

A novel case of quartet tumor: meningioma, angiomyolipoma, ependymoma and sarcoma: report of a case and review of the literature

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► Case report

ABSTRACT

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Multiple primary tumors in a single patient are relatively rare when four or more distinct lesions are considered. Herein, we report a case of woman with four different primary tumors: meningioma, renal angiomyolipoma, spinal ependymoma and high-grade soft tissue sarcoma. There was no family history and hereditary syndrome. The genetic analysis was completely normal. To best of our knowledge, the present patient is the first case in the literature, who presented with these four types of tumors.

Keywords: Angiomyolipoma, ependymoma, meningioma, sarcoma.

INTRODUCTION

The phenomenon of multiple primary neoplasms in the same individual was described firstly by Warren and Gates ⁽¹⁾. Recently, the early detection and the advances in therapy for malignant diseases have contributed to prolonged survival of patients, resulting in an increment of multiple primary tumors. However, the reports of multiple primary tumors are still uncommon. They appear more frequently in the upper digestive tract, respiratory system, head and neck region, or urogenital system. The incidence ranges from 2% to 10% ⁽²⁾. Among those with multiple primary malignancies, double cancers is commonly seen, while triple cancers occur in 0.5% of patients, and quadruple or quintuple cancers occur in only less than 0.1% of the population ⁽³⁾. Autopsy series have estimat-

ed the incidence of a second primary cancer ranges from 3% to 7% with the higher percentage representing the older age groups ⁽⁴⁻⁵⁾. Herein we report a case with four primary tumors, all involving different organ systems.

CASE REPORT

A 59-year-old woman admitted to the hospital, with a complaint of progressive weakness on her lower extremities over a 6-month history in January 2011. She denied tobacco usage or alcohol consumption. She was a housewife living in a small village. There was no family history.

The patient had a past history of meningioma. The mass located in the right parieto-occipital region 2.5×2×1.5 cm in size, the first of her cancers. It was curatively resected in November

2004. Pathological examination revealed that the tumor characterized was due to the formation of multiple, discrete, concentrically laminated, calcareous bodies (psammoma bodies). It was diagnosed as psammomatous meningioma, grade I (WHO, 2000) (figure 1). In 2010 she admitted to the hospital with left flank pain which was increased progressively within 3 months. The physical examination was unremarkable. Ultrasound demonstrated a hyperechoic mass on the left kidney. The CT revealed a heterogeneous mass in the left kidney measuring 8×5×3 cm. grossly; the tumor was confined within the renal capsule. A radical left nephrectomy was performed. The major histological components of the tumor were characterized by abnormally thick-walled vessels, mature fat cells, and smooth muscle

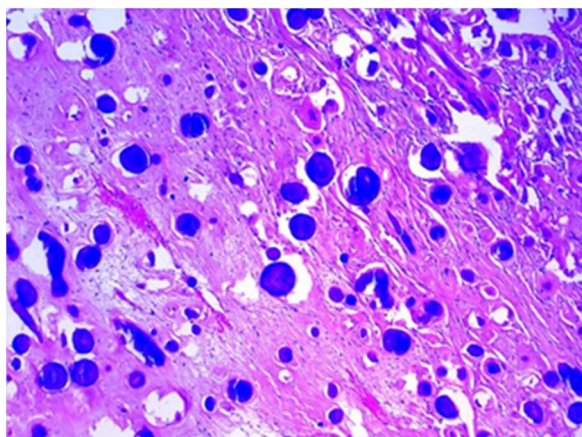


Figure 1. The tumor characterized by the abundance of psammoma bodies (H&E ×40).

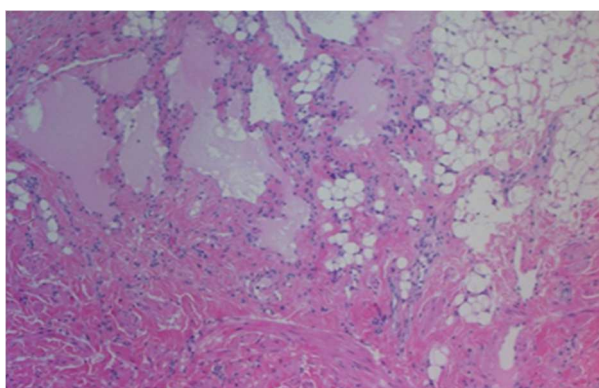


Figure 2. Renal angiomyolipoma showing mature fat cells, blood vessels, and smooth muscle cells (H&E ×100).

bundles. Pathologic examination revealed an angiomyolipoma which was her second tumor. The tumor composed of adipose tissue, smooth muscles and blood vessels (figure 2). After surgery the patient refused any further diagnostic work and treatment so she did not go to her routine follow-up until (a year later) the development progressive weakness on her lower extremities.

Neurological examination revealed a bilateral hemiparesis (3/5). Lumbar magnetic resonance imaging (MRI) revealed an intradural and extramedullary mass located in the level of L2-L3. On T1-weighted images, the mass appeared isointense whereas on T2-weighted images, it was hyperintense relative to the normal cord. A subtotal excision of the mass was then performed, which was followed by transient improvement. Histological findings indicated a diagnosis of tanycytic ependymoma grade II (WHO, 2007). The tumor characterized by markedly elongated spindle shaped cells, which were immunopositive for S-100 protein and glial fibrillary acidic protein (figure 3). Since the tumor subtotally resected, a total dose of 5000 cGy radiotherapy (RT) with 2 Gy/fraction was planned. RT field was defined as the preoperative tumor volume (determined by T1 magnetic resonance imaging (MRI) scan) plus 2

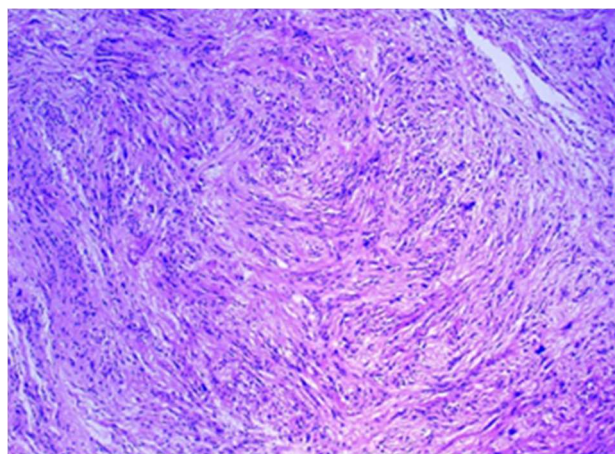


Figure 3. The tumor consistent of elongated cells with highly fibrillary processes, forming a fascicular architecture (H&E ×40). The tumor characterized by markedly elongated spindle shaped cells, which were immunopositive for S-100 protein and glial fibrillary acidic protein.

cm margin a dose of 50Gy was applied.

Three months after the RT, she came to routine follow-up. She had no complaint about her three other tumors although she had a mass on her right gluteal region. Physical examination revealed a 10 cm fixed irregular mass located on her right buttock. We inspected her previous planning tomography for spinal ependymoma however; there was no mass on her right gluteal region. MRI revealed a 15×10 cm mass on the right gluteal region. We performed position emission tomography (PET)-CT, and it demonstrated 10×15 cm heterogenous hypermetabolic mass with a standardized uptake (SUV) value of 43.81. The tumor excised from right gluteal area characterized by an extreme degree of pleomorphism with numerous typical and atypical mitotic figures and a fascicular growth pattern. Hemorrhage and necrosis were extensive in tumor. Immunohistochemically tumor cells were positive for Vimentin, but negative for CD45, AE1/AE3, SMA, S-100, Desmin and Myogenin. Histological and immunohistochemical findings indicated diagnosis of high grade sarcoma (figure 4). During the operation the tumor was disintegrated so the surgical margins could not be determined. We planned a dose of 66-70 Gy RT to the tumor bed, with 5 cm and 2 cm margins in craniocaudal radial directions respectively; however she could not tolerated the doses above 62 Gy.

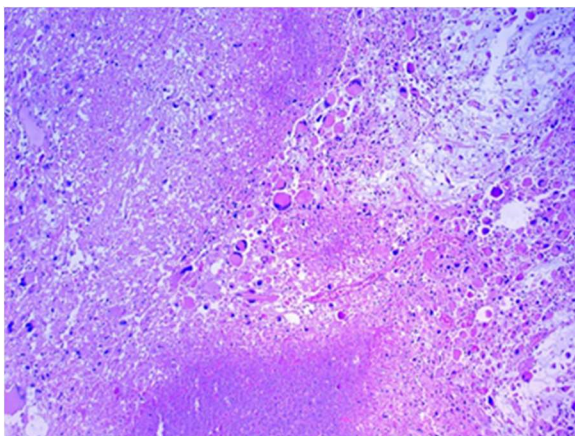


Figure 4. Anaplastic tumor cells are arranged haphazardly in sheets and necrotic areas (H&E ×40). Immunohistochemically tumor cells were positive for Vimentin, but negative for CD45, AE1/AE3, SMA, S-100, Desmin and Myogenin.

We thought that she might have had a genetic syndrome which was associated with multiple primary tumors. Thus conventional cytogenetic analysis and FISH (fluorescence in situ hybridization) with P53 gene were done. Both cytogenetic analysis and FISH analyses showed a normal karyotype and p53 gene.

During follow-up the patient was admitted to the hospital with shortness of breath and severe cough. A contrast enhanced CT revealed multiple nodules in her lungs, which were identified as metastases. The patient was hospitalized. However; her dyspnea was progressively increased and 15 months after the completion of the last RT, the patient died of respiratory failure.

DISCUSSION

Multiple primary tumors in a patient are extremely low conditions but have increase in frequency in recent decades. This may be due to the medical improvements in both diagnostic and therapeutic strategies, which eventually increase the overall survival time of the patents with multiple malignancies. On the other hand, as the age increased, the risk of developing a tumor increases as well. We report a patient who developed four different tumors: a meningioma, angiomyolipoma, tanycytic ependymoma and high grade sarcoma. To best of our knowledge, the present patient is the first case in the English literature, who presented with these four types of tumors.

In reviews of the literature with respect to the multiple primary malignancies, it is interesting that, the Japanese population seems to have higher likelihood of developing multiple malignancies. This may be due to longer life span, gene susceptibility or advancement in the field of the oncology. Table 1 summarizes the reported cases of four or more primary malignancies in the literature during 1981-2011 (6-27). Although the appearance of four and more primary tumors in one patient is not very common, should not be considered as such a rare event. As it is seen in the table, most of the cases were

reported from Japan. Moreover a case with six metachronous primary malignancies was recently reported by Takada and colleagues from Japan ⁽⁶⁾. As can be seen from the table 1, the case with four primary tumors same with our case has not been reported previously.

Li Fraumeni syndrome comprises of breast cancer, brain tumors, acute leukemia, soft tissue sarcomas, bone sarcomas, and adrenal cortical carcinoma. It is a rare autosomal dominant

hereditary disorder linked to germline mutations of p53 tumor suppressor gene. Although we analyzed constitution of karyotype beside p53 alterations we could not find any genetic changes in our case.

Multiple primary tumors occur more often in elderly patients, as the incidence of tumors increases with age. A family history of cancer and genetic predisposition to cancer may be associated with a risk of multiple neoplasms ⁽⁷⁾.

Table 1. The reported cases of four or more primary malignancies in the English literature during 1974-2011.

| Malignancies | | | | | | |
|------------------------------|-------------------|------------------|-----------------|-------------------------------|-----------------|-----------------|
| Author | 1 st | 2 nd | 3 rd | 4 th | 5 th | 6 th |
| Kenyon GS ⁸ | Caecum | Uterus | Renal pelvis | Anus | Bladder | |
| Kenyon GS ⁸ | Caecum | Choroid Melanoma | Bowel | Colon | Pancreas | |
| Bjerium ⁹ | Rectum | Breast | Uterus | Colon | | |
| Kobayashi T ¹⁰ | Uterus | Stomach | Breast | Brain | | |
| Megighian D ¹¹ | Parotid Gland | Tongue | Soft Palate | Larynx | Hypopharynx | |
| Hori N ¹² | Bladder | Penis | Stomach | Lung | | |
| Hori N ¹² | Bladder | Lung | Buccal mucosa | Rectum | | |
| Craig DM ¹³ | Mouth | Lung | Larynx | Tongue | | |
| Oagawara K ¹⁴ | Breast | Breast | Lung | Brain | Thyroid | |
| Kiyo ¹⁵ | Stomach | MM | Bladder | Bladder | | |
| Kuriara ¹⁶ | Breast | RCC | Thyroid | Colon | | |
| Abe ¹⁷ | Stomach | Colon | Ureter | Rectum | | |
| Melkert PW ¹⁸ | Skin | Vulva | Vagina | Anus | Cervix | |
| Brugieres L ¹⁹ | Soft tissue tumor | Brain | Thyroid | Breast | | |
| Murata ²⁰ | Skin | Stomach | Colon | Larynx | | |
| Bumpers HL ⁷ | Larynx | Lung | Breast | Colon | | |
| Sakashita ²¹ | Stomach | Lip | Oral cavity | Oral cavity | | |
| Potzsch ²² | Breast | Lung | RCC | Acute myelomonocytic leukemia | | |
| Keshishian ²³ | Oropharynx | Oesophagus | Lung | Oral cavity | | |
| Nakayama ²⁴ | Breast | Breast | Vater's papilla | Bladder | | |
| Mussari case 1 ²⁵ | Anus | Esophagus | Lung | Oral cavity | | |
| Mussari case 2 ²⁵ | Lung | Stomach | Rectum | Lung | | |
| Mussari case 3 ²⁵ | Oral cavity | Oropharynx | Esophagus | Melanoma | | |
| Mussari case 4 ²⁵ | Oral cavity | Larynx | NHL | Esophagus | | |
| Mukai ²⁶ | Stomach | Duodenum | Esophagus | RCC | Colon | |
| Hu NC ² | Colon | MALT | Lung | Breast | HCC | |
| Takada K ⁶ | Lymphoma | Stomach | Ureter | Lung | Bladder | Lung |
| Sherriff JM ²⁷ | Ovary | RCC | Melanoma | Breast | | |
| Current study | Brain | Kidney | Spinal Cord | Soft Tissue Sarcoma | | |

HCC: Hepatocellular Carcinoma, RCC: Renal cell carcinoma, MALT: Mucosa associated lymphoid tissue, MM: Multiple myeloma, NHL: Non-Hodgkin's lymphoma.

The present case was 59 years old and there was no relevant family history. The patients described in the current report never used tobacco or alcohol. Additionally she did not receive any chemotherapy or radiotherapy for her first two tumors. There wasn't any predisposing factor to these four tumors.

Interestingly, her fourth tumor, high grade sarcoma, was developed up to 10 cm within three months of period. When she was receiving RT to her spinal region she was regularly followed-up in every week; however she did not have any mass on the gluteal region. Moreover when she admitted to the hospital three months after her spinal RT, we checked again her planning tomography scans and it was completely normal.

There was no predisposing factor, family history and genetic abnormality in the case we presented. We considered that the multiple primary tumors may not be associated with hereditary syndrome and risk factors including smoking, chemotherapy and radiotherapy. However patients with a diagnosis of either benign or malign tumor should be followed for the development of subsequent cancers.

Conflict of interest: Declared none

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