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Case report

Peritoneal mesothelioma metastasis to the tongue – Comparison with 8 pleural mesothelioma reports with tongue metastases

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HIGHLIGHTS

- MM incidence in "Western" men has stabilised in the last 10 years.
- Our case of MM with tongue metastasis was unfortunately very young, in fact the least aged amongst all reported cases.
- Our case is the only recorded one with peritoneal MM metastasising to the tongue.
- Our case probably presents an unusual pattern of mesothelioma metastatic progression, specifically from the abdomen to the chest, and from there, to the oral cavity.
- All reports of MM with tongue metastases concisely tabulated and compared.

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ABSTRACT

Purpose: Malignant mesothelioma (MM) rarely arises from the peritoneum. We describe the 1st such case which metastasised to the head and neck region (tongue).
Methods: We briefly surveyed the American Surveillance Epidemiology and End Results (SEER) database, and the British Cancer Research UK database for the latest trends in MM incidence. We did a systematic Pubmed search for other MM reports with tongue metastases.
Results and presentation of case: American and British data show that MM incidence in men has stabilised in the last 10 years, earlier than previously predicted. The tongue is an unusual site for MM spread, with ours being only the 9th such case described. Our summary of published cases of MM metastasising to the tongue brings out our patient to be the least in age(35 years), and the only one to have peritoneal MM as the primary. Seven of the 9 cases were male. Only 2 had a recorded history of exposure to asbestos. All 9 patients had the epithelioid subtype of MM. Surgery was done as the exclusive reported intervention in 4 out of the 9 patients. Only 2 cases received radiotherapy, amongst whom, only our patient responded.
Conclusions: Metastasis of MM to the tongue is rare and usually in the uncommon context of MM with multiple sites of extra-thoracic or extra-abdominal spread. We have described a unique clinical manifestation of a rare subtype of mesothelioma. Moreover, we have tabulated and summarised details (including responses to surgery or/and radiotherapy) regarding all reported cases of mesotheliomas with tongue metastasis.

1. Introduction

Malignant mesothelioma (MM) is an uncommon tumour which arises from the visceral or parietal pleura, and less commonly from the peritoneum or pericardium [1]. MM is usually confined to the body cavities, distant metastasis for either type being uncommon. The major risk factor for MM is asbestos exposure, with other

Abbreviations: cm, Centimetre (s); CT, Computerised tomography; Gy, Gray; HIPEC, Hyperthermic intraperitoneal chemotherapy; mm, millimetre; MM, Malignant mesothelioma; MRI, Magnetic resonance imaging; PET, Positron emission tomography; R_x, Recipe (Treatment); SEER, Surveillance epidemiology and end results.

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possible, but debated lesser risk factors [2].

Several studies [3] have quantitated the risk of mesothelioma development with cumulative asbestos exposure, but not with the magnitude of mesothelioma aggressiveness. In one study [4], 9 out of 13 cases of the aggressive, but rare sarcomatoid peritoneal mesothelioma variant, had objective markers of asbestos exposure or history of mesothelioma-associated occupations."

Pleural MM [1,5] is the most common form, with mostly undetectable symptoms such as mild persistent chest pain and constitutional symptoms in its early stages. Pleural effusion development may eventually produce symptoms such as dyspnea. A standard TNM staging of pleural MM is available for prognosis estimation.

Peritoneal MM [1], [5] is a rare form, originating in the abdominal peritoneum, and potentially spreading to the liver, spleen, and gut. Symptoms include abdominal pain, ascites, intestinal obstruction, and constitutional symptoms. To date, no standard staging system exists for peritoneal mesothelioma, although experimental [6] staging systems have been proposed.

Pericardial MM [1,5] is the least common form, producing symptoms such as nausea, chest pain, and dyspnoea. Prognosis is poor in all 3 forms of MM.

The use of amphibole asbestos (crocidolite and amosite) in the US reached its peak in the 1960s, and declined soon after [7]. Similarly, other developed countries had different chronological patterns of amphibole use cessation. Estimated chronologies of mesothelioma incidence-stabilisation are statistical projections based on the known latency period for mesothelioma development, and data pertaining to the different chronological patterns of amphibole use cessation [7]. Our survey of the Surveillance, Epidemiology, and End Results (SEER) database over the 1980–2011 time-period, demonstrate that standardised mesothelioma incidence increases proportionately with age, and is more in men (owing to later mortality-induced decrease) [8] (Fig. 1A). A bit earlier than previously predicted [5,7,9,10], the SEER data show that mesothelioma incidence in men has stabilised after 2006 (Fig. 1B) [8]. In women, the incidence has been relatively unchanged over the past 3 decades (Fig. 1B) [8]. These SEER data patterns [8] are almost identical to data from the United Kingdom [11] over a near-identical period of time (1979–2011). In this report, we present a rare case of peritoneal MM with multiple metastases, including to the tongue.

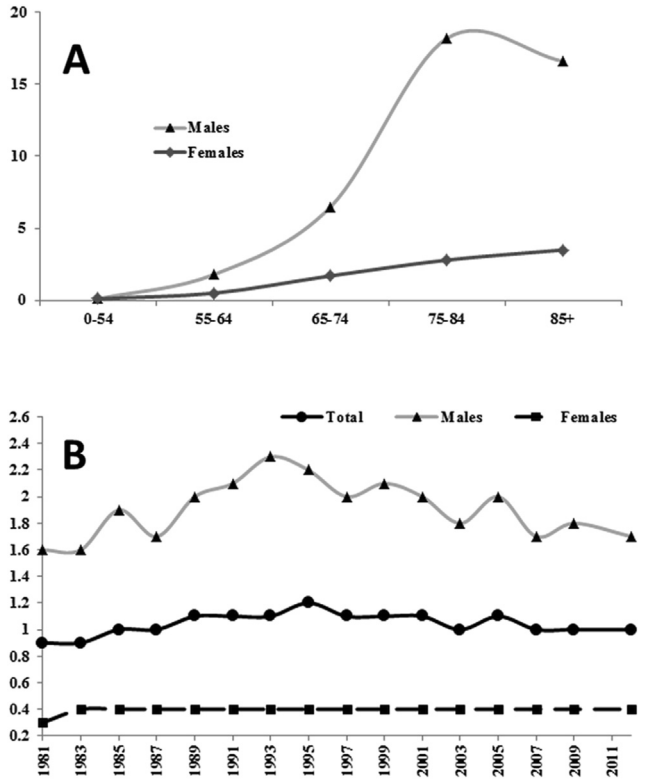

Fig. 1. SEER data depicting mesothelioma incidence per 100,000; age-adjusted to the 2000 US standard population. A Mesothelioma incidence increases proportionately with age, and is more in men. B Mesothelioma incidence in men has stabilised after 2006. In women, the incidence has been relatively unchanged over the past 3 decades. SEER, Surveillance epidemiology and end results.

2. Methods

We briefly surveyed the American Surveillance Epidemiology and End Results (SEER) database, and the British Cancer Research United Kingdom database for the latest trends in MM incidence. In addition to information extracted from our patient case files, we did a systematic Pubmed search for other MM reports with tongue metastases.

3. Presentation of case

A 35 year old male developed ascites associated with fatigue and weight loss of 20 kg over 2 months. The ascites was moderate, with shifting dullness and fluid thrill present. The patient had no relevant personal-, family-, and previous medical-history. Abdominal computed tomography (CT) showed extensive small bowel wall thickening and a soft tissue mass on the lower anterior abdominal peritoneal surface. Biopsy of an omental mass revealed well differentiated papillary MM. The patient underwent

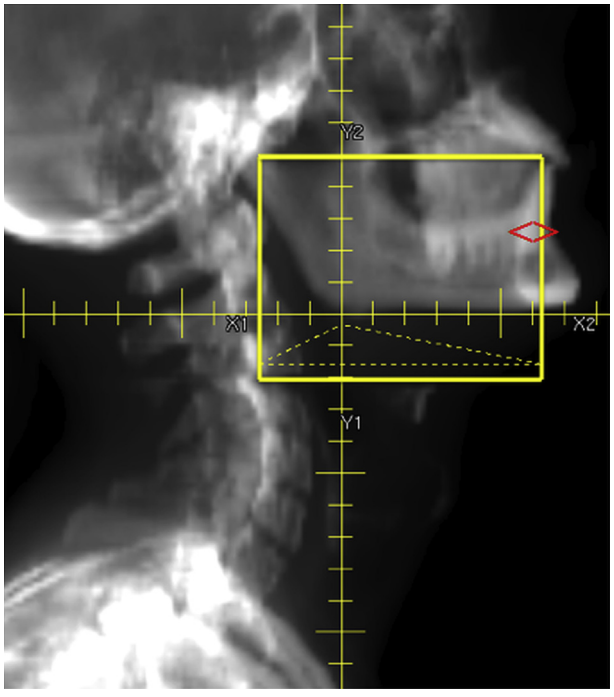

Fig. 2. Radiotherapy field for irradiating the patient's metastatic MM tongue lesion. In this figure, the radiotherapy field used for irradiating the metastatic MM tongue lesion in our case is depicted by the yellow rectangle. The red <> denotes the major area of metastatic involvement. MM, Malignant mesothelioma. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 1
Published cases of MM metastasising to the tongue.

Age	Sex	Primary	Details of tongue metastasis	Other secondaries	R_X of tongue metastasis	Response to R_X	Asbestos exposure
35 [This case]	M	Peritoneal MM of lower anterior abdomen, well-differentiated papillary pattern	3 cm mass in the anterior 2/3rd tongue. Entire tongue thickness, mouth floor, and adjacent bone involved. Metastatic focus in left submandibular gland (tertiary?)	Gallbladder, omentum, colon, inguinal canal, pleura, spermatic cord, diaphragm, chest wall, ribs, subcutis soft tissue	50 Gy in 20 fractions	Possible reduction in size	–
46 [27]	F	Pleural MM, left hemithorax	Tongue metastasis was the first presentation: • 10 × 5 mm firm, painless mass on the left posterior dorsum. • 3 × 3 mm lesion on the right dorsolateral aspect	Approximately 6 months after completing treatment, developed a subcutaneous metastasis over right posterior chest wall	Cisplatin and pemetrexed chemotherapy for initial 2 lesions	3 more small tongue lesions appear shorty after subcutis metastasis noted. Nodules were excised. More cisplatin and pemetrexed given	–
52 [28]	M	Pleural MM	?	Facial skin, thoracic surgical scar	Excision	Lost to follow up	–
59 [29]	F	Pleural MM	5 mm mass on dorsum	Skin, lung, peritoneum	Excision	Died 9 months post-excision	+
68 [17]	M	Pleural MM	22 × 9 mm submucosal lesion in intrinsic muscles of anterior aspect	Suspected metastatic mass in right gluteus 4 months post-radiotherapy	50 Gy in 20 fractions (2 lateral fields)	Stable tongue disease at 4 months	–
70 [30]	M	Pleural MM, right hemithorax	20 × 10 mm lesion left lateral border	?	Patient rejects treatment	?	+
71 [31]	M	Pleural MM	Poorly delimited, bleeding and ulcerated nodular consolidation over the right dorsal-lateral aspect	AUTOPSY- Pericardium, myocardium, adrenal glands, peritoneum, liver, gastric & splenic nodes	Excision	Died 3 months post-excision	–
71 [32]	M	Pleural MM	3 cm anterior right tongue mass. Left septum displacement	Neck lympadenopathy, postoperative liver & pancreatic deposits, postoperative scar seeds	Excision and radical neck node dissection	Died 19 days after surgery of aspiration pneumonia	?
73 [33]	M	Pleural MM	2 cm firm swelling	Contralateral lung, skin	Adriamycin	More metastases noted 6 months after treatment. Died of heart failure (chemotherapy-induced)	–

This table summarises the salient clinical and interventional features of all published MM cases with tongue metastases. Our patient was the least in age (35 years), and the only one to have peritoneal MM as the primary. Seven of the 9 cases were male. Only 3 had a previous history of exposure to asbestos. All 9 patients had the epithelioid subtype of MM (not mentioned in the table contents). Surgery was exclusively done in 4 out of the 9 patients.
?, Details not available; +, Present; -, Absent; cm, centimetre; F, Female; M, Male; mm, millimetre; MM, Malignant mesothelioma; R_X, Recipe (Treatment).

peritonectomy, cholecystectomy, omentectomy, and left colectomy; with the addition of hyperthermic intraperitoneal chemotherapy (HIPEC) using mitomycin (30–40 mg total, at titres > 5 μg per millilitre), and cisplatin (200–300 mg per square metre), in conformity with standard protocols [12,13]. After 3 months, a revision peritonectomy was performed with more HIPEC given (cisplatin and doxorubicin). During the same year, he received 4 cycles of cisplatin and pemextred.

Eight months later, the patient developed a right groin mass and CTs showed soft tissue thickening in the right inguinal canal and a right-sided pleural effusion. Histology of a local resection confirmed MM at the right spermatic cord with positive margins and at the right diaphragm and parietal pleura. Consequently, a month later, a right thoracotomy and pleurectomy was performed with the addition of HIPEC (cisplatin) and 50 Gy of radiotherapy given to the right groin in 25 fractions. No further recurrence was documented at this site.

Nineteen months later, he noticed a mass over the right posterolateral chest wall and a CT showed lobulated right pleural thickening and involvement of the lower ribs by a soft tissue mass, extending through the chest wall to involve subcutaneous soft tissues. The mass and involved ribs were resected and more HIPEC was given. Intraoperatively, the mass was noted to have invaded the latissimus dorsi and erector spinae muscles, and MM was confirmed on histology. A positron emission tomography (PET) scan revealed recurrent metabolically active disease in the peritoneum and mid-abdomen. Follow-up CT showed progression of the disease with extensive nodular pleural thickening and a soft tissue mass in the anterior peritoneal cavity. Five more cycles of intravenous cisplatin and pemextred were given. Surgery and further HIPEC was performed 9 months later for the peritoneal recurrence.

Ten months later, palliative radiotherapy was given to the paravertebral region of the thorax and posterior chest at 42 Gy in 21 fractions. Later that year, he detected a mass on the right side of his tongue extending to the midline. This caused dysphagia and difficulty with chewing due to pain, reducing oral intake to a minimal amount and restricted to fluids. As a result, the patient lost approximately 15 kg. On examination, the ovoid metastatic lesion was diffuse (not circumscribed), tongue-coloured, and approximately 2.5 cm in diameter. It was fixed to the anterior 1/3rd of the

tongue (immobile), and seemed to extend further down to the mouth-floor. There was no associated regional lymphadenopathy. The lesion measured 3 cm on CT (Fig. 2). Magnetic resonance imaging (MRI) showed a mass in the anterior 2/3rd of the tongue with involvement of its entire thickness and adjacent bone. The findings were also suggestive of an invasion of the floor of the mouth, with a metastatic focus in the left submandibular gland. As tongue-involvement was observed 3 years after the patient's first presentation (35 years-old), he was 38 years-old at the time of oral tumour diagnosis. The biopsy result of the tongue lesion indicated MM. Since the lesion was deemed inoperable, radiotherapy was given to the tongue to 50 Gy in 20 fractions. During examination prior to a gastroscopy for an unrelated condition, the tongue mass was noted to have responded to radiotherapy. The patient was lost to official follow up because of progressive deterioration in his condition over a few months until his death, 5 years after initial diagnosis.

4. Discussion

MM is an uncommon tumour with an estimated incidence of 720 cases and 620 mortality cases in 2010 in the Australian population [14]. The major risk factor for MM is asbestos exposure. Other possible risk factors include genetic predisposition, Simian virus 40 infection, previous radiotherapy, ageing, and gender (males) [2]. MM usually arises from the visceral or parietal pleura, but less commonly from the peritoneum.

Extant time-estimates of the stabilisation of mesothelioma incidence are statistical projections contingent on mesothelioma pathogenesis and geographical differences in the timing of stopping amphibole use [7]. However, the slightly earlier (Fig. 1B) than projected [5] stabilisation cannot be explained by known reasons, although it is tempting to point to probable statistical errors in the projection, and to differences in the reference population used.

It is variously claimed that “20%–33%” of mesotheliomas [15] or “30%” of mesotheliomas [16] are peritoneal, but those unreliable claims are cited from another citation instead of the original source (or outdated), with the cited sources not positing those figures. Reliable sources indicate that incidence rates of peritoneal mesothelioma (males) were “one order of magnitude lower than those of pleural mesothelioma” [1].

Distant metastasis is rare, although studies have demonstrated a prevalence of extrathoracic metastasis up to 10–15% on CT and PET of pleural MM at the time of presentation [17]. The most common sites of metastasis of pleural MM are liver, adrenal glands, kidney, and contralateral lung [17]. Other rare sites of documented distant spread include lip and skin [18], oral cavity including the tongue [19,20], brain [21], skeletal muscle [22], subcutaneous tissue and small bowel [23,24]. Spread of peritoneal MM has been reported to liver, lung, heart, brain, thyroid gland, adrenal glands, kidneys, pancreas, bone, soft tissue, skin, lymph nodes, and subcutaneous tissue [25].

The tongue is an unusual site for MM spread, with ours being only the 9th such case on record. Table 1 summarises the published cases of MM with metastasis to the tongue. Ours was the youngest case at 35 years, and the only one originating from the peritoneum. Our case probably presents an unusual pattern of mesothelioma metastatic progression, specifically from the abdomen to the chest, and then to the oral cavity. This may be considered as a “serosal/subserosal version of Troisier's sign and Virchow's node” [26]. Seven of the 9 cases were male and only 2 had a previous history of exposure to asbestos. All 8 had the epithelioid subtype of mesothelioma.

Surgery was the mainstay of therapy for MM tongue metastasis, with 4 cases out of the 9 having surgical excision as a sole treatment or a component of their treatment. However, these reports did not describe local tumour control after surgery. For MM in general, radiotherapy has been used with some success, usually for advanced, non-resectable MM. Pertaining to the 2 cases receiving radiotherapy, only our patient responded positively. In contrast, the other case was described as having stable disease after 4 months. As may be expected, recorded survival after treatment was poor amongst all patients (3–9 months).

5. Conclusions

We have described the only case of peritoneal MM metastasising to the tongue, on record. This is a unique clinical manifestation of the peritoneal variant of mesothelioma, probably demonstrating an unusual pattern of mesothelioma metastatic progression from the abdomen to the chest, and next to the oral cavity. Furthermore, we have compared and succinctly posited aspects of our case to the other 7 MM with tongue metastases, in literature.

Ethical approval and consent

Not applicable.

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None.

Author contribution

Melisa V Vazquez – Study design, data collection.
Selwyn Selvendran – Data collection.
Rajkumar Cheluvappa – Writing, rebuttal-framing, submission.
Michael J McKay – Study design, data collection, writing.

Conflicts of interest

None.

Guarantor

Prof. Michael J McKay.

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