Rare disease

Krukenberg tumour arising from adenocarcinoma of the gastro-oesophageal junction in a 28-year-old female presenting as lower abdominal swelling mimicking an inguinal hernia

Hosam E Matar,¹ Ashraf S Elmetwally,² Iliya Salu,² Rudi Borgstein,³ Olu Oluwajobi²

¹Department of General Surgery, Royal Free Hampstead NHS Trust, London, UK;

²Department of General Surgery, North Middlesex University Hospital NHS Trust, Sterling Way, London, UK;

³Department of Radiology, North Middlesex University Hospital NHS Trust, Sterling Way, London, UK

Correspondence to Hosam E Matar, hematar@doctors.org.uk

Summary

Krukenberg tumours arising from gastro-oesophageal adenocarcinomas prior to the fourth decade are extremely rare. The authors present the case of a 28-year-old patient who was then 4 years of age, residing close to the Chernobyl nuclear reactor at the time of the nuclear disaster in 1986, and was found to have late-stage Krukenberg tumours from a gastro-oesophageal primary. Her presentation with right groin pain initially raised a suspicion of an occult groin hernia. Clinicians are reminded to delve deeply into the social history in their enquiries with Eastern European patients who present with unusual clinical features and were in utero, young and living in proximity to the nuclear fallout zone at the time of the incident.

BACKGROUND

Krukenberg tumours are rare metastatic ovarian tumours arising from primaries in the gastrointestinal tract, first described in 1896.¹ Symptoms are either absent or extremely variable with an average age of 45 years at diagnosis. Only 25–30% of patients are known to have a primary elsewhere at initial diagnosis.² Krukenberg tumours unfortunately are advanced malignancies with extremely poor prognosis and median survival of 7–14 months.^{3 4}

The aetiology and management of adenocarcinoma of the gastro-oesophageal junction (GOJ) continues to be a matter of debate despite the rising incidence.⁵ We report, what we believe is the first case in the literature of a 28-year-old female with Krukenberg tumour secondary to signet-ring adenocarcinoma of the GOJ that presented solely with groin pain and lower abdominal swelling that mimicked a right-sided inguinal hernia.

Figure 1 (A) CT scan image showing thickening in the antrum and pyloric region (arrowed). (B) pelvic CT scan showing uterus and ovarian masses. (C) pelvic CT scan showing bilateral ovarian masses and pelvic fluid. (D) CT scan showing one of the vertebral lytic lesions (arrowed).

Figure 2 (A,B) Endoscopic findings at the gastro-oesophageal junction.

CASE PRESENTATION

A 28-year-old female manual worker presented to Accident and Emergency with a 3-day history of troublesome right groin pain radiating globally in the pelvic area and to the lower back after lifting heavy objects. The pain was constant, dull, of gradual onset and progressively worse on movement. It was not associated with nausea, vomiting, dyspepsia or alteration of bowel habits and responded partially to Ibuprofen.

She also had 3 months of recurrent right groin swelling extending to the labia which was investigated in her native Poland by means of transvaginal ultrasound with needle aspiration of a cyst. There was no cytological or histological diagnosis or follow-up.

Her menstrual periods were normal and regular and there were no prior or current gynaecological symptoms. A non-smoker and an occasional consumer of alcohol, she was otherwise fit and well, with no family history of malignancy. However, direct questioning, revealed that the patient was 4 years old and lived only about 60 miles away from the Chernobyl reactor, Ukraine when the disastrous nuclear explosion occurred in 1986.

INVESTIGATIONS

General examination and vital signs were normal. Abdominal examination was soft and non-tender with slight fullness in the right inguinal region without a cough impulse. Slight tenderness was elicited over the lower lumbar vertebrae. Physical examination of the breasts was normal.

The basic blood tests were normal, but the liver function tests showed markedly elevated alkaline phosphatase of 848 U/l. Pregnancy test and urinalysis were both negative. Tumour marker values were carcinoembryonic antigen 4 µg/l, CA-125 29 U/ml, CA 19-9 404 U/ml and human chorionic gonadotropin <1 U/l.

CT scan of the abdomen and pelvis (figure 1A) showed several small rounded densities adjacent to the GOJ with some irregularity and thickening of the gastric antrum/pyloric region and no focal lesions within the liver. In the

pelvis (figure 1B,C), two large heterogeneous, part-cystic masses were present, the largest of these measured 9.8 cm while the smaller measured 5.8 cm. Free fluid was present in the pouch of Douglas. Furthermore, multiple lytic areas (figure 1D) were seen within the vertebrae and pelvic bones. The pancreas, kidneys, adrenals and other intra-abdominal organs appeared normal. Staging CT scan of the chest showed soft tissue thickening at the GOJ with adjacent lymph nodes, but no evidence of mediastinal lymphadenopathy. Notable were several small lytic areas in the vertebral bodies consistent with metastatic deposits.

Oesophagogastroduodenoscopy demonstrated erythematous, thickened and raised mucosa at the GOJ which was biopsied (figure 2). Colonoscopy with random biopsies was completely normal.

Histopathology of the GOJ biopsies revealed poorly differentiated adenocarcinoma with foci of signet ring features in association with heavily inflamed gastric fungal mucosa in keeping with primary gastric tumour. Immunohistochemistry confirmed patchy positivity for CK7 and CK20 while staining was negative for oestrogen receptors and progesterone receptors in keeping with GOJ carcinoma. There was no *Helicobacter pylori* in the specimens.

Transvaginal ultrasonography showed a right ovary measuring 5.7×5×5.4 cm with cystic areas that were less than 2.4 cm each. The left ovary measured 11×7.7×10.9 cm and contained cystic areas under 2.7 cm each. Breast ultrasonography was normal.

OUTCOME AND FOLLOW-UP

The diagnosis of metastatic adenocarcinoma in the GOJ was established and palliative chemotherapy started using Epirubicin, Cisplatin and Capecitabine regimen.

DISCUSSION

Krukenberg tumours with characteristic mucin-filled, signet-ring cells may affect a wide age range.⁶ In a case

series of 28 women, Savey *et al*⁷ reported a mean age of 42 years, while Mrad *et al*⁸ reported 15 cases with patients' ages ranging from 13 to 71 years. Similarly, a large Latin American series reported ages ranging from 18 to 84 years in 56 patients.⁹

The predominant location for the primary tumour is the stomach in 40–94%,^{2 6–10} a finding supported by data from the Peruvian National Institute of Neoplasia. 58.9% of patients had gastric primaries, presenting mainly with abdominal pain and swelling.⁹

The definition of what constitutes GOJ tumours may be mired in controversy.⁵ Nevertheless, to the best of our knowledge, there are no previous reports of Krukenberg-associated primaries of the GOJ in anyone so young. In stark contrast to our patient, the peak age group for tumours of the GOJ in the general population is between 50 and 60 years with male-to-female ratio of 2:1 and 12:1 respectively.^{11–13}

This patient presented with a Type II tumour by Siewert's classification,⁵ being a true carcinoma of the oesophagogastric junction. Type II tumours resemble proximal gastric cancer more closely than do distal oesophageal adenocarcinoma.⁵ In a population-based analysis of patients with gastric cancer, Theuer *et al*,¹⁴ found young patients <40 years with adenocarcinoma have a more aggressive form and therefore a poorer prognosis than older patients. Younger patients were more likely to have distant metastases with signet ring cell type, however, they were less likely to have GOJ adenocarcinoma.¹⁴ Krukenberg tumours arising from gastric carcinomas selectively spread in the stomach-ovarian axis with the retrograde lymphatic spread being the most likely route of metastasis.¹⁵ However, our patient presented with carcinoma of the oesophagogastric junction where the mode of lymph node spread yet to be understood.¹⁶

Our patient presented with non-specific and potentially misleading symptoms, advanced disease evident with bony metastasis and Krukenberg tumours in the presence of a mainly negative gynaecological history. The diagnosis was potentially missable or subject to delay without recourse to CT scanning. Her unquantifiable exposure to nuclear irradiation from proximity to the 1986 Chernobyl reactor number 4 disaster, which released about 5% of its radioactive core into the atmosphere is a plausible risk factor for the uncommon primary site and younger age in this case.

Juxta-Chernobyl contaminated areas were mainly exposed to I¹³¹ and Cs¹³⁷ radioactivity with half-lives of 8 days and 30 years respectively, resulting in evacuation within 2 weeks of over 160 000 inhabitants within a 30 km radius. The exclusion zone was later extended to just under 60 km with evacuation of a further 210 000 people. Immediate radiation doses of the evacuees ranged from under 50 mSv to over 100 mSv.¹⁷ Our patient, who was only 4 years old at the time, though nearby, was never evacuated.

Many reports of post-Chernobyl developmental and neoplastic anomalies exist in the literature, chief of which is a huge rise in thyroid cancers, particularly of the papillary type of around 4000 cases reported in exposed children by the year 2000. Leukaemias, neural tube defects, conjoined

twins, teratomas and other congenital malformations have also increased.¹⁸

Despite recognised chronic low dose radiation exposure in the region, particularly in view of the very long half-life of Cs¹³⁷, some authorities, including the Chernobyl Forum scientists believe the consequences from the nuclear fallout have been far less than was originally feared. The Forum scientists concluded in 2005 that apart from the increase in thyroid malignancies, there was no major public health impact from the fallout.¹⁷

Nevertheless, there needs to be awareness that a subgroup of juxta-Chernobyl residents exist who were in utero, neonates, children or adolescents at the time of the nuclear fallout in 1986 that may be at increased risk of unusual and early-onset cancers, but may have emigrated to other parts of the world. With increased migration, clinicians need to include some enquiry about proximity to the affected zone in their enquiries, especially when Eastern European patients present with unusual symptoms, signs or rare malignancies.

Learning points

- Krukenberg tumours are extremely rare with variable presentations.
- Clinicians are reminded to delve deeply into the clinical history.
- Social history of Eastern European patients is of special relevance particularly those in proximity to the nuclear fallout zone at the time of the Chernobyl disaster.

Competing interests None.

Patient consent Obtained.

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