Gastrointestinal Cancer: Research & Therapy

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Austin Publishing Group

Case Report

A Rare Association of Pheochromocytoma and Gastrointestinal Stromal Tumor in a Patient with Recklinghausen's Disease: A Case Report

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Received: June 10, 2017; **Accepted:** July 06, 2017; **Published:** July 13, 2017

Abstract

Neurofibromatosis type 1 (von Recklinghausen's disease-NF1) is a genetic disease characterized by neoplastic and non neoplastic disorders involving tissues of neuroectodermal and mesenchymal origin. It comprises 90% of neurofibromatosis cases. It is characterized by abnormal skin pigmentation (cafe au lait spots and axillary freckling), skeletal dysplasias, cutaneous and plexiform neurofibromas, and Lisch nodules.

Other tumours can also develop like pheochromocytoma, optic nerve and brain stem gliomas, carcinoids and rarely gastrointestinal stromal tumours.

A combination of pheochromocytoma and gastrointestinal stromal tumour is very rare. Only about 16 cases documented till 2015 in the English literature.

Here, we are reporting a rare combination of pheochromocytoma and gastrointestinal stromal tumour in a patient with neurofibromatosis type 1.

Keywords: Pheochromocytoma; Gastrointestinal stromal tumour (GIST); Inherited syndromes Neurofibromatosis 1 (NF1)

Background

Neurofibromatosis (NF) is a rare autosomal dominantly inherited syndrome with an incidence of 1 in 3000 live births [1]. Of the two types, neurofibromatosis 1 and 2 (NF1 and NF2, respectively), NF1 comprises 90% of the cases.

The NF1 gene encoding the protein neurofibromin has been localized to chromosome 17q11.2, and the NF2 gene encoding the protein merlin is on chromosome 22. NF shows complete penetrance but variable expressivity. Apart from multiple neurofibromas, many other neoplasms may be seen in such patients. The risk of pheochromocytoma in neurofibromatosis I is small: A pheochromocytoma is diagnosed in approximately 0.1% to 6% of all patients with neurofibromatosis I [2]. Gastrointestinal stromal tumour (GIST) is also described in NF1 patients, because 20% of the patients with gastrointestinal stromal tumor are asymptomatic, the tumors can be easily missed [3].

This article describes a female with the simultaneous occurrence of neurofibromatosis I, pheochromocytomas, and gastrointestinal stromal tumors.

Observation

We report the case of a 64-year-old female with epilepsy under Carbamazepine who reported pain in the left flank with cramps associated with post-prandial vomiting and constipation.

On clinical examination, the patient had about 15 Café-au-lait spots, the size of which was more than 1.5cm predominant in the trunk. Inguinal and axillary freckling was present. On further enquiry, patient revealed that her sister is also having similar lesions in the body. The rest of the clinical examination was normal.

The abdomino-pelvic CT scan revealed digestive tissue thickening in the left flank measuring 46.6mm long (Figure 1) and a heterogeneous mass of the right adrenal gland measuring 35.3mm in diameter (Figure 2).

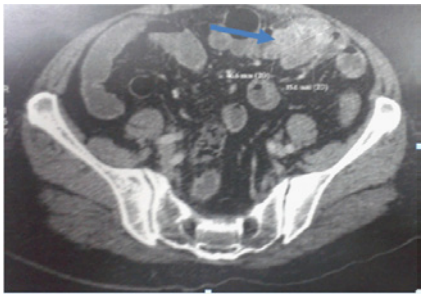

Figure 1: Soft tissue masse, arising from the wall of small bowel.

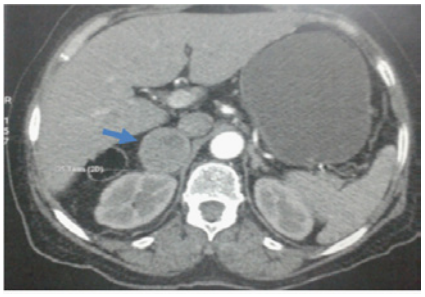

Figure 2: CT abdomen note the large, heterogeneous masse with areas of necrosis in the right adrenal area.

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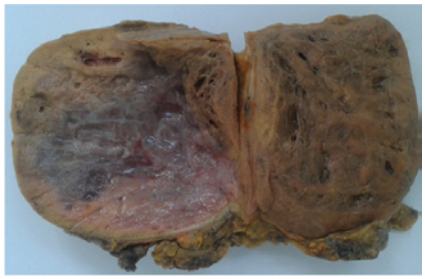

Figure 3: Gross specimen of left adrenalectomy. Cut section of pheochromocytoma with brownish/tan colour of the tumour.

Figure 4: Jejunal wall nodule.

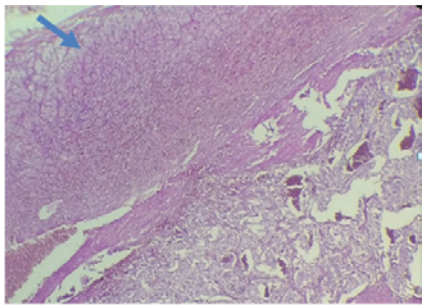

Figure 5: Microscopy of the adrenal mass showed normal adrenal tissue in the periphery (arrow) with a circumscribed neoplasm showing histological features of pheochromocytoma (hematoxylin-eosin staining (HE) x 100).

Biochemical analysis results were in normal range including urinary cathecholamine (Vanyl mandelic acid and normetaneprine).

After all these examinations, we performed transabdominal right adrenelectomy and partial small bowel resection, and end to end anastomosis.

We received in the pathology department the right adrenalectomy specimen (Figure 3) and excision specimen of the jejunal wall nodule (Figure 4).

Right adrenalectomy specimen measured as 6 x 4,6 x 2 cm and weighed 32g (Figure 3). The cut section showed brownish/tan colour of the tumour with presence of necrotic and haemorrhagic foci. At the level of the jejunal segment, there is a nodular lesion measuring 5.5x5 x 3.5 cm, located at a distance from the limits of surgical resections (Figure 4).

Microscopic examination of adrenal mass shows à pheochromocytoma with a characteristic nested or "zellballen"

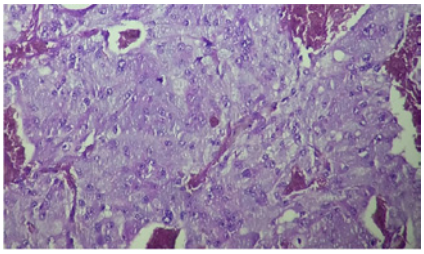

Figure 6: Histology of pheochromocytoma, different areas highly pleomorphic cells with interspersed vascular channels (hematoxylin-eosin staining (HE) ×400).

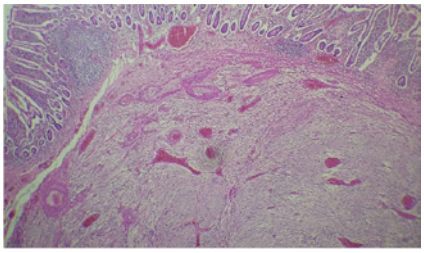

Figure 7: Lesion in the submucosa of the jejunum with spindle cells arranged in a fascicular pattern (HE x 100).

growth pattern This is composed of nests of epithelioid cells with variably eosinophilic, finely granular cytoplasm to more basophilic cytoplasm. The cells are epithelioid with indistinct cell membranes and vesicular nuclei with nucleoli. This tumor shows nuclear clearing in some nuclei (Figure 5, 6). The delicate spindled sustentacular cells around the nests generally require S100 immunostaining to identify.

Nodules from the jejunal wall showed a spindle cell neoplasm arranged in sheets and fascicles. Immunohistochemical staining (IHC) of this was positive for CD117, CD34 and DOG1. SMA was negative confirming the diagnosis of gastrointestinal stromal tumour (Figure 7).

Discussion

Neurofibromatosis (NF) is a familial syndrome with complete penetrance and variable expressivity. There are two types—NF1 and NF2—according to the specific molecular defect. The present case was diagnosed clinically as NF1 because three of the seven criteria of the National Institute of Health (NIH) consensus conference of 1987 [4] were met in this case, namely, (1) six and more café-au-lait spots more than 15mm in size were present, (2) freckling in the inguinal/axillary regions were noted and (3) the sister diagnosed to have NF1. (Two or more of the seven defined criteria are needed for diagnosis of NF1).

Pheochromocytoma occurs in less than 1% of NF1 patients [5]. The tumour presents clinically with features of hypertension. Our patient had a flank pain. Without arterial hypertension or increase in catecholamine.

The tumour can be clearly delineated by imaging studies is bilateral or multifocal in 10% to 15% of patients [6]. In the present case, only the left adrenal was involved by the tumour; the right adrenal was normal in imaging studies.

The incidence of GISTs among NF1 patients varies from 3.9 to 25%, while the overall ratio of NF1 among GIST patients is about 6% [7].

The most frequent signs and symptoms of gastrointestinal stromal tumors are abdominal pain, abdominal mass, gastrointestinal hemorrhage, and bowel obstruction or perforation. In at least 20% of patients with a gastrointestinal stromal tumor, the tumor(s) remain asymptomatic.

Although sporadic gastrointestinal stromal tumors occur predominantly in the stomach, the small intestine is most frequently involved in patients with neurofibromatosis I [8].

The coexistence of pheochromocytoma and GIST is very rare. Only a few cases have been reported in the English literature. This combination without the genetic background of neurofibromatosis type I have been described and is known as the Carney-Stratakis dyad. In most cases, prototypical lesions of the triad-pulmonary chondromas are also seen. But in the present case, there was no lung lesion.

Conclusion

Although rare, this association should be kept in mind; pheochromocytoma should be excluded before a patient with neurofibromatosis I undergoes surgery for gastrointestinal stromal tumors because an undiagnosed pheochromocytoma carries a high risk of life-threatening perioperative complications.

Authors' Contributions

All authors contributed and approved the final version of the manuscript.

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