

CASE REPORT

Isolated Polypoid Ganglioneuroma of Gall Bladder - A Case Report

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Abstract: A ganglioneuroma is a very rare neoplasm in the gastrointestinal tract and a benign neoplasm of sympathetic nervous system. They predominantly affect the colon and rectum and are rare to arise in gall bladder. Gastrointestinal ganglioneuromas occur as rare isolated (solitary) polypoid lesions or more commonly as ganglioneuromatous polyposis and diffuse ganglioneuromatosis. Isolated polypoid lesions are clinically asymptomatic and incidentally detected during endoscopy or surgery. We report a case of a 42-year-female who presented clinically with features of chronic cholecystitis and was operated. There was no association of any hereditary disease. Incidentally the cholecystectomy specimen showed a small sessile polypoid lesion. Histopathological examination showed the lesion to be polypoid ganglioneuroma arising in gall bladder. The isolated polypoid ganglioneuroma is invariably benign. They do not have increased risk of von Recklinghausen's disease or multiple endocrine neoplasia IIB and show no evidence of recurrence with excellent prognosis after total excision.

Key words: gall bladder, isolated, polypoid, ganglioneuroma

Introduction

Ganglioneuromas [GNs] are benign tumors of sympathetic nervous system. Gastrointestinal GNs fall into three groups—Isolated (solitary) polypoid GN, ganglioneuromatous polyposis and diffuse ganglioneuromatosis [1-2]. GNs of gastrointestinal tract are considerably less common. They can occur at any level, from stomach to anus and have been even described in the gall bladder [1]. In gall bladder, benign mesenchymal tumors are rarely documented except leiomyoma. Isolated polypoid GN occur as solitary lesions and are incidentally noted during endoscopy or surgery as we have in this case. We report this case due to its unusual location in gall bladder.

Case History

A 42-year-female patient presented with a history of pain in right hypochondriac region for three months and clinically was diagnosed as chronic cholecystitis. Ultrasonography of the gall bladder revealed thickened contracted gall bladder with cholelithiasis. There was irregular nodule at the region of neck adherent to wall. Routine haematological, urine and serology investigations were found to be normal. Liver function tests showed only raised serum alkaline phosphatase levels. Cholecystectomy was performed and specimen was sent for histopathological examination.

Grossly, specimen of gall bladder weighed 15 gm and measured 5x2x2 cm. Cut section showed thickened fibrous areas with cholelithiasis. The neck region showed a sessile polypoid lesion measuring 0.3x0.2 cm in size. The cut surface was gray white and homogenous.

Figure-1: Hyperplastic spindle cell proliferation in the lamina propria, H & E stain, 10 X

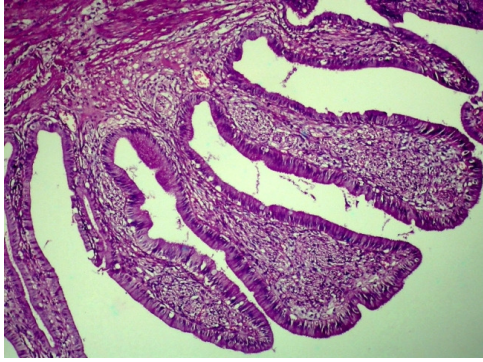


Figure-2: Another area showing expanded lamina propria, 10 X; with inset showing ganglion cells, H & E stain, 40 X

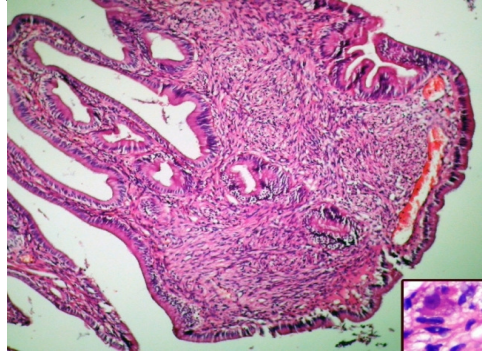


Figure-3: Clusters of ganglion cells amongst fascicles of spindle cells, H & E stain, 40 X

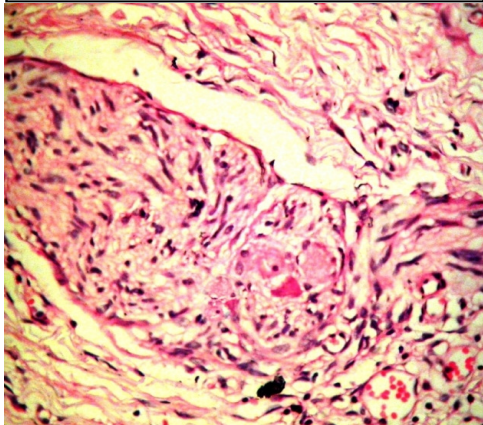
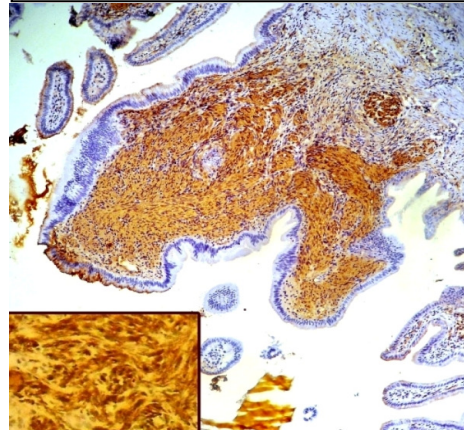


Figure-4: Schwann cell proliferation showing S-100 positivity, 10 X; inset shows 40 X view



Histopathologically, section from a polypoid lesion of neck showed mucosa overlying hypercellular, expanded lamina propria with diffusely proliferating wavy spindle cells arranged in whorls in the lamina propria against the fibrillar matrix; dissecting even the muscularis and adventitia. The margins were poorly circumscribed (Figure1,2). Amidst these fascicles of spindle cells were seen isolated and clusters of ganglion cells (Figure3). Some bundles showed mucoid change. Mucosa showed flattening and reparative atypia in some areas.

Mucosal fibrosis with mild chronic inflammation was also noted. Sections from the fundus and other areas showed features of chronic cholecystitis. Immunohistochemically, the spindle cells demonstrated a strong positivity for S-100 protein (Figure4).

Discussion

Ganglioneuroma [GN] is a tumor that originates from neural crest sympathogonia which are completely undifferentiated cells of the sympathetic nervous system. Neuroblastomas, ganglioneuromas and ganglioneuroblastomas are collectively known as neurogenic tumors [3]. Most frequently occurring in abdomen, these tumors can grow wherever sympathetic nervous tissue is found. Common locations for GN include adrenal gland, paraspinal retroperitoneum, posterior mediastinum, head and neck. It is uncommon to find them in urinary bladder, bowel wall, abdominal wall and gall bladder. GNs are rare benign fully differentiated tumors that contain mature schwann cells, ganglion cells, fibrous tissue and nerve fibers. These tumors can arise de novo or result from the maturation of ganglioneuroblastoma or a neuroblastoma into GN. These tumors may be hormonally active and hypertension, diarrhoea, flushing and virilization may occur as a result of secretion of catecholamine, vasoactive intestinal polypeptide or androgenic hormone [4]. These neoplasms are histologically classified into risk groups by using Shimda classification and Paediatric Oncology Group classification. GNs are staged using the INSS (International Neuroblastoma Staging System) [5].

Gastrointestinal GNs fall into three groups – Isolated (solitary) polypoid GN, ganglioneuromatous polyposis and diffuse ganglioneuromatosis. These categories have different clinical implications. Patients with isolated polypoid GN do not have increased risk of developing von Recklinghausen's disease or multiple endocrine neoplasia IIB [6]. Polypoid GNs develop equally in men and women. They peak between 20 – 40 years. Polypoid GNs are present as small, single, sessile or pedunculated polyps that range in size from 0.1 to 2.0 cm in diameter and grossly resemble juvenile or hyperplastic polyps or adenomas. Most are located in large intestine with colon and rectum as the frequent site [2]. GNs are very rarely seen in gall bladder and their location in the gall bladder is hardly ever reported. They are usually asymptomatic. Polypoid GNs have been reported in a few cases of Cowden's syndrome, a case of tuberous sclerosis, a case of familial polyposis coli and in a family with juvenile polyposis [6]. The diagnosis of ganglioneuromatous lesions centers mainly on the identification of ganglion cells in nodular or diffuse neural setting. In some ganglioneuromas the ganglion cell component is readily identifiable, whereas in others it is rare or even absent. Haematoxylin and eosin stain is usually sufficient for identifying the ganglion cells but NSE is helpful in a minority of cases when ganglion cells are sparse. S-100 protein identification is useful in confirming the neural background and extent of a diffuse lesion [6]. To know neural origin we did S-100 immunostaining but as we could easily locate and identify the ganglion cells with Haematoxylin and eosin stain so we did not opt for NSE immunostain.

The differential diagnosis of polypoid GN includes neurofibroma, schwannoma and gangliocytic paraganglioma. Ganglion cells are not normally found within mucosa [6]. Ectopic ganglion cells in the lamina propria can occur in response to mucosal injury but such cells associated with reparative lesions lie within a normal appearing lamina propria without characteristic S-100 positive spindle cell proliferation seen in GNs [2]. The pathogenesis of these ganglioneuromatous lesions remains unclear. Diffuse ganglioneuromatosis, referred to as neuronal intestinal dysplasia, is thought to represent an unusual hyperplasia of the nerve plexuses, related to abnormal levels of circulating nerve growth factors and or selective expression of the mutated neurofibromatosis gene (NF-1) within subpopulations of autonomic neurons [6-7]. Solitary polypoid GN appears more likely to represent a hamartoma or choristoma. Former may be the accurate term, because of lack of ganglion cells in normal intestinal mucosa and prevalence of polypoid GN to occur as mucosal based lesions [6]. The nature of polypoid lesions of the gall bladder is difficult to define before operation. The risk factors for malignancy include age more than 60 years, coexistence of gallstones and size of polypoid lesions more than 10 mm [8]. GNs have completely mature and differentiated cells and stroma. So removal of isolated GN is curative and patients have good prognosis. These lesions are not associated with systemic manifestations and do not require long term follow up [2].

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