Primary large cell neuroendocrine carcinoma of the presacral region

P Theunissen, M Fickers, R Goei

Abstract

A 7 cm diameter presacral tumour, not related to the intrapelvic organs, was found in a 51 year old woman. The needle biopsy showed a poorly differentiated large cell carcinoma. The patient died of urosepsis after chemotherapy. Postmortem examination revealed no other primary or metastatic tumour. Histological examination of the presacral tumour showed a large cell carcinoma with a trabecular pattern and strong immunoreactivity for neuroendocrine markers. The tumour was finally classified as a primary large cell neuroendocrine carcinoma of the presacral region.

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Malignant tumours in the presacral region or retrorectal space are extremely rare in adults. In the literature, we found 10 reported cases of primary neuroendocrine tumours in the presacral region, all carcinoid tumours.[1 2] In one of these reports, it was assumed that these carcinoids probably arise from neuroendocrine cells located in presacral hindgut rests, whether associated with identifiable tailgut cysts (retrorectal cystic hamartoma) or not.[1] Our patient seems to be the first documented case of a primary large cell neuroendocrine carcinoma (LCNEC) of the presacral region.

Case report

A 51 year old woman was referred to the department of internal medicine for lower abdominal pain with rectal tenesmi. Rectal and vaginal examinations were normal. Sigmoidoscopy revealed no abnormalities. Barium enema showed a stricture in the rectosigmoidal region. Computed tomography (CT) and magnetic resonance imaging of the pelvis showed a soft tissue mass (7 × 5 × 5 cm) in the presacral region (fig 1). The erythrocyte sedimentation rate was 20 mm in one hour, but other laboratory tests were normal. A needle biopsy was taken. The tumour was initially interpreted microscopically as a poorly differentiated large cell carcinoma. Immunohistochemically tumour cells showed expression of keratin (antibody clone MNF116; Dako, Glostrup, Denmark) and focally vimentin. Immunohistochemical stains for carcinoembryonic antigen, CA125, and S-100 were negative. Workup for a primary tumour and other metastatic disease was negative. The patient was treated with four courses of chemotherapy with etoposide and cisplatin. After two courses the patient showed clinical benefit (diminution of pain and faecal continence), but without objective tumour regression on CT scan. At that time, a surgical approach was considered but rejected by the patient because of serious morbidity afterwards. Irradiation was also contemplated. The patient died of urosepsis in the haematological nadir after the fourth course of chemotherapy. Permission to perform a necropsy was granted. The postmortem examination confirmed a 7 cm solid tumour in the presacral space firmly attached to the sacrum. There was no relation to pelvic organs. No metastasis or other primary tumour was found. Microscopically (fig 2) the tumour showed an infiltrative trabecular growth pattern. There was no necrosis present. The tumour cells

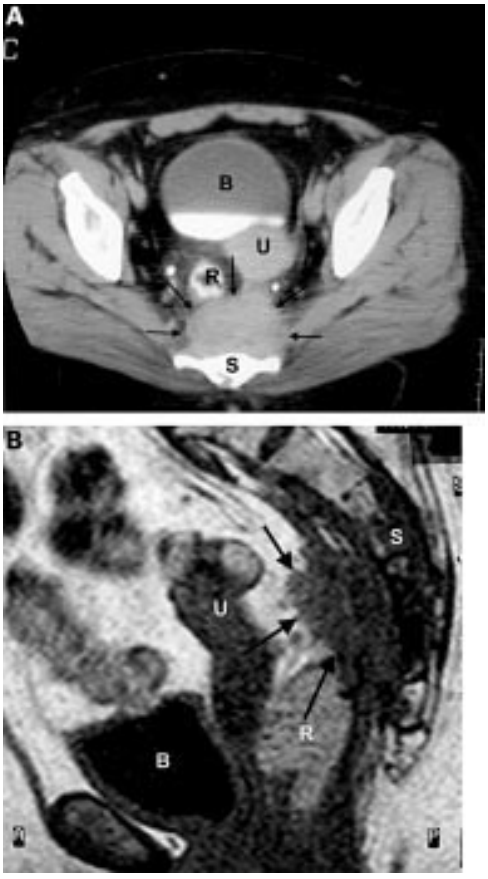

Figure 1 (A) Axial computed tomography scan cut through the pelvis depicting the presacral tumour (arrows). Notice the adjacent structures: B, bladder; R, rectosigmoid; U, uterus; S, sacrum. (B) Sagittal T1 weighted magnetic resonance image through the pelvis. Notice the invasive growth of the tumour (arrows) in the sacrum (S), as demonstrated by the low signal intensity of the involved vertebral bodies. Notice adjacent structures: B, bladder; U, uterus; R, rectum.

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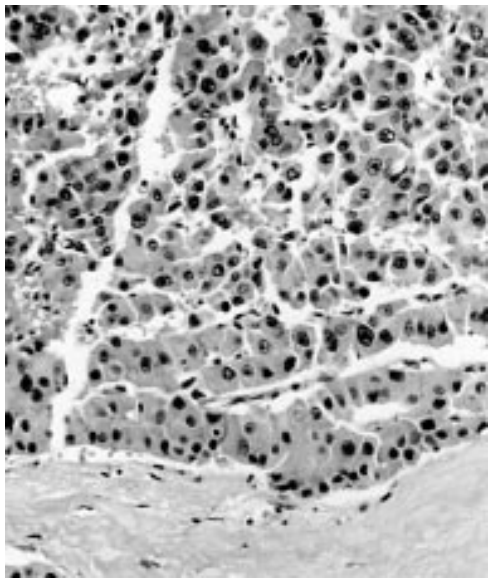

Figure 2 Microscopic picture of the tumour (postmortem specimen) showing a trabecular pattern with large sized cells that possess vesicular nuclei with prominent nucleoli (haematoxylin and eosin; original magnification, ×250).

were of large size and of polygonal shape, with wide eosinophilic cytoplasm. The nuclei were large, vesicular, and with prominent nucleoli. The mitotic activity was 2 mitoses/2 mm^2. Immunohistochemistry (fig 3) was repeated and extended to neuroendocrine markers because of the now recognisable trabecular pattern that was not evident in the histological sections of the needle biopsy. The tumour showed strong expression of both chromogranin and synaptophysin. No demonstrable sustentacular cells were present in the S-100 stain. The tumour was finally classified as primary LCNEC of the presacral region. The differential diagnosis of a paraganglioma could be ruled out because of the trabecular pattern, the lack of sustentacular cells, and the diffuse strong expression of keratin. The histological diagnosis was confirmed by Professor G Klöppel (department of pathology, University of Kiel, Germany) who was consulted.

Discussion

Tumours in the presacral space are extremely rare. An incidence of one in 40 000 admissions in a review of 120 patients with presacral tumours treated at the Mayo Clinic over a period of 29 years has been reported.[3] Presacral tumours have been classified as congenital, inflammatory, neurogenic, osseous, and miscellaneous.[4] In an overview of the literature, 276 cases of retrorectal tumours were reported.[2] According to this overview, chordomas are the most common malignant tumours, comprising over 50% of all tumours. In this overview, only one carcinoid was reported in the miscellaneous group. In another paper, three new cases of presacral carcinoid tumours were reported and an additional six cases were referred.[1] In five of these 10 cases, the carcinoid tumours were associated with a tailgut cyst or retrorectal cystic hamartoma. The age range of the patients was 19–61 years. Five patients were female, two male, and in three cases the sex of the patient was not documented.

To our knowledge, our case is the first documented case of a primary LCNEC of the presacral region. Whether this tumour could eventually be classified as atypical carcinoid is controversial. The large cell size and the large vesicular and polymorphic nuclei with prominent nucleoli are morphological characteristics supporting the diagnosis of a LCNEC, but the low mitotic activity and the lack of necrosis are in favour of an atypical carcinoid. There was no associated tailgut cyst or retrorectal cystic hamartoma present. The origin of this tumour remains speculative: because documented cases of other primary neuroendocrine tumours (carcinoid tumours) of the presacral region often show an association with a tailgut cyst, it is possible that these neoplasms

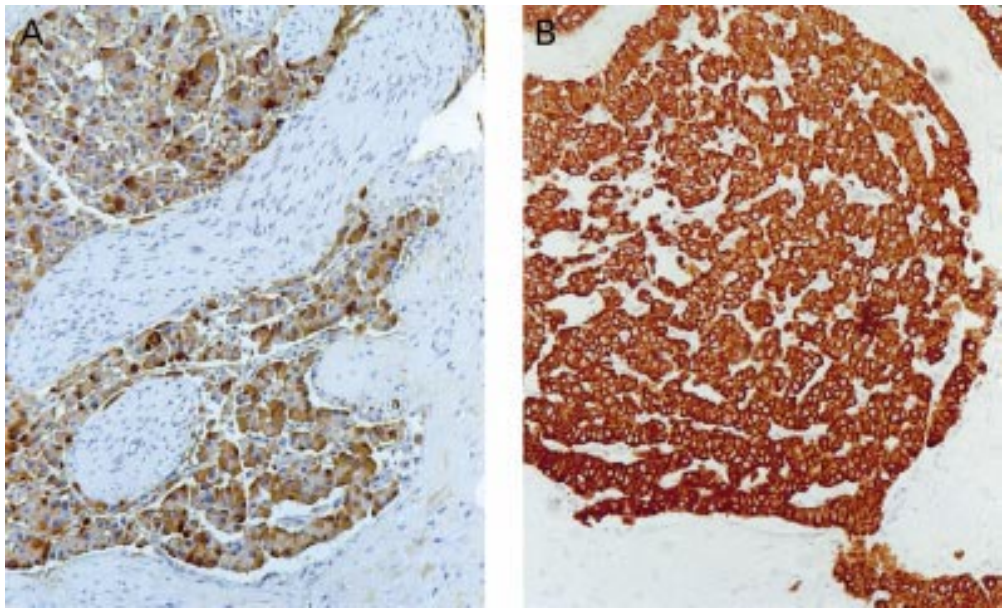

Figure 3 Immunohistochemical stain of the tumour. (A) Staining for chromogranin A: notice the perineural tumour growth. (B) Staining for cytokeratin, highlighting the trabecular growth pattern (original magnification, ×100).

could arise from neuroendocrine cells in presacral hindgut rests.

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