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Case Report

Rare occurrence of triple primary malignant tumors: Dermatofibrosarcoma protuberans, lung adenocarcinoma and papillary thyroid carcinoma in a patient with genetic evaluation ☆,☆☆

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ABSTRACT

Triple primary malignancies are rare, involving the occurrence of three distinct, unrelated cancers in a single patient, requiring a personalized, multidisciplinary treatment approach. A 69-year-old male was diagnosed with dermatofibrosarcoma protuberans (DFSP), lung adenocarcinoma, and papillary thyroid carcinoma. After amputation for DFSP, following staging and genetic evaluation, a multidisciplinary tumor board designed a tailored treatment plan, adjuvant chemotherapy for lung adenocarcinoma while monitor regularly the thyroid carcinoma via ultrasound. This case highlights the extreme rarity of this triple primary cancers combination and emphasizes the need for individualized treatment planning. Each cancer's unique characteristics, prognosis, and potential interactions must be considered, alongside the patient's overall health and treatment tolerability, to optimize outcomes in such complex cases.

Introduction

Triple cancer in a single patient, is a rare and challenging phenomenon in clinical oncology. This condition involves the simultaneous or sequential development of three distinct, unrelated cancers within one individual. The occurrence of multiple primary malignancies (MPMs) may be influenced by genetic predispositions, environmental factors, lifestyle choices, or previous cancer treatments. Managing

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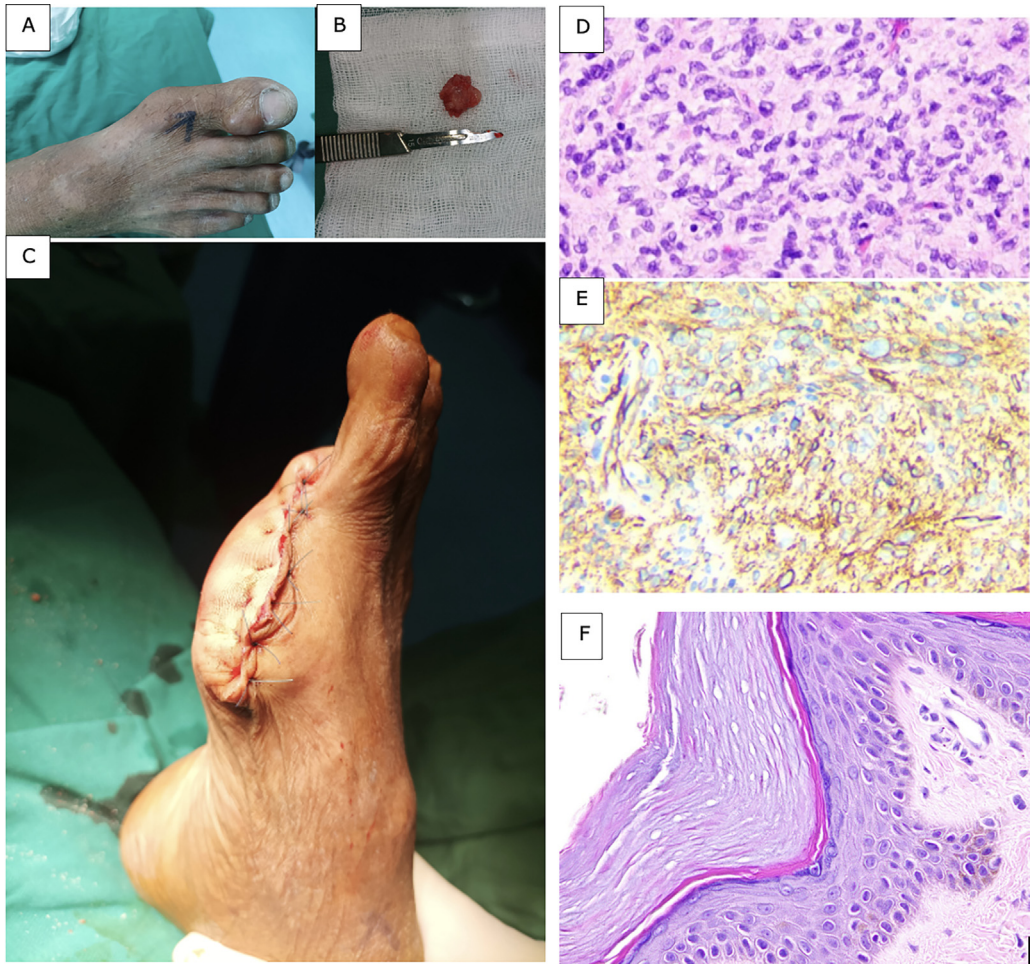

Fig. 1 – (A) The appearance of the tumor suggested a neurofibroma; (B) Complete excision of the mass on the toe; (C) Amputation of metatarsal head of the right foot; (D) Pathological biopsy revealed spindle cells with elongated, hyperchromatic nuclei, scanty cytoplasm, arranged in fascicles with a collagenous stroma and infiltrated by inflammatory cells; (E) Immunohistochemical stain shows that tumor cells are strongly and diffusely positive for CD34; (F) No tumour cells at the resection margin.

such patients requires a tailored, multidisciplinary approach to address the complexities of diagnosis, staging, and treatment planning. The interactions between these distinct malignancies, potential treatment conflicts, and the overall impact on prognosis make triple cancer cases particularly difficult to manage and highlight the need for personalized and coordinated care. This article presents a detailed analysis of the diagnosis and treatment of a patient with three primary malignancies—dermatofibrosarcoma protuberans, lung adenocarcinoma, and papillary thyroid carcinoma—accompanied by genetic analysis.

Case report

A 69-year-old male patient was admitted because of a painful mass on his right big toe that had been present for 4 years, gradually increasing in size. Examination revealed a 1 × 2 cm firm, poorly defined, painful mass on the right big toe (Figure 1A). A biopsy and complete excision of the mass was performed (Fig. 1B), and pathology confirmed dermatofibrosarcoma protuberans (DFSP).

The patient was re-admitted for an amputation of the metatarsal head (Fig. 1C). The final pathology report has reconfirmed a diagnosis of dermatofibrosarcoma protuberans (DFSP) (Fig. 1D, Fig. 1E). Postoperative results were favorable with the stump healing well and no tumor cells found at the resection margin (Fig. 1F).

During hospitalization, a chest X-ray revealed a lung lesion. Further chest CT scan identified a 37.7 × 30.3 × 15.7mm consolidation in the S9 segment of the left lung (Fig. 2A). A biopsy confirmed primary lung adenocarcinoma (Fig. 2B).

The patient underwent thoracoscopic left lower lobectomy (Fig. 3A) and mediastinal lymph node dissection, with the final diagnosis of left lower lobe lung cancer (pT2bN0M0) – primary adenocarcinoma (EGFR (-), CK7 (+), CK20 (-), TTF-1 (+)). Postoperative pathology confirmed invasive lungs adenocarcinoma (Fig. 3B) and no mediastinal lymph node metastasis (Fig. 3C).

A comprehensive health check post-lobectomy included thyroid ultrasound revealing: TI-RADS 3-4 nodules in both lobes. The right lobe had several mixed-echo nodules, pre-

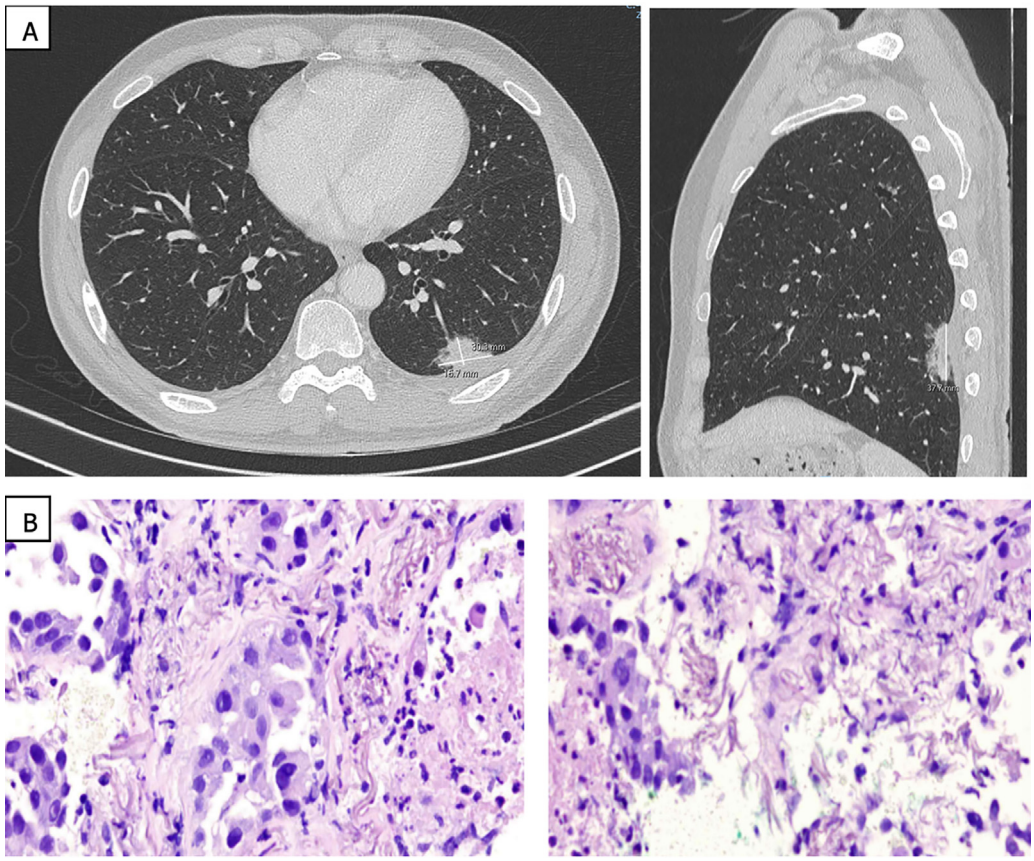

Fig. 2 – (A) Consolidation in S9 segment of the left lung; (B) Hematoxylin-eosin stain shows adenocarcinoma of lung: cells have large, hyperchromatic, pleomorphic nuclei with high N/C ratio and are arranged in a glandular pattern.

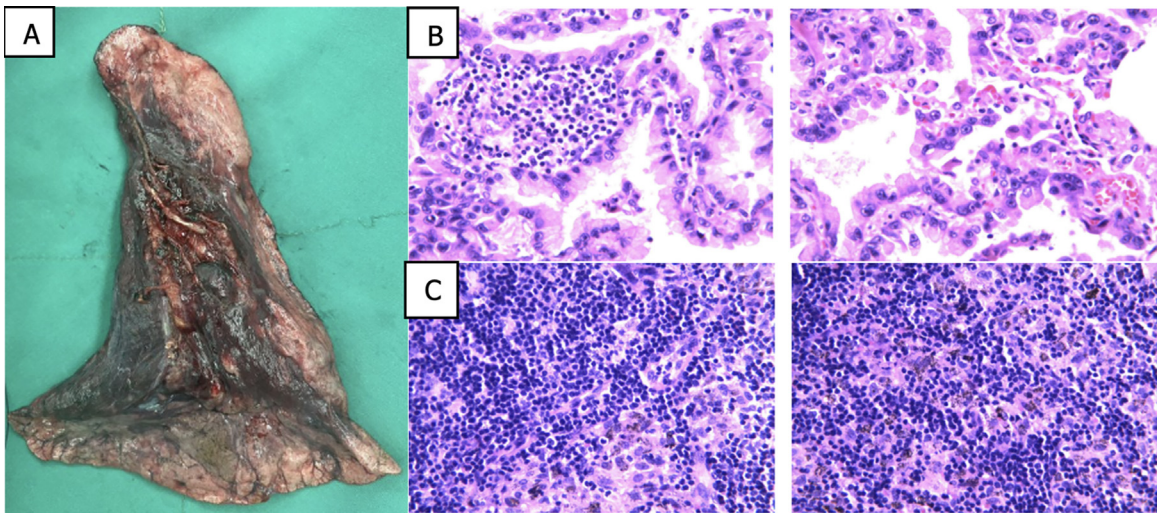

Fig. 3 – (A) lower lobe of the left lung; (B) Hematoxylin-eosin stain. Epithelial cells with large, hyperchromatic, pleomorphic nuclei and glandular growth patterns; (C) Hematoxylin-eosin stain. Section of mediastinal lymph node shows no tumor cells.

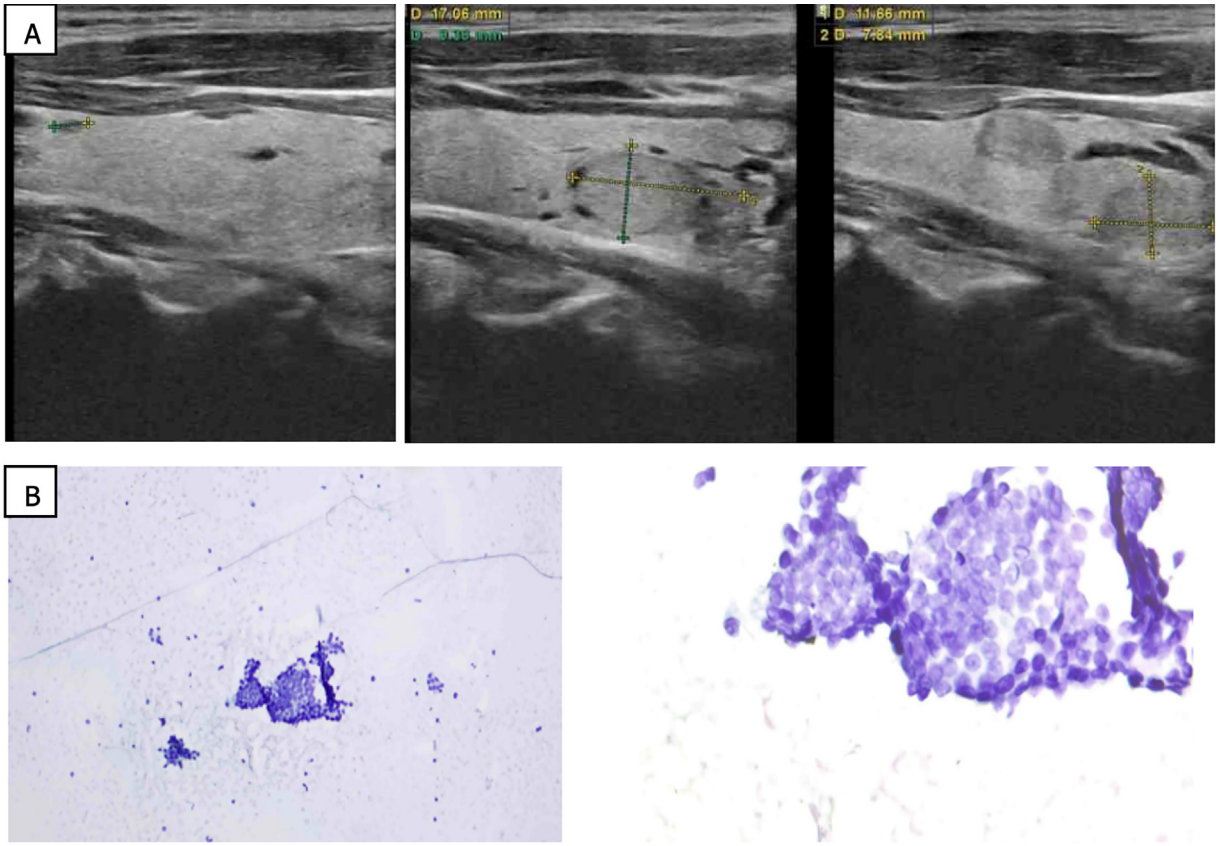

Fig. 4 – (A) Multiple thyroid nodules on ultrasould; (B) Papanicolaou stain. Bethesda V: Suspicious for papillary thyroid carcinoma. Fine-needle aspiration of thyroid nodule shows clusters of cells with nuclear enlargement, elongation and overlapping, chromatin clearing.

dominantly solid, up to 17 × 9 mm (Fig. 4A). Multiple cysts ≤ 3 mm were noted. The left lobe had several mixed-echo nodules, predominantly solid, up to 12 × 8 mm. Multiple cysts ≤ 3 mm were noted. A fine-needle aspiration biopsy (FNA) was performed, yielding findings consistent with papillary thyroid carcinoma in the left thyroid lobe (Fig. 4B).

A multidisciplinary team comprising a thoracic surgeon, a radiologist, a pathologist, and an oncologist determined the patient's treatment plan. Based on the findings, the team agreed that the patient should underwent adjuvant chemotherapy for lung cancer and continued to monitor thyroid cancer via ultrasound. Following the surgery, chemotherapy with carboplatin and paclitaxel was given once a month for five consecutive months. In the most recent thoracoabdominal enhanced CT scan performed on July 18, 2024, no tumor metastasizes was indicated, and the thyroid cancer showed no change on ultrasound (Fig. 5).

Due to the presence of multiple primary cancers, a comprehensive genetic test for germline mutations in 133 genes associated with hereditary cancer was conducted, but no pathogenic variants in the genes tested were revealed. The gene panel tested is available in supplementary data. Genetic test was performed in commercial laboratory with ISO 15189:2012 certification.

Discussion

We described a MPMs in a patient who was subsequently treated. Our patient had no prior medical history of any serious illness, but had a remote smoking history. The simultaneous occurrence of triple primary tumors, though reported, remains exceedingly rare, occurring in less than 0.1% of cancer patients [1]. The increasing frequency of these cases can be attributed to advancements in diagnostic techniques, more sophisticated treatments, and enhanced screening and surveillance in oncology [2]. To our knowledge, this is the first documented case of a patient presenting with dermatofibrosarcoma protuberans, lung adenocarcinoma, and papillary thyroid carcinoma.

MPMs are characterized by histopathological confirmation of malignancy, distinct anatomical sites without continuity, and confirmation that the second tumor is not a metastasis of the first [3]. MPMs are classified as synchronous or metachronous based on timing of diagnosis between two malignancies. Surveillance, Epidemiology, and End Results (SEER) registry defines synchronous tumors if the interval between two diagnosis is within two months, while the International Association of Cancer Registries (IARC) recommends

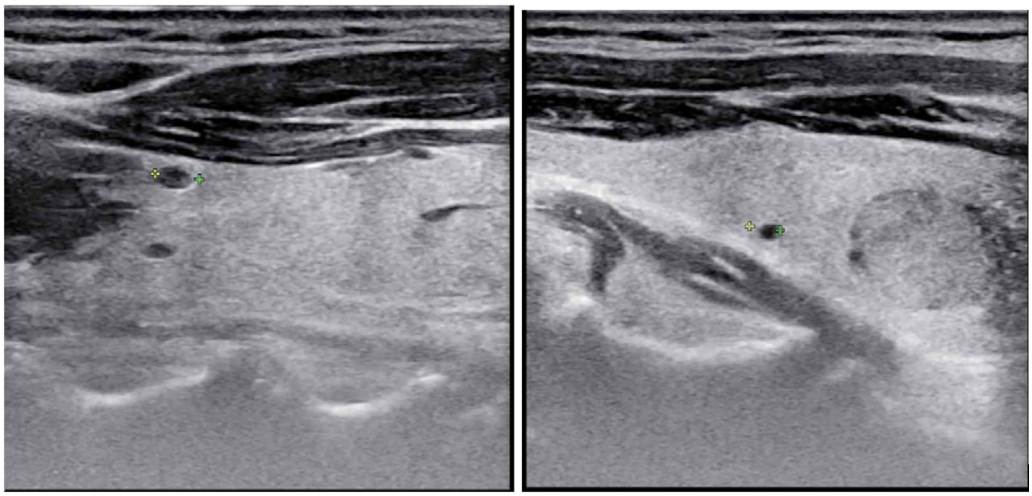

Fig. 5 – Thyroid ultrasound after 5 months.

classifying tumors as synchronous if diagnosed within an interval of less than six months, and as metachronous if diagnosed more than six months apart. Currently, there is no universally accepted diagnostic technique or guideline for detecting MPMs. The choice of imaging—such as CT, MRI, PET, or ultrasound—depends on the tumor type and location. Contrast-enhanced multidetector CT (MDCT) is the most commonly recommended method for cancer staging, offering rapid, whole-body evaluation and detailed multiplanar reconstructions. However, there remains debate about the optimal scanning protocols, as no universal standard exists. With increased CT use, radiologists often play a key role in suggesting or confirming diagnoses, such as colon cancer, based on imaging findings [4].

The underlying cause of the association between dermatofibrosarcoma protuberans, lung adenocarcinoma, and papillary thyroid carcinoma remains unclear.

DFSP is the most common malignancy arising from dermal sarcoma [5]. In DFSP diagnosis, ultrasound offers quick and accurate assessment of tumor size, including thickness and depth, while improving loco-regional staging by evaluating deeper layer involvement. Calatano, Corvino et al. described DFSP ultrasound features as an irregular, ill-defined mixed echogenic lesion with hyperechoic and hypoechoic bands, reflecting mucinous degeneration and fibrous tissue hyalinization. Characteristic pseudopodia-like protrusions extending into surrounding adipose tissue may create a swirling (whirlpool) appearance [6]. In our patient, the diagnosis is confirmed exclusively through histopathological examination.

Early-stage lung cancer patients, like our patient, are more likely to develop additional primaries, particularly in the context of smoking. According to Rosso, the prevalence of multiple primary malignancies in patients with lung cancer may be as high as 13.4% [7].

Several clinical scenarios should call a clinician's attention towards the possibility of an underlying cancer predisposition, in particular the occurrence of multiple primary cancers like in our case. Genetic testing is crucial for identifying predispositions [8]. However, no abnormalities were detected in our patient after evaluating 133 common cancer-related genes.

The management of multiple primary malignancies remains complex due to the absence of standardized guidelines, particularly in rare cases involving triple primary tumors. Treating these patients is challenging because they represent a minority group often excluded from large clinical trials, resulting in treatment approaches that rely on individualized case-by-case assessments. Long-term survival with multiple primaries is variable and is influenced by cancer type and stage at diagnosis. CT remains the most commonly used imaging modality for staging newly diagnosed tumors, and in some cases it is the only imaging test needed prior to surgical management [3]. A multidisciplinary, patient-centered approach is essential, as individualized treatment plans are necessary to address the unique characteristics of each tumor.

Selecting an anticancer strategy that effectively targets all malignancies without increasing toxicity, causing drug interactions, or compromising overall outcomes is critical, making multidisciplinary team management indispensable. Treatment modalities may include surgical resection, adjuvant chemotherapy, and radiotherapy depending on the clinical scenario.

In our case, all tumors were histologically confirmed as primary. The prognosis for primary cancers is generally more favorable than for metastatic diseases. This patient had a relatively positive outlook given the early stage of his three malignancies, without lymph node involvement.

Although dermatofibrosarcoma protuberans is aggressive, but in our patient, the tumour was localized and treated radically with amputation. It was proved that when it is resected widely and achieved negative margins, DFSP can be controled with favorable prognosis [9]. In the case of synchronous MPNs, the malignancy with the most critical prognosis or greatest risk to life should be prioritized for treatment, whereas for metachronous MPNs, each tumor can be addressed sequentially, one at a time. As in our case, the lung cancer histology indicated a high risk of metastasis, necessitating additional chemotherapy to improve postoperative outcomes. The papil-

lary thyroid carcinoma, known for its favorable prognosis [10], can be monitored closely.

Given the rarity of simultaneous triple primary malignancies involving dermatofibrosarcoma protuberans, lung adenocarcinoma, and papillary thyroid carcinoma, further research is needed to explore the potential links between these tumor types and their shared etiological factors.

Conclusion

In conclusion, several key insights should be taken from this case. When managing multiple primary tumors, clinicians must carefully assess whether the tumors are truly primary or metastatic, as this distinction is critical in determining the appropriate surgical and oncological strategy. Comprehensive genetic testing can help identify patients who may be suitable candidates for targeted therapies, including immunotherapy. Lastly, a multidisciplinary approach has proven necessary, ensuring that all relevant factors are considered to choose the most appropriate treatment plan.

Ethical approval and consent to participate

All procedures performed in studies involving the human participant were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from the individual included in the study.

Availability of data and material

The datasets generated and/or analysed during the current study are not publicly available in order to protect patient privacy but are available from the corresponding author on reasonable request.

Author contributions

NMV and THN collected the necessary data. LMBT and NMV was responsible for writing. MDD reviewed the case report.

Patient consent

Written, informed consent was obtained from this patient about the case report that we are submitting for publication.

REFERENCES

[1] Almasan I, Vogt A, Piciu D, et al. Triple primary malignancies: tumor associations, survival, and clinicopathological analysis: a 25-year single-institution experience. Healthcare 2023;11(5):1–16. doi:10.3390/healthcare11050738.
[2] Vogt A, Schmid S, Heinimann K, et al. Multiple primary tumours: challenges and approaches, a review. ESMO Open 2017;2(2):e000172. doi:10.1136/esmoopen-2017-000172.
[3] Corvino A, Setola SV, Sandomenico F, Corvino F, Catalano O. Synchronous tumours detected during cancer patient staging: prevalence and patterns of occurrence in multidetector computed tomography. Polish J Radiol 2020;85:e261. doi:10.5114/pjr.2020.95781.
[4] Corvino A, Corvino F, Radice L, Catalano O. Synchronous mucinous colonic adenocarcinoma and multiple small intestinal adenocarcinomas: report of a case and review of literature. Clin Imaging 2015;39(3):538–42. doi:10.1016/j.clinimag.2014.12.019.
[5] Thway K, Noujaim J, Jones RL, Fisher C. Dermatofibrosarcoma protuberans: pathology, genetics, and potential therapeutic strategies. Ann Diagnostic Pathol 2016;25:64–71. doi:10.1016/j.anndiagpath.2016.09.013.
[6] Catalano O, Corvino A. Ultrasound of skin cancer: what we need to Know. Semin Ultrasound, CT MRI 2024;45(3):216–32. doi:10.1053/j.sult.2023.11.003.
[7] Rosso S, De Angelis R, Ciccolallo L, et al. Multiple tumours in survival estimates. Eur J Cancer 2009;45(6):1080–94. doi:10.1016/j.ejca.2008.11.030.
[8] Borja NA, Silva-Smith R, Calfa C, Sussman DA, Tekin M. Triple primary cancers: an analysis of genetic and environmental factors. Cancer Prev Res (Phila) 2024;17(5):209–15. doi:10.1158/1940-6207.CAPR-23-0395.
[9] Chen S, Xiong L, Zhao L, Li Y, Li L. Survival outcomes and prognostic factors of dermatofibrosarcoma protuberans: a population-based retrospective cohort analysis. Dermatol Surg 2023;49(9):825–31. doi:10.1097/DSS.0000000000003853.
[10] Sebastian SO, Gonzalez JMR, Paricio PP, et al. Papillary thyroid carcinoma: prognostic index for survival including the histological variety. Arch Surg 2000;135(3):272–7. doi:10.1001/archsurg.135.3.272.