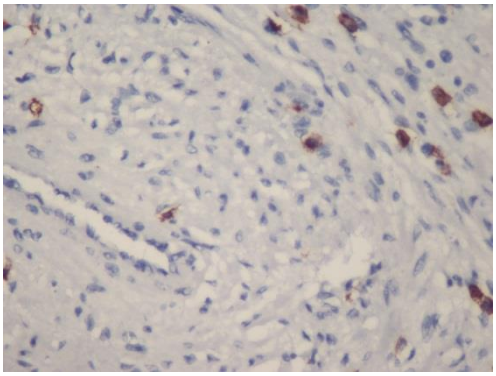

Figure 8: CD-117 in colonic lesion.

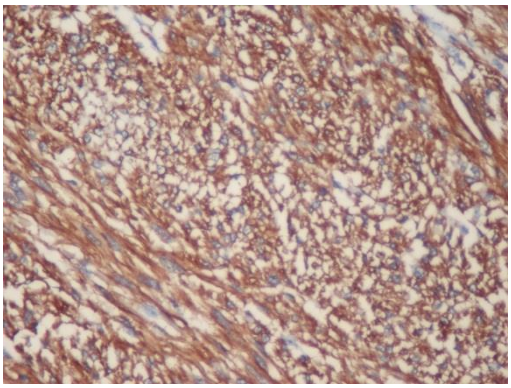

Figure 9: CD-117 in jejunal nodule.

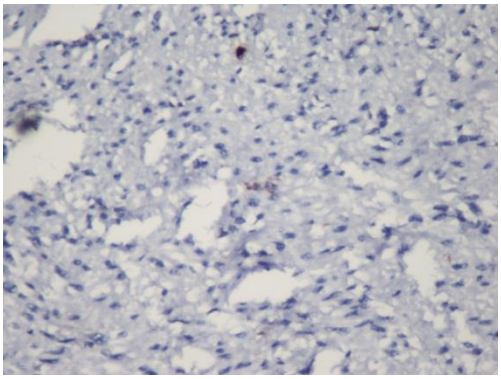

Figure 10: S-100 in jejunal nodule.

On the basis of clinical, histological and immunohistochemistry, diagnosis of diffuse intestinal ganglioneuromatosis and very low risk gastrointestinal stromal tumour (GIST) was made.

DISCUSSION

The gastrointestinal manifestations occurring in neurofibromatosis are usually under recognised in routine practise (Table 1). These manifestations usually start in later life, along with appearance of cutaneous manifestations.

Table 1. Reported gastrointestinal manifestations in NF-1.

1. True neurogenic neoplasms
Solitary neurofibroma
Diffuse or plexiform neurofibroma
Gastric schwannoma (single case reported)
Diffuse mucosal/submucosal neurofibromatosis
Ganglioneuromatosis
Gangliocytic paraganglioma
Malignant peripheral nerve sheath tumor (very rare)
2. Interstitial cell of Cajal lesions
Multifocal clinical gastrointestinal stromal tumors [GISTs]
Minute incidental GIST tumorlets (usually non-gastric)
Microscopic diffuse or multifocal interstitial cell of Cajal lesions
Motility disorders related to Cajal cell lesions
3. Neuroendocrine tumors
Carcinoid tumors at any gastrointestinal location
Periampullary somatostatinoma
Rarely, insulinoma and gastrinoma
4.Miscellaneous neoplasms and lesions
Adenocarcinoma at different gastrointestinal sites
Vasculopathy

Gastrointestinal neurofibromatosis

Neurofibromatosis may present with diffuse neuromatous proliferation expanding the lamina propria, submucosa of GIT. This may take the form of pure neurofibromatosis or be admixed with ganglion component.[2]

Neurofibromatosis & GIST

GIST have been increasingly documented as an abdominal manifestations of the disease. GIST was detected in 25% of neurofibromatosis patient.[3] Most NF-1 associated GIST are small asymptomatic lesion with low mitotic activity & follow a benign course. Histologically they display spindle cells with brightly eosinophilic PAS positive collagen fibres that have been referred as skeinoid fibres.

Coexistence of GIST & peripheral nerve sheath tumour

The concurrence of gastrointestinal benign peripheral nerve sheath tumour with GIST seems to be unique. Literature search revealed only 4 such reported cases of association.[4] All the GIST showed low grade morphology except gastric GIST.[5]

Molecular pathogenesis of GIST & other gastrointestinal manifestation

GIST in the setting of NF-1 don't harbour mutations in KIT. Despite their molecular profiles NF-1 associated with GIST are uniformly KIT positive by IHC.[6] The NF-1 gene product, neurofibromin, is a member of GAP family of ras regulatory proteins that functions as tumour suppressor by negatively regulating the ras pathway. The biallelic NF-1 inactivation results in constitutive ras activation of downstream mitogenic signalling through the ras-MAP kinase cascade. Gain of function mutations of KIT also result in constitutive activation of downstream signalling pathways including ras-MAP kinase cascade.

CONCLUSION

Though there are 4 reported cases of benign nerve sheath tumour association with GIST, this case report is the first of association of ganglioneuromatosis with very low risk GIST in neurofibromatosis patient.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Fuller CE, Williams GT. Gastrointestinal manifeatations of type-1 Neurofibromatosis (Von Recklinghausen's disease). Histopathology. 1991;19:1-11.
2. Abbas Agaimy, Nikolas Vassos, Roland S. Crow. Gastrointestinal manifeatations of neurofibromatosis type-1. J Clin Pathol. 2012;5(9):852-62.
3. Zooler ME, Rembeck B, Samuelsson M, Angervall L. Malignant & benign tumours in patients with neurofibromatosis type-1 in a defined Swedish population. Cancer. 1997;79:2125-31.
4. Agaimy A, Markl B, Kitz J, Wunschph, Arnhold H, Fuzesi L, et al. Peripheral nerve sheath tumours of gastrointestinal tract: a multicenter study of 58 patients including anf-1 associated gastric scwanomma & unusual morphologic variants. Virchows Arch. 2010;456:411-22.
5. Schaldenbrand JD, Appelman HD. Solitary solid stromal gastrointestinal tumors in von Recklinghausen's disease with minimal smooth muscle differentiation. Hum Pathol. 1984;15:229-32.
6. Kinoshita K, Hirota S, Isozaki K, Ohashi A, Nishida T, Kitamura Y, et al. Absence of C-kit gene mutation in gastrointestinal stromal lesion from neurofibromatosis type-1. J Pathol. 2004;202:80.

Cite this article as: Sreedharan S, Rao V, Thomas M. Diffuse intestinal ganglioneuromatosis with coexisting gastrointestinal stromal tumour - gastrointestinal manifestations of neurofibromatosis: an unusual case report. Int J Res Med Sci 2015;3:2499-502.