An Unusual Case of Presacral Carcinoid Tumor and the Approach of Management

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Abstract

Introduction: Gut derived neuroendocrine tumors (NETs) are a heterogenous group of tumors classified as Gastroenteropancreatic (GEP) NETs. These tumors can be found along the gastrointestinal tract from the foregut, mid, to the hindgut. They are referred to as carcinoid tumors due to their potential to secrete bioactive hormones. Presacral tumors are a subset of GEP NETs that are histologically similar. They are uncommon tumors that are found at the presacral space and are often clinically silent with no associated carcinoid syndrome.

Presentation of Case: We report a case of 49 year old female who was diagnosed with a presacral carcinoid tumor. Her initial presentation, investigations that led up to the final diagnosis and management of the tumor are discussed.

Conclusion: Presacral carcinoid tumors are NETs that are clinically and histologically similar to GEPs arising from the colon or rectum. Management of such tumors is often surgical resection of localized disease with a long follow-up of surveillance to detect recurrence and metastasis.

Keywords: Carcinoid tumor; Presacral; Tailgut cyst; Neuroendocrine; Gastroenteropancreatic

Abbreviations: 5-HIAA: 5- hydroxyindoleacetic acid; CgA: Chromogranin A; CEA: Carcinoembryonic Antigen; CT: Computed Tomographic; GEP: Gastroenteropancreatic; LVI: Lymphovascular Invasion; MRI: Magnetic Resonance Imaging; NET: Neuroendocrine tumors; PAP: Papanicolaou smear; TGC: Tailgut Cyst; THBSO: Total Hysterectomy and Bilateral Salpingoopherectomy; WHO: World Health Organization

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Received: February 19, 2012; Accepted: March 2, 2013; Published: March 25 2013

Competing Interests: The authors have declared that no competing interests exist.

Consent: Written informed consent was obtained from the patient for publication of this report and accompanying images. A

Introduction

Presacral carcinoid tumors are rare entities and are known to be less aggressive than carcinoid tumors found elsewhere in the gastrointestinal tract. Patients are frequently asymptomatic and patients usually do not present with carcinoid syndrome even with metastatic disease. We report a case of a 6cm presacral tumor that was detected incidentally during a physical examination and had no clinical symptoms. The diagnosis was confirmed pre-operatively in a biopsy. The patient went on to have a transabdominal excision of the pelvic lesion with the final histology of a carcinoid tumor.

The tumor was subsequently resected enbloc in an open surgery and patient recovered well.

Case report

A 49 year old Indian perimenopausal female first presented after the discovery of a mass during a physical examination done prior to a routine screening papanicolaou (PAP) smear. Her medical history includes osteoporosis on Fosamax and a
previous ovarian cystectomy for a benign ovarian cyst more than fifteen years ago. Her family history is significant for breast cancer, prostate cancer and leukemia.

She had complaints of vague abdominal bloatedness and constipation for many years but had no other symptoms of abdominal pain, nausea, vomiting, change in bowel habits, per rectal bleed or melena. There was no history of loss of appetite or weight loss. Physical examination revealed a palpable mass on the left adnexa with no cervical excitation on bimanual palpation per vaginally. Her other system reviews were insignificant. Review of other body systems was unremarkable.

She did not report of symptoms like skin flushing, wheezing, dyspnoea or watery diarrhoea, typical of the carcinoid syndrome.

A pelvic ultrasound showed a retro uterine mass measuring 4cm (Figure 1). A computed tomographic (CT) scan similarly showed a 4x4cm mass at the left presacral space displacing the rectum to the right. The rectum and urinary bladder close to the mass displayed mural thickening with suggestion of invasion. There were no other suspicious lesions or lymphadenopathy seen in the gastrointestinal tract (Figure 2 A, B).

Figure 1 CT imaging of the presacral tumor. (A) Axial view. (B) Coronal view

Figure 2 MRI imaging of the presacral tumor. (A) Saggital view. (B) Axial view
Further investigations included an oesophagoduodenoscopy and colonoscopy that showed antral gastritis and no suspicious colonic lesions. Blood tests for tumor markers like CEA, alpha-feto protein, CA 125 and CA 19-9 were all normal.

She had an ultrasound guided biopsy of the pelvic lesion and histology of the presacral mass was suggestive of a carcinoid tumor.

A magnetic resonance imaging (MRI) of the pelvis was performed to further characterize the pelvic tumor as well as to delineate its relations to the other structures within the pelvis. The presacral tumor was seen as predominantly solid and located posteriorly to the rectum in the presacral region. It appeared to be separate from the left ovary with vascular supply deriving from the lateral pelvic side wall rather than the uterine vessels. There was also an enlarged uterus suggestive of adenomyosis and multiple Nabothian cysts in the cervical region. The tumor was localized with a visible resection plane and there were no suggestion of osseous or neurogenic involvement. The bladder was not seen to be involved with the tumor mass. There was no regional lymphadenopathy to suggest nodal spread [Fig 3a/b].

Her case was discussed at a multidisciplinary tumor board during which a decision was made to proceed with surgical resection of the pelvic tumor.

The patient underwent an open, transabdominal surgical resection of the presacral tumor. The anterior approach (transabdominally) was taken for the resection of the tumor to facilitate an extensive local resection. Intraoperative findings confirmed that the tumor was non-adherent to the rectum, mesorectum, bladder or other gynaecological organs. Hence decision was made for no bowel resection during the enbloc removal of the presacral tumor. Sacrectomy was not performed as there was no evidence of posterior invasion of the tumor to its bony relations.

Frozen section of the pre-sacral tumor was performed, which was interpreted as a neoplasm with differential diagnosis of tumor arising from either epithelial, neuroendocrine, sex cord or stromal cells. A THBSO was performed in view of the frozen section findings and considering adenomyosis of the uterus.

Her post-operative recovery in the general ward was uneventful. She was discharged on post-operative day eight. She recovered well but on her first follow-up appointment, she complained of fever and abdominal pain. She spiked a temperature of 39 Degrees Celcius. However septic workup, which included urine and blood cultures, was negative and the only abnormality was her raised total white counts of 16.9x 109/L (normal range 8-10x109/L). A CT scan performed on post operative day twelve showed a pelvic collection and mild left hydronephrosis. She was treated with a seven-day course of oral antibiotics – ciprofloxacin and recovered well and remained afebrile after completion of the medication. A surgical drain left in situ was removed on post-operative day 17 after the output showed a downward trend.

**Histopathological Results**

Based on the World Health Organization (WHO) classification of neuroendocrine tumors (NETs), the final histology of the pelvic tumor confirms the diagnosis of a well differentiated 6cm grade 2 neuroendocrine neoplasm (atypical carcinoid) with a mitotic rate of 7 per 10 high power field. The resection margin and capsular surface were free of tumor. Macroscopic description indicated features of a well encapsulated tumor with fleshy cut surface and focal cystic and haemorrhagic areas. Microscopic examination showed cords and trabeculae of neuroendocrine cells, similar to the histological characteristics of carcinoids. The characteristic “salt-and-pepper” nuclear chromatin was seen.

The tumor cells were positive for CK20 only and CK7 and CDX2 were both negative. Immunohistochemistry staining was unable to conclude the primary site of the carcinoid tumor. The THBSO specimen was negative for malignancy with the myometrium showing adenomyosis. Both ovaries and tubes had benign cysts and there were
nabothian cysts on the cervix, detected on the pre-operative scans.

**Discussion**

Majority of NETs are found in the gastrointestinal tract (67%) [1]. These tumors are referred to as gastroenteropancreatic (GEP) NETs. GEP NETs are most common in the small intestine, followed by the rectum and appendix. GEP NETs or carcinoid tumors found in the presacral region are rare and to our knowledge twenty five cases have been reported in the literature [2-12]. Most of these reported cases were associated with carcinoid tumors derived from tailgut cysts (TGCs).

TGCs are persistent remnants of the embryonic primitive hindgut. These are multiculated cysts lined by a variety of epithelial types [14]. Malignant transformation is possible and there had been reports of transformation of tailgut cysts to adenocarcinomas [14-16], carcinoid tumors [3-13], squamous cell carcinomas [18] and sarcomas [19].

Regardless of association with identifiable TGCs or not, presacral carcinoid tumors have been often hypothesized to arise from neuroendocrine cells in the presacral hindgut rests [5, 13, 27]. Due to the similarity in histological patterns of presacral carcinoids, it is often associated with carcinoid tumors of the rectum [14].

Presacral carcinoid tumors are indolent growths that usually produce symptoms only as a consequence of growth. Patients typically do not display signs of carcinoid syndrome. This is similar to patients with colonic or rectal carcinoids that tend to be clinically silent tumors until they are advanced. Most patients would complaint of local mass effects like pelvic pain or rectal fullness with or without associated constipation or haematochezia. Our reported case complained of vague abdominal bloatedness for many years and was fairly asymptomatic otherwise. Occasionally, the tumor mass is detected during routine digital rectal or per vaginal examination or detected incidentally on imaging.

A pelvic ultrasound or CT scan can be performed to evaluate a mass discovered on per rectal or vaginal examination. CT scans are ideal for identifying the primary tumor located at the presacral region and hepatic metastases that are common in advanced disease. Imaging like a MRI is also important in the pre-operative planning stage for delineation of the pelvic structures that are in close proximity with any retrorectal or pre-sacral tumor. It also facilitates the planning of the operative approach [20].

Surgical resection is the definitive treatment for localized pre-sacral carcinoid tumors. The presacral tumor can be approached in three ways: the transabdominal, the perineal or the combined abdominoperineal approach [21]. Low lying and small lesions that do not extend above S3 can be approached from a posterior approach via a parasacral incision. The other two approaches are taken to facilitate the need for any concomitant sacrococcygeal resection.

In the event a sacrectomy is indicated, patients must be counselled adequately regarding potential functional sequelae of anal incontinence if the sacral nerve roots are sacrificed. In general, the preservation of at least unilateral S3 nerve roots allows for normal bowel and bladder function post sacrectomy [22]. Pelvic stability must be ensured to avoid stress fractures if adjuvant radiation therapy is required or was given to the patient pre-operatively. The spinopelvic stability can be maintained by preservation of more than half the S1 vertebral body or restored with a fusion. Though not common, carcinoid tumor spreading to the bone has been reported mostly of foregut or midgut origin [23, 24]. Common sites of bony metastasis are the axial skeleton like the spine, ribs and pelvis [25]. There has been one report of a rectal carcinoid tumor invading the sacrum requiring partial sacrectomy [26].

With reference to current published guidelines in the literature [28, 29, 30], there are no separate guidelines for the specific management of presacral carcinoid tumors. However, treatment strategies for gastrointestinal carcinoids are all categorized anatomically, implying the common clinical behaviour of tumors arising from the same embryological origin.

Carcinoid tumors arising in the retrorectal/
presacral region are often treated surgically, just like rectal carcinoids, with the objective of symptomatic treatment and cure. Like all gastrointestinal carcinoids, presacral carcinoids can metastasize to regional lymph nodes and distant sites. Common sites of metastasis include liver, lungs and bone [24]. The risk of metastasis increases with primary tumor size, nodal status, histologic growth pattern and microinvasion and presenting symptoms [23, 31, 32]. Rectal carcinoids are known to be least aggressive with 82% of the carcinoids at this location being localized tumors with no metastasis [31]. The propensity of primary rectal carcinoid tumors to metastasize is low with high reported 5-year survival rate of more than 87% compared to 30-60% of those originating from the foregut and midgut [31,1].

In our patient, the final histology revealed a well differentiated, well circumscribed carcinoid tumor with clear resection margins and capsular surface clear of tumor cells. There was no involvement of the resected reproductive organs. However the patient has a grade 2 carcinoid, based on mitotic rate and would hence be classified as an intermediate grade rectal carcinoid based on the WHO classification guidelines. In Fahy’s [33] attempt to predict the risk stratification of rectal carcinoids, poorer outcome was associated with large tumor size, deep invasion, presence of LVI, and increased mitotic rate.

Considering the long-natural history of carcinoid tumors and its ability to metastasize, post treatment follow-up would require regular imaging like triphasic CT scans or MRI of the abdomen and pelvis. Our reported case would be followed up closely with postoperative imaging for local recurrence and distal metastasis.

It is also recommended to perform blood and urine measurements of circulating peptides and amines. Baseline tests should include regular plasma chromogranin A (CgA) and 5- hydroxyindoleacetic acid (5-HIAA). The recommended follow-up period as suggested in the National Comprehensive Cancer Network (NCCN) guidelines should be at least 7 years for midgut carcinoid [28]. The initial re-evaluation duration to be 3 to 12 months post surgical resection and every 6-12 months thereafter.

In summary, presacral carcinoid tumors are rare entities but when a case is encountered, the management approach should always take the course similar to that of any GEP NETs. A comprehensive history to outline clinical signs and symptoms, clinical examination and family history to exclude complex cancer syndromes (eg Multiple Endocrine Neoplasm 1, 2) are important. Due to their indolent and silent presentation, imaging plays an important role in diagnosis and staging.

Patients may or may not present with symptoms attributable to hormonal hypersecretion in presacral carcinoid tumors. Laboratory urine and blood tests should be performed routinely to rule out carcinoid syndrome and also to provide useful clues to the origins of the tumor since about 10% of midgut carcinoid tumors are often associated with carcinoid syndrome. The incidence is usually lower for carcinoid tumors from the foregut and hindgut. Tumor markers like CEA, ca 19-9 and ca 125 are useful in excluding other types of malignancies like adenocarcinoma or squamous carcinoma and should be performed during any investigation involving carcinoid tumors. Surgical resection is the definitive treatment for locoregional disease.

Conclusion

Carcinoid tumors in the presacral region are unusual growths. These tumors do not differ clinically or histologically from carcinoid tumor of the colon and rectum. Hence the approach to management can be similar. However presacral compared to hindgut carcinoid tumors may be less aggressive and more localized with no regional lymph node involvement. Hence surgical resection may occasionally not require resection of the rectum or surrounding pelvic organs. The long term follow-up with clinical examination and appropriate imaging is required in view of the long natural history of carcinoid tumors.

Author’s contribution

WFSJ performed critical appraisal of the literature and wrote the manuscript. MTCC supervised,
assisted in the critical appraisal of the included studies and editing of the manuscript. Both authors contributed to the final proof-reading of the manuscript.

Reference


