Metastasis of Occult Prostatic Carcinoma to the Sphenoid Sinus: Report of a Rare Case and a Review of the Literature

Fredrik Petersson · Tan Sien Hui · David Loke · Thomas Choudary Putti

Received: 11 October 2011 / Accepted: 27 October 2011 / Published online: 5 November 2011
© Springer Science+Business Media, LLC 2011

Abstract We present a case (55-year-old) with a metastasis to the sphenoid sinus from an occult prostatic adenocarcinoma as the first evidence of disease. The patient's symptoms were progressive left-sided headache of a few months duration and a 2-week history of blurred vision with diplopia. Clinical examination revealed a left cranial nerve III palsy and ptosis. A computed tomography scan showed a 2 cm large, well delineated soft tissue lesion involving the left sphenoid sinus and extending to the left cavernous sinus with sclerosis of the adjacent sphenoid bone. Histological and immunohistochemical examinations revealed a poorly differentiated adenocarcinoma that was positive for prostate specific antigen (PSA) and broad-spectrum cytokeratins (Cam 5.2). Subsequent urological examination confirmed a locally advanced prostatic carcinoma with significantly increased serum-PSA (4,561 µg/l) and bone scintigraphy showed widespread metastasis.

Keywords Metastasis · Sphenoid sinus · Sinonasal · Prostatic carcinoma · Carcinoma · Occult

Introduction

Metastatic presentation of an occult prostatic carcinoma (Pca) is not an uncommon event. The vast majority of these patients present with osseous metastases to the axial

skeleton. Pca-metastasis to the head and neck region is unusual and metastasis to the sphenoid sinus is a rare event with only 8 documented cases in the English literature [1–7]. In only 2 of these patients was the sphenoid metastasis related to the presenting symptom [4, 7]. In this paper we present, to the best of our knowledge, the third case of metastasis to the sphenoid sinus from an occult Pca and review the literature on this subject.

Case Report

A 55-year-old paraplegic (secondary to trauma), but otherwise healthy, man was referred to the otolaryngology department for a soft tissue lesion with focal bony abnormality involving the left sphenoid sinus identified on magnetic resonance imaging (MRI) of his brain which was performed because of progressive left-sided headache of a few months duration and a 2 week history of blurred vision with diplopia.

Clinical examination showed left cranial nerve III palsy with ptosis. His cranial nerves IV to XII were intact and the rest of the ear, nose, and throat examination was unremarkable. A computed tomography (CT) scan confirmed the presence of a 2 cm large, well-delineated soft tissue lesion involving the left sphenoid sinus, extending to the left cavernous sinus with sclerosis of the adjacent greater wing and left lateral body of the sphenoid bone (Fig. 1a).

The patient underwent a left sphenoidotomy which showed a polypoid tumorous mass lined by normal appearing mucosa (Fig. 1b). After the final histopathological diagnosis (“PSA-positive poorly differentiated adenocarcinoma, highly suggestive of metastatic Pca”), the patient underwent urological work up including a digital rectal examination which revealed a hard and irregular prostate, and a serum

F. Petersson (✉) · T. C. Putti
Department of Pathology, National University Health System,
5 Lower Kent Ridge Road, Singapore 119074, Singapore
e-mail: fredrikpetersson@live.se

T. S. Hui · D. Loke
Department of Oto-Rhino-Laryngology,
Khoo Teck Puat Hospital, Singapore, Singapore

Fig. 1 A computed tomography (CT) scan showed a 2 cm large, well-delineated soft tissue lesion involving the *left* sphenoid sinus, extending to the *left* cavernous sinus with sclerosis of the adjacent greater wing and *left* lateral body of the sphenoid bone (arrows; **a**). Intra-operative finding of a polypoid mass within the (*opened*) *left* sphenoid sinus lined by normal appearing mucosa (arrow; **b**)

prostate specific antigen (PSA) level which was markedly elevated at 4,561 $\mu\text{g/l}$. Findings on bone scintigraphy were compatible with extensive skeletal metastases to the skull, ribs, vertebrae, humerus, pelvis, and femur.

The patient was initiated on goserelin therapy and is currently on close follow-up.

Materials and Methods

The tissue was fixed in formalin, embedded in paraffin and 4 μm thin sections were cut and stained with hematoxylin and eosin. An immunohistochemical study was performed using commercially available antibodies to the following antigens according to the protocols of the manufacturers: cytokeratins (CK AE1-3, MNF 116 and Cam 5.2), CK7 and 20, epithelial membrane antigen (EMA), CDX2, S100 protein, CD56, vimentin, HER2, prostate specific antigen (PSA), prostatic specific acid phosphatase (PSAP), chromogranin A, and synaptophysin.

Results

Frozen Section

The tissue submitted for FS consisted of four fragments measuring 0.4–0.7 cm in maximum dimension. The frozen

sections showed a cellular tumor forming vague lobules and sheets separated by thin fibrous septae (Fig. 2a). Imprints showed cells with malignant features—high nuclear-to-cytoplasmic ratio, enlarged, irregular nuclei and variably vacuolated cytoplasm (Fig. 2b). Occasional mitotic figures were identified, as were small areas of necrosis. Focally, the tumor formed vague gland-like or, alternatively, pseudorosette-like structures (Fig. 2c). The FS report was that of a malignant neoplasm NOS.

Permanent Histology

Three additional formalin fixed fragments of tissue measuring 0.4–0.5 cm were received for histological examination. Hematoxylin and eosin stained sections of these revealed neoplastic tissue composed of sheets of moderately pleomorphic epithelial appearing cells in solid and variably cribriform arrangements. The tumor cells displayed moderately pleomorphic nuclei with distinct to prominent centrally located nucleoli (Fig. 3a, b). No squamous differentiation, true (Flexner-Wintersteiner) rosettes, pigment or neurofibrillary matrix was identified. Scattered mitotic figures and focal necrosis were present.

Immunohistochemistry

The immunohistochemical study showed that the neoplastic cells were positive for PSA (Fig. 3c) and broad-spectrum

Fig. 2 Frozen section shows a cellular tumor forming sheets and vague lobules separated by *thin* fibrous septae (**a**). Imprint from the unfixed biopsy specimen (for frozen section) shows malignant cells with high nuclear-to-cytoplasmic ratio, enlarged irregular nuclei and

variably vacuolated cytoplasm. Note the two ciliated columnar cells of the respiratory mucosa (*arrows*; **b**). High power view from the frozen section showing malignant cell with pleomorphic nuclei forming vague gland- or pseudorosette-like structures (*arrows*; **c**)

CKs; (Cam 5.2; Fig. 3d). No immunoreactivity was discerned for MNF 116, and AE1-3, CK7, CK20, EMA, vimentin, synaptophysin, chromogranin A, CD56, HER2, S100 protein, CDX2 and PSAP (data not shown).

Discussion

Metastasis from Pca to the head and neck region is very uncommon. Reportedly, the most commonly involved sites are brain, dura, cervical (including left supraclavicular) lymph nodes [6, 8–16]. In addition, cases of Pca with spread to the parotid [17–19], pituitary gland [6, 20], optic canal [21], cervical spine (epidural space and vertebral body) [6], and skin of the head and neck region [22] are on record. Metastasis to the sphenoid sinus is a rare event. The largest series to date was published by Mickel et al. [2] and comprises 26 cases (7 from the authors' own institution and 19 cases compiled from the literature). The most common primary tumor sites were prostate and lung. Of the 7 cases presented by Mickel et al., 2 patients had the metastasis to the sphenoid sinus as the first clinical manifestation of the disease and primary carcinomas of the lung were subsequently diagnosed. Also on record are isolated case reports of metastasis to the sphenoid sinus from clear cell renal cell carcinoma [23, 24], rectal carcinoma [25], papillary and follicular thyroid carcinoma [26, 27], endometrial clear cell

carcinoma [28], hepatocellular carcinoma [29, 30], fallopian tube carcinoma [31], gastric cancer [32] and Ewing's sarcoma [33]. To the best of our knowledge, we are only aware of 8 well-characterized cases of metastatic Pca to the sphenoid sinus in the English literature [1–7]. Prostatic carcinoma not infrequently presents with osseous metastases to the axial skeleton. Apart from this, metastasis from an occult Pca is rare. For example, in a large series on solitary cerebral metastasis from one center, Giordana et al. [34] found one patient with metastasis from an occult Pca among 99 patients with unknown primary tumors (all carcinomas) at the time of surgery and van der Waal et al. found no cases of metastatic occult Pca in their series on 24 oral metastases [35]. In a series by Hunt et al. on metastatic Pca to the head and neck area comprising 14 cases, 2 patients had an occult primary tumor with metastasis to the left supraclavicular lymph nodes and 2 patients had pituitary metastasis [6]. In all the other cases with adequate clinical information, the Pca was known. Moreover, 3 reports of well-documented cases of Pca presenting as a parotid mass are on record [17–19]. In addition, one case of metastatic occult Pca to the hyoid bone [36] and one case of pulmonary metastasis from an unknown Pca [37] have been documented.

With, to the best of our knowledge, only 2 cases of occult Pca presenting with metastasis to the sphenoid sinus, this becomes a diagnostic challenge [4, 7]. The differential

Fig. 3 Low-power magnification (Hematoxylin and Eosin; formalin-fixed tissue) showing a cellular tumor composed of irregular, variably-sized nests giving a lobular impression. The *nests* are separated by limited amounts of collagenous stroma (**a**). The tumor cells show focal formation of luminal structures and the neoplastic

cells have variably prominent nucleoli (**b**). The tumor cells display strong immunoreactivity for PSA growing under (immunonegative) ciliated respiratory epithelium (**c**) and variable expression of cytokeratins (Cam 5.2). Note the strong immunoreactivity in the areas bordering the glandular lumina (**d**)

diagnostic spectrum is influenced by the type and degree of differentiation of the Pca. For example, a moderately-differentiated (gland-forming) acinar adenocarcinoma with a significant component of Gleason pattern 3 is probably more likely to give the diagnostic histopathologist the correct association, especially if the neoplastic cells contain the commonly encountered single central prominent nucleolus (focally present in our case), compared with a predominantly Gleason grade 4 tumor with less well-developed glands and/or neoplastic cells with foamy cytoplasm or a ductal Pca with prominent papillary structures. A high-grade (non-gland forming) Pca corresponding to Gleason grade 5 would invoke a whole range of poorly-differentiated malignant tumors predominantly composed of solid nests, sheets, and isolated tumor cells. This plethora of differential diagnostic alternatives would include both metastases and primary tumors, such as high-grade olfactory neuroblastoma, sinonasal malignant melanoma, sinonasal undifferentiated carcinoma, high-grade neuroendocrine carcinoma, NUT-translocation carcinoma, the solid variant of alveolar rhabdomyosarcoma, solid and

dedifferentiated adenoid cystic carcinoma, pituitary carcinoma, a neuroblastoma-like or high-grade carcinomatous component of sinonasal teratocarcinosarcoma and high-grade haematolymphoid malignancies. In cases where a glandular component is identified, a high-grade intestinal-type adenocarcinoma, a salivary gland-type carcinoma such as salivary duct carcinoma, high-grade mucoepidermoid carcinoma, basal cell adenocarcinoma/basal cell adenoma, a gland-forming component of a sinonasal teratocarcinosarcoma, and even cellular pleomorphic adenoma could be contemplated. It is obvious from the broad list of differential diagnoses (which in addition also include the possibility of a metastasis), that performing a broad enough immunohistochemical study and close clinicopathological correlation are of vital significance to arrive at the correct diagnosis. In the case presented herein, we initially considered several of the diagnostic possibilities mentioned above. However, the combination of the histological features and the finding of immunoreactivity for broad-spectrum cytokeratins (Cam 5.2) in conjunction with “double negativity” for CK 7 and CK 20 prompted us to

investigate the possibility of a metastatic Pca which then turned out to be the case.

Pca, together with a limited number of non-squamous cell carcinomas, such as most conventional renal cell (cRCC), hepatocellular, and adrenal carcinomas (ADC) are characteristically negative for CK 7 and 20. Both cRCC and ADC are positive for vimentin (negative in our case).

Of note is, that apart from being expressed by Pca, PSA has been shown to be expressed in salivary duct carcinoma, rare cases of invasive ductal and apocrine carcinomas of the breast, urothelial carcinoma, dedifferentiated epithelial-myoepithelial carcinomas of the parotid gland, salivary gland adenocarcinoma NOS, mucoepidermoid carcinoma and even some pleomorphic adenomas [38–42].

In conclusion, we present, to the best of our knowledge, the third case in the English literature, of a patient with prostatic carcinoma presenting with a metastasis to the sphenoid sinus. This case highlights that a high level of suspicion for rare metastatic events should be a component of the diagnostic approach to sinonasal malignant tumors.

References

1. Saleh HA, O'Flynn P, Jones NS. Prostatic metastases in the nose and paranasal sinuses. *J Laryngol Otol*. 1993;107:629–32.
2. Mickel RA, Zimmerman MC. The sphenoid sinus—a site for metastasis. *Otolaryngol Head Neck Surg*. 1990;102:709–16.
3. McClatchey KD, Lloyd RV, Schaldenbrand JD. Metastatic carcinoma to the sphenoid sinus. Case report and review of the literature. *Arch Otorhinolaryngol*. 1985;241:219–24.
4. Matsumoto I, Furusato M, Inomata I, et al. Prostatic cancer presenting as metastatic adenocarcinoma of sphenoid sinus. *Acta Pathol Jpn*. 1986;36:1753–6.
5. Lavasani L, Zapanta PE, Tanna N, et al. Metastasis of prostatic adenocarcinoma to the sphenoid sinus. *Ann Otol Rhinol Laryngol*. 2006;115:690–3.
6. Hunt JL, Tomaszewski JE, Montone KT. Prostatic adenocarcinoma metastatic to the head and neck and the workup of an unknown epithelioid neoplasm. *Head Neck*. 2004;26:171–8.
7. Barrs DM, McDonald TJ, Whisnant JP. Metastatic tumors to the sphenoid sinus. *Laryngoscope*. 1979;89:1239–43.
8. Penley MW, Kim YC, Pribram HF. Subdural metastases from prostatic adenocarcinoma. *Surg Neurol*. 1981;16:131–4.
9. McMenamin PG, Anderson JD, Baker JJ. Prostatic carcinoma presenting with neck metastasis. *J Otolaryngol*. 1989;18:119–24.
10. Lynes WL, Bostwick DG, Freiha FS, et al. Parenchymal brain metastases from adenocarcinoma of prostate. *Urology*. 1986;28:280–7.
11. Leibman BD, Dilliogluligil O, Wheeler TM, et al. Distant metastasis after radical prostatectomy in patients without an elevated serum prostate specific antigen level. *Cancer*. 1995;76:2530–4.
12. Kasabian NG, Previte SR, Kaloustian HD, et al. Adenocarcinoma of the prostate presenting initially as an intracerebral tumor. *Cancer*. 1992;70:2149–51.
13. Jones H, Anthony PP. Metastatic prostatic carcinoma presenting as left-sided cervical lymphadenopathy: a series of 11 cases. *Histopathology*. 1992;21:149–54.
14. Gupta A, Baidas S, Cumberlin RK. Brain stem metastasis as the only site of spread in prostate carcinoma. A case report. *Cancer*. 1994;74:2516–9.
15. Chung TS, Thannikkary C. Carcinoma of the prostate with brain metastasis. *J Surg Oncol*. 1986;33:103–5.
16. Bland LI, Welch WC, Okawara SH. Large cystic intraparenchymal brain metastasis from prostate cancer. *Neuroradiology*. 1992;34:70–2.
17. Simpson RH, Skalova A. Metastatic carcinoma of the prostate presenting as parotid tumour. *Histopathology*. 1997;30:70–4.
18. LiVolsi VA. Prostatic carcinoma presenting as a primary parotid tumor. *Oral Surg Oral Med Oral Pathol*. 1979;48:447–50.
19. Kirkali Z, Koyuncuoglu M, Pabuccuoglu U, et al. Prostatic carcinoma presenting with painless parotid mass. *Urology*. 1995;46:406–7.
20. Couldwell WT, Chandrasoma PT, Weiss MH. Pituitary gland metastasis from adenocarcinoma of the prostate. Case report. *J Neurosurg*. 1989;71:138–40.
21. Kattah JC, Chrousos GC, Roberts J, et al. Metastatic prostate cancer to the optic canal. *Ophthalmology*. 1993;100:1711–5.
22. Azana JM, de Misa RF, Gomez MI, et al. Cutaneous metastases from prostatic cancer. *J Dermatol*. 1993;20:786–8.
23. Singh I, Khaitan A. Diplopia - an unusual primary manifestation of metastatic renal cell carcinoma. *Urol Int*. 2004;73:285–6.
24. Morvan JB, Veyrieres JB, Mimouni O, et al. Clear-cell renal carcinoma metastasis to the base of the tongue and sphenoid sinus: Two very rare atypical ENT locations. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2010;128:91–4.
25. Tanaka K. A case of metastases to the paranasal sinus from rectal mucinous adenocarcinoma. *Int J Clin Oncol*. 2006;11:64–5.
26. Yamasoba T, Kikuchi S, Sugawara M, et al. Occult follicular carcinoma metastasizing to the sinonasal tract. *ORL J Otorhinolaryngol Relat Spec*. 1994;56:239–43.
27. Argibay Vazquez S, Lancha Hernandez C, Martinez Muniz A. Metastases in the sphenoidal sinus in a patient with papillary thyroid cancer. *Clin Transl Oncol*. 2005;7:324–7.
28. Ilvan S, Akyildiz EU, Calay Z, et al. Endometrial clear cell carcinoma metastatic to the paranasal sinuses: a case report and review of the literature. *Gynecol Oncol*. 2004;94:232–4.
29. Sim RS, Tan HK. A case of metastatic hepatocellular carcinoma of the sphenoid sinus. *J Laryngol Otol*. 1994;108:503–4.
30. Aung TH, Po YC, Wong WK. Hepatocellular carcinoma with metastasis to the skull base, pituitary gland, sphenoid sinus, and cavernous sinus. *Hong Kong Med J*. 2002;8:48–51.
31. Merimsky O, Inbar M, Groswasser-Reider I, et al. Sphenoid and cavernous sinuses involvement as first site of metastasis from a fallopian tube carcinoma. Case report. *Tumori*. 1993;79:444–6.
32. Hirai O, Kikuchi H, Hashimoto N. Skull base metastasis from gastric cancer—case report. *Neurol Med Chir (Tokyo)*. 1992;32:908–10.
33. Handler SD, Lange B, Bilaniuk LT. Ewing's sarcoma metastatic to the sphenoid sinus. *Trans Pa Acad Ophthalmol Otolaryngol*. 1979;32:72–9.
34. Giordana MT, Cordera S, Boghi A. Cerebral metastases as first symptom of cancer: a clinico-pathologic study. *J Neurooncol*. 2000;50:265–73.
35. van der Waal RI, Buter J, van der Waal I. Oral metastases: report of 24 cases. *Br J Oral Maxillofac Surg*. 2003;41:3–6.
36. Wang S-H, Lee JC, Liu T-C. Occult prostate cancer detected by hyoid bone metastasis after resection of thyroglossal duct cyst. *Int J Oral Maxillofac Surg*. 2011. doi:10.1016/j.ijom.2011.04.010.
37. Greenberg BE, Young JM. Pulmonary metastasis from occult primary sites resembling bronchogenic carcinoma. *Dis Chest*. 1958;33:496–505.
38. Sarode VR, Truelson J, Zaidie M. Dedifferentiated epithelial-myoepithelial carcinoma of the parotid gland with aberrant

- expression of prostate specific antigen: a case report. *Int J Surg Pathol*. 2010;18:401–5.
39. Fan CY, Wang J, Barnes EL. Expression of androgen receptor and prostatic specific markers in salivary duct carcinoma: an immunohistochemical analysis of 13 cases and review of the literature. *Am J Surg Pathol*. 2000;24:579–86.
 40. Chen JC, Ho CL, Tsai HW, et al. Immunohistochemical detection of prostate-specific antigen expression in primary urothelial carcinoma of the urinary bladder. *Anticancer Res*. 2008;28:4149–54.
 41. Alanen KA, Kuopio T, Koskinen PJ, et al. Immunohistochemical labelling for prostate specific antigen in non-prostatic tissues. *Pathol Res Pract*. 1996;192:233–7.
 42. van Krieken JH. Prostate marker immunoreactivity in salivary gland neoplasms. A rare pitfall in immunohistochemistry. *Am J Surg Pathol*. 1993;17:410–4.