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COMMUNICATION

Metastatic neuroendocrine malignancy presenting as Sister Mary Joseph's nodule

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Abstract Sister Mary Joseph's nodule (SMJN) is often the first sign of intra-abdominal and/or pelvic malignancy. We present an interesting case of SMJN in an 84-year-old woman referred by a rheumatologist to a gynaecological oncology team with mass in her umbilicus. Histology identified it as a metastatic neuroendocrine carcinoma origin, which was not clear from biopsy.

Keywords Umbilicus · Sister Mary Joseph's nodule (SMJN) · Neuroendocrine tumor.

Introduction

Sister Mary Joseph's nodule (SMJN) can be the first manifestation of an underlying malignancy or an indication of a recurrence in a patient with a previous malignancy [1]. More than 400 cases of this well-described clinical presentation of advanced gastrointestinal and gynaecologic cancers have been reported [2]. We present what we believe to be the first case of metastatic neuroendocrine malignancy presenting as SMJN.

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Case report

An 83-year-old Caucasian woman was referred to the joint gynaecological oncology clinic with mass in her umbilicus. She was 34 years post-menopausal. There was no history of post-menopausal bleeding, discharge or use of hormone replacement.

Her past medical history included dermatomyositis, which had been diagnosed 4 years ago. Her condition was well controlled with 7.5 mg methotrexate weekly since July 2006. She also had a past history of osteoarthritis, hypothyroidism and mild asthma well controlled with Salmeterol 250 mg twice a day. She had an appendectomy and total left knee and hip replacement. She had no allergies and was taking levothyroxine 75 μg and folic acid 5 mg once a day, respectively.

Her abdominal examination revealed a nodule in the umbilicus 4×3 cm in diameter hard in consistency with clear margins. Vaginal examination revealed an anteverted bulky uterus and no adnexal masses. Endometrial pipelle sampling was attempted. Investigations included a normal full blood count, which showed a haemoglobin level of 12 g, erythrocyte sedimentation rate of 11 mm in the first hour and C-reactive protein of 33 mg/l, normal renal and liver profile.

The computed tomography (CT) scan before assessment in clinic revealed a small necrotic mass anterior to the IVC at L2 level, a sliding type of hiatus hernia and small surrounding but not pathologically enlarged lymph nodes. Furthermore, a central pelvic mass was noted originating from the uterus or ovary. The uterus was enlarged and irregular in outline and enhanced homogenously. A trans-vaginal ultrasound scan showed an anterverted uterus with thickened bright, cystic endometrium measuring 15 mm. The anterior wall of the uterus appeared to be smooth, but

the posterior wall was grossly enlarged and irregular in outline and measured 8×4.7×4.3 cm. The right adnexa contained a cystic mass measuring 2.5 cm that could have been of ovarian origin. The left ovary was not identified.

Hysteroscopy revealed a large fundal endometrial polyp, which was removed with polypectomy forceps and appeared benign. Afterwards, through a transverse incision round the umbilicus, the mass was dissected down to the rectus sheath. It contained omentum only. Manual examination of abdominal cavity revealed multiple nodules on the underside of the abdominal wall. In view of the unresectable disease, only a Mayo repair was performed to close the defect after resection of the umbilical nodule. The patient had an uneventful postoperative period and was discharged home on the second postoperative day.

The histology report of the endometrial polyp indicated that it was benign showing menopausal features. The umbilical sample was reported a poorly differentiated tumour. Initial histological examination identified no particular differentiation. Immunostains showed intense reactivity with mixed cytokeratine indicating epithelial origin and intense reactivity with S100 protein. The appearances indicated neuroendocrine differentiation. Further immune stains were undertaken and showed faint reactivity with chromogranin A and CD56. The final histological report was a metastatic neuroendocrine carcinoma, the origin of which was unclear.

The patient declined any further treatment but agreed to undergo one more CT scan, which revealed that the previously noted central irregular pelvic mass had enlarged and measured 6.3 cm in depth × 7 cm in width on the axial scans and 10.4 cm in height on the sagittal scans. There was also considerable omental thickening and infiltration. A small amount of abdominal and pelvic ascites was noted. The liver had changes compatible with fatty infiltration, but no focal was lesion seen. No significant abnormality was revealed in the spleen, pancreas, adrenal glands or kidneys. Diverticular disease was noted in the sigmoid colon. The radiological opinion was that the pattern of the disease was compatible with an infiltrating ovarian malignancy. There was also a small soft tissue nodule seen peripherally in the right lower lobe and slightly smaller calcified nodule in the same lobe, but it was uncertain whether both were granulomas or one of them was a secondary deposit. There were two small nodules in the left mid-zone, which could very well represented lung metastases.

In the view of the extensive nature of the disease, palliative treatment only was recommended. Her symptoms were relatively minor at the time of last review in the clinic before discharge under the care of a palliative team. She still had palpable induration around the area of the excised umbilical nodule that was also tender in the right iliac fossa area.

She was referred to the Community Palliative service with no follow-up with the Oncology team. She was admitted to the Hospice for palliative care where she died 1 month later (Fig. 1).

Discussion

Umbilical metastasis (SMJN) is rare. It is encountered in 1–3% of patients with intra-abdominal and/or pelvic malignancy; with gastric carcinoma being the commonest origin in men and ovarian carcinoma in women [3], of which serous papillary cystadenocarcinoma (34%) is the most frequent. Furthermore, endometrial carcinoma, cervical, vaginal and vulval may also be responsible for metastasis to the umbilicus [4]. Overall metastases to the umbilicus represent only 10% of all secondary tumours, which have spread to the skin [5, 6]. In 15% to 30% of patients, the source of the primary site of the tumour is unknown [7–9]

Presentation is usually as a painful or painless lump in the umbilicus. The size of the nodule usually ranges from 0.5 to 2 cm, although some nodules may reach up to 10 cm in size [10]. In our case, the nodule was noted by a rheumatologist during the follow-up visit for the longstanding dermatomyo-

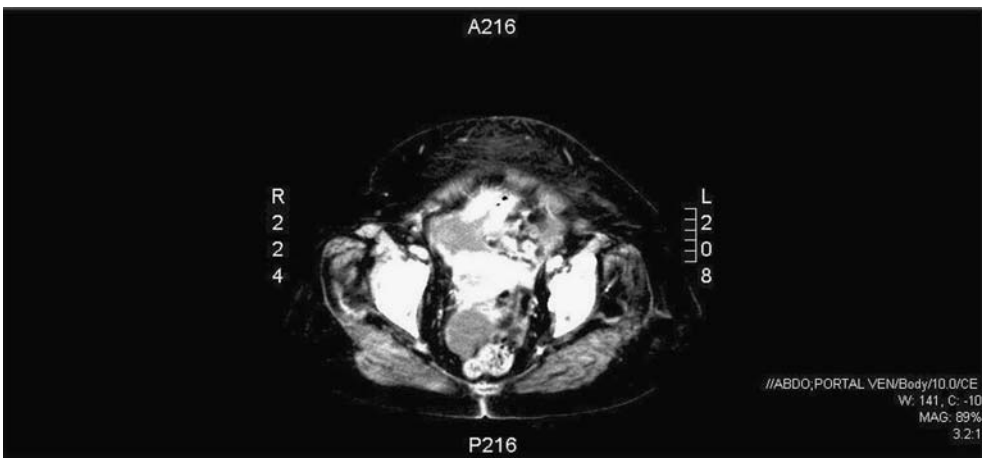

Fig. 1 Pelvic CT scan

sitis, which we should now consider to be a para-neoplastic manifestation of her malignancy as is often the case with autoimmune conditions.

The exact mechanism of tumour spread to the umbilicus still remains unclear. However, several hypotheses have been proposed, which describe the arterial, venous and lymphatic systems as possible routes by which tumour cells could implant into the umbilical region, especially from gynaecological cancers [11, 12]. The presence of an umbilical metastasis usually suggests an advanced metastatic process characterised by poor prognosis [13, 14]. Identification of the primary tumour is important for treatment planning. Therefore, obtaining histological confirmation of tumour type is recommended. However, sometimes clinical, cytological, histological, radiological and/or surgical investigations may not be sufficient to identify the primary site of the metastasis [15]. In our case, the patient had surgery that involved excision of the nodule and investigation of the abdominal cavity. Extensive metastases involving peritoneum and omentum disease made it impossible to assess the pelvis and identify a possible gynaecological primary tumour. However, the CT scan report performed before surgery suggested a possible ovarian malignancy. The final histology confirmed the excised SMJN as a metastatic neuroendocrine carcinoma. To our knowledge, this is the first ever reported case of metastatic neuroendocrine tumour presenting as SMJN.

Neuroendocrine tumours (NET) are tumours arising from neuroendocrine cells of neural crest origin. They are characterised by the presence of neurosecretory granules, which react positively to silver stains and to specific markers including neuron specific enolase, synaptophysin and chromogranin. In our case, the final histology confirmed the neuroendocrine origin of the excised tumor by the use of chromogranin A. NET most commonly originate in the appendix, small intestine, rectum and bronchus [16, 17]. Metastasis of the skin has been reported but typically occurs in association with metastases elsewhere [18, 19]. There have been no reports of NET metastasising to the umbilicus. Quite commonly, NET gives rise to the carcinoid syndrome, consisting of flushing, diarrhoea, wheezing, facial oedema and periodic abdominal pain. None of those symptoms were present in our patient. The origin of tumor has not been confirmed, although an ovarian origin was suspected by radiologist. The neuroendocrine gynaecological cancers are usually rare and aggressive. Reported cases include neuroendocrine carcinoma of vagina, cervix, ovary and even fallopian tube. But none of those cases had tumor metastasised to the umbilicus and presented as SMJN.

The average survival time of patients with SMJN is 11 months with <15% of the patients surviving >2 years. In some patients, however, depending on the state of the primary neoplasm and the patient's general condition, surgery and/or chemotherapy may improve survival [1]. In our case, it was only 11.,5 months between the time of initial diagnoses and death.

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