Judi Clinical Journal | 2025;1(2):99-117
Journal home page: https://judijournal.com

Systematic Review

Check for updates

Complex Collision Tumors: A Systematic Review

Dua Abuquteish[1], Mohammad A. Al-Qudah[1]*

[1]*Department of Microbiology, Pathology and Forensic Medicine, Faculty of Medicine, Hashemite University, Zarqa 13133, Jordan.*

**Corresponding author: Mohammad A. Al-Qudah (Department of Microbiology, Pathology and Forensic Medicine, Faculty of Medicine, Hashemite University, Zarqa, Jordan). m.alqudah12@just.edu.jo*

Received: *Sep 14, 2025* ***Revised:*** *Oct 11, 2025* ***Accepted:*** *Nov 09, 2025* ***First Published:*** *Nov 22, 2025*

Introduction: A collision tumor consists of two distinct neoplastic components located within the same organ, separated by stromal tissue, without histological intermixing. These rare tumors are usually identified incidentally in surgical specimens. This study systematically reviews complex collision tumors (those with three or more distinct histological types) to explore their features and clinical behavior.

Methods: A comprehensive literature search was conducted using Google Scholar, Consensus AI, and Perplexity AI to identify all articles that describe collision tumors comprising more than two distinct pathologies. Studies lacking full texts, reviews, or those from predatory journals were excluded. Data extracted included publication details, patient demographics, clinical and diagnostic findings, tumor characteristics, treatments, outcomes, and follow-up. Findings were analyzed qualitatively and summarized using frequencies, percentages, and means with standard deviations.

Results: A total of 2,798 articles were identified, and 26 studies (28 cases) met the inclusion criteria. Female patients accounted for 17 cases (60.71%), with a mean age of 63.46 ± 14.00 years. Surgery was performed in 26 cases (92.86%). Triple collision tumors were reported in 26 cases (92.86%), and quadruple collision tumors in 2 cases (7.14%). The thyroid gland was affected in 7 cases (25.00%), and papillary thyroid carcinoma was identified in 9 cases (32.14%). At the last follow-up, 22 patients (78.57%) were alive.

Conclusion: Complex collision tumors represent rare and histologically diverse entities with significant diagnostic and therapeutic implications. They are most frequently found in the thyroid and skin. Accurate diagnosis typically requires comprehensive histopathological and immunohistochemical analysis of the entire lesion.

Keywords: Collision tumors, Complex neoplasia, Multicomponent malignancy, Triple tumors, Quadruple neoplasms

How to cite this article: Abuquteish D, Al-Qudah MA. Complex Collision Tumors: A Systematic Review. Judi Clin. J. 2025;1(2):99-117. https://doi.org/10.70955/JCJ.2025.13

1. Introduction

A collision tumor is defined by the presence of two histologically distinct neoplastic components situated adjacent to each other within the same organ. These components are separated by intervening stromal tissue and lack histological intermingling, thereby classifying the tumor as a type of multiple synchronous neoplasm [1]. The concept of collision tumors was first introduced by Bernet in 1902 and later refined by Meyer in 1919 [2]. They most commonly arise in the liver, stomach, adrenal glands, ovaries, lungs, kidneys, and colon [3].

Collision tumors are exceedingly rare and are typically discovered incidentally during the pathological examination of surgically resected specimens. Due to their rarity, the biological behavior and optimal treatment strategies for collision tumors remain poorly understood, with most available evidence limited to case reports and small case series [4].

From a histopathological viewpoint, collision tumors typically contain both epithelial and mesenchymal components. Therefore, they must be carefully differentiated from other biphasic neoplasms such as carcinosarcomas, which show squamous epithelial and spindle cell elements; composite tumors, which display mixed histologic patterns within one lesion; and tumor-to-tumor metastasis [5].

The exact mechanisms underlying the development of collision tumors remain poorly understood. These neoplasms are thought to originate from a common malignant progenitor cell, which subsequently differentiates into two distinct lineages, each retaining its own malignant characteristics [5].

Collision tumors can consist of different combinations, including two benign neoplasms, a benign and a malignant tumor, or two malignant tumors [6]. A defining feature is that each component preserves its own morphological, immunohistochemical, and sometimes genetic identity, despite its close anatomical proximity [7]. This study aims to systematically review complex collision tumors (defined here as neoplasms composed of three or more distinct histological types within a single anatomical site without any intermixing) and offer comprehensive insights into their characteristics and clinical behavior.

2. Methods

2.1. Study Design

This systematic review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

2.2. Data Sources and Search Strategy

A comprehensive literature search was conducted using Google Scholar, Consensus AI (Pro), and Perplexity AI to identify all articles that describe collision tumors comprising more than two distinct pathologies. In Google Scholar, the search strategy incorporated the use of the "allintitle" and "excluding citation" features. Each of the following terms: Collision, Triple, Quadruple, Triad, Colliding, Combined, Simultaneous, Coexisting, Coexistence, Multicomponent, and Concurrent was individually paired with pathology-related terms using Boolean operators: Tumor, Tumors, Tumour, Tumours, Malignancy, Malignancies, Neoplasm, Neoplasms, Cancer, Cancers, Histology, Histologies, Carcinoma, and Carcinomas. The search was restricted to English-language publications.

In Consensus AI and Perplexity AI, searches were performed using natural language queries formulated in a systematic review format (e.g., "reports of collision tumors involving three or more histologically distinct malignancies"). Retrieved responses were screened for primary literature sources, with cross-verification through direct journal links to ensure inclusion of peer-reviewed articles only.

2.3. Eligibility Criteria

All studies or case reports describing collision tumors involving more than two distinct pathological components were considered eligible for inclusion. Exclusion criteria included inaccessible full texts, review articles, or publications appearing in journals with insufficient peer review standards. The authenticity of the included studies was confirmed by comparing their publishing journals against recognized lists of predatory journals [8].

2.4. Study Selection and Data Extraction

Titles and abstracts were screened to remove studies of dual-component collision tumors, non-human publications, and irrelevant study designs, such as review articles and studies that did not align with the research objectives. Full-text articles that passed the initial screening were then reviewed in detail, with exclusions made for irrelevant studies.

Data extracted from the eligible studies included: the first author's name, year of publication, patient demographics, clinical presentations, affected organs, initial diagnostic methods, imaging findings, type of surgery performed, histological diagnosis, histopathological features, immunohistochemical markers, lymph node involvement, organ metastasis, adjuvant therapies, postoperative complications, follow-up duration, recurrence, and patient status at the last follow-up.

2.5. Statistical Analyses

The data were compiled using Microsoft Excel (version 2021) and analyzed qualitatively with the Statistical Package for the Social Sciences (SPSS, version 27.0). Results were presented as frequencies with corresponding percentages, and means with standard deviations.

3. Results

3.1. Study Identification

A total of 2,798 articles were identified through the comprehensive search. After the initial screening, 616 articles were excluded for the following reasons: duplication (n = 359), non-English language (n = 104), unretrieved data (n = 77), abstract-only publications (n = 58), non-article formats (n = 10), and preprints (n = 8). The titles and abstracts of the remaining 2,182 articles were screened, and 2,145 were excluded due to irrelevance (n = 1,187), including dual-component collision tumors (n = 892), non-human studies (n = 19), review articles (n = 16), and publications in journals with inadequate peer review standards (n = 31). The remaining 37 articles underwent full-text screening, 11 of which were excluded due to lack of relevance. Consequently, 26 eligible articles, encompassing 28 cases of complex collision tumors, were included in the review [1, 5, 9-32] (Table 1). The steps taken to identify relevant studies are represented in the PRISMA diagram (Figure 1).

3.2. Demographic and Clinical Characteristics

The mean age at diagnosis was 63.46 ± 14.00 years. Of the 28 patients, 17 female cases (60.71%) and 11 male cases (39.29%) were identified. The most commonly affected organs were the thyroid, with 7 cases (25.0%), and the skin, with 5 cases (17.86%). The esophagus, kidney, lung, and uterus were each involved in 3 cases (10.71%). Clinical manifestations varied according to tumor location. In thyroid tumors, thyroid nodules were the most common presenting symptom, observed in 3 cases (42.86%). Among skin tumors, lesions were reported in 3 cases (60.0%). All esophageal tumors presented with dysphagia (Table 1).

3.3. Diagnostic Modalities and Interventions

The most frequently used initial diagnostic method was biopsy, performed in 21 cases (75.0%), followed by CT scan in 9 cases (32.14%) and ultrasound in 7 cases (25.0%) (Table 1). Surgical intervention was performed in 26 cases (92.86%), tailored to tumor type and location (Table 2). Among all cases, 15 cases (53.57%) received adjuvant therapy, most commonly radiotherapy in 9 cases (60.0%), followed by chemotherapy in 5 cases (33.33%) (Table 3).

3.4. Histopathology and Tumor Components

Regarding tumor composition, 26 cases (92.86%) were triple collision tumors, while 2 cases (7.14%) were quadruple collision tumors (Table 2). The most common tumor types identified in collision neoplasms were papillary thyroid carcinoma in 9 cases (32.14%) and squamous cell carcinoma in 8 cases (28.57%), followed by adenocarcinoma in 7 cases (25.0%), medullary thyroid carcinoma in 6 cases (21.43%), small cell carcinoma in 4 cases (14.28%), and both basal cell carcinoma and follicular thyroid adenoma in 3 cases each (10.71%) (Table 4).

3.5. Metastatic Spread and Patient Outcomes

Lymph node metastasis was present in 13 cases (46.43%), and organ metastasis occurred in 8 cases (28.57%), most commonly to the lungs in 4 cases (50.0%) and to the liver in 3 cases (37.50%). Recurrence was reported in 4 cases (14.28%) (Table 5). At the time of last follow-up, 22 cases (78.57%) were alive, 5 cases (17.86%) had died, and 1 case (3.57%) was lost to follow-up. Follow-up durations varied widely, ranging from one week to over 8 years (Table 3).

Table 1. Demographics, Clinical Features, and Imaging Findings of the Included Cases

Author (yr)	Study design	Age (yr)/ Sex	Country of origin	Cause of presentation	Duration	Medical history	Surgical history	Family history of cancer	History of radiation exposure	Site of tumors	Initial diagnostic method	Imaging findings
Luo et al., 2024 [5]	Case report	58/M	China	Progressive dysphagia	2 Months	None	N/A	None	N/A	Esophagus	Barium swallow + gastroscopic biopsy	**Barium:** Irregular filling defect 8.9×5.0 cm mid-esophagus. **CT:** Emphysema, bullae, mass. **Gastroscopy:** Mass 28-32 cm from incisors, blocks ⅔ of the lumen.
Bahbahani et al., 2023 [9]	Case report	57/M	Kuwait	Routine checkup	N/A	Hypertension, dyslipidemia, GERD	None	Thyroid, breast	N/A	Left kidney	Urinalysis, US, Contrast CT, PET/ CT	**US:** multiple left renal cysts; **CT:** multiple complex cystic lesions (Bosniak III & IV); **PET/ CT:** hypermetabolic lesions in the left kidney.
Boukhannous et al., 2022 [10]	Case report	59/M	Morocco	Febrile right flank pain	Not specified	Type 2 diabetes, hypertension	N/A	N/A	N/A	Right kidney	CT, MRI, ultrasound-guided biopsy	**CT:** Right renal abscess, bilateral septic emboli. **MRI:** Right renal lesion (8.1×7.8×8.2 cm), possible infection vs. tumor.
Rose et al., 2021 [11]	Case report	82/M	United Kingdom	Ulcerated keratotic lesion on the upper right ear	3 months	Hypertension, multiple non-melanoma skin cancers	N/A	N/A	N/A	Right ear	Clinical examination, excisional biopsy	**CT**: no evidence of distant metastasis
Rupchandani et al., 2021 [12]	Case report	89/M	United Kingdom	Right forearm lesion	N/A	Osteoarthritis, glaucoma, Klinefelter syndrome, DVT, paroxysmal atrial fibrillation, SCC, and actinic keratoses	Previous excisions for SCCs and actinic keratoses; wide local excisions for the current lesion	N/A	N/A	Right forearm skin	Clinical evaluation, excisional biopsy	**CT:** local extension to axilla, right subpectoral and axillary lymphadenopathy, chest wall extension; no distant visceral metastasis

Table 1. Continued...

Author (yr)	Study design	Age (yr)/ Sex	Country of origin	Cause of presentation	Duration	Medical history	Surgical history	Family history of cancer	History of radiation exposure	Site of tumors	Initial diagnostic method	Imaging findings
Toyoshima et al., 2021 [13]	Case report	63/F	Brazil	Longstanding thyroid nodules, neck pain, and dysphagia	25 years	Chronic lymphocytic thyroiditis, Hashimoto's thyroiditis	Total thyroidectomy	N/A	N/A	Thyroid gland	US, FNA	**US:** heterogeneous nodules with calcifications in the left thyroid lobe (largest 6.4 cm)
Hobbs et al., 2020 [14]	Case report	66/M	United States	Asymptomatic enlarging lesion on the right anterior shoulder	1 year	End-stage renal disease (post-kidney transplant), cirrhosis (post-liver transplant), immunosuppression, multiple NMSCs	Kidney and liver transplant	N/A	N/A	Right anterior shoulder skin	Biopsy	**CT chest/abdomen/ pelvis:** no metastatic disease detected
Lai et al., 2020 [15]	Case report	62/F	Taiwan	Epigastric pain and dysphagia	Not specified	N/A	N/A	N/A	N/A	Esophagus	Upper GI endoscopy with biopsy	**CT:** esophageal mass at mid-third esophagus (T2N0M0); **PET**: no distant metastasis; **endoscopic US:** T1N0.
Mizoguchi et al., 2020 [16]	Case report	63/F	Japan	Recurrent abnormal uterine bleeding and anemia	N/A	Diabetes mellitus, hypertension	Appendectomy	N/A	N/A	Uterus	Hysteroscopy, pelvic exam, MRI, CT	**MRI:** 3.4 cm multiple nodular mass confined to the uterine cavity, no myometrial invasion; CT: confined to the uterus, no lymphadenopathy or metastases.
Roshini et al., 2018 [17]	Case report	27/F	India	Right-sided neck swelling	1 year	None	N/A	None	None	Thyroid gland	Ultrasound + FNA	**US:** 3.8×2.4 cm hypoechoic solid nodule with small cystic areas in the right lower thyroid lobe; left lobe and isthmus normal.
Liu et al., 2017 [18]	Case report	58/F	United States	Fevers, chills, abdominal fullness, chest/ back pain	1 month	Invasive ductal carcinoma of left breast	Lumpectomy for breast cancer	N/A	Post-lumpectomy radiation therapy	Right adrenal gland	CT scan of the abdomen	**CT:** 6.2×4.3 ×5.1 cm heterogeneous right adrenal mass, increased in size compared to prior imaging (3.2 cm in 2005); irregular enhancement.

Table 1. Continued...

Author (yr)	Study design	Age (yr)/ Sex	Country of origin	Cause of presentation	Duration	Medical history	Surgical history	Family history of cancer	History of radiation exposure	Site of tumors	Initial diagnostic method	Imaging findings
Schizas et al., 2017 [19]	Case report	76/M	Greece	Progressive dysphagia, weight loss (15 kg over 4 months)	4 months	GERD	N/A	N/A	N/A	Esophagus	Upper GI endoscopy, biopsy, CT scan	**Endoscopy:** Barrett's esophagus, 2 nodules (mid-esophagus and cardia); **CT:** diffuse esophageal wall thickening; no lymphadenopathy or distant metastasis.
Masuyama et al., 2016 [20]	Case report	52/F	Japan	Genital bleeding	N/A	N/A	N/A	None	N/A	Uterus	Transvaginal US, MRI, PET-CT, biopsy	**Transvaginal US:** 4.9×4.9×5.7 cm mixed echogenic cervical mass; **MRI:** 5.5×5.1×5.2 cm hyperintense mass invading lower uterine segment; **PET-CT:** high FDG uptake in cervical and endometrial masses, no distant metastasis.
Bloom et al., 2014 [21]	Case report	68/F	United States	Large, red-brown plaque on left buttock	Since childhood	Hypertension, hyperlipidemia, non-alcoholic steatohepatitis	Cholecystectomy	None	N/A	Left buttock skin	Clinical examination, shave biopsy	N/A
Kim et al., 2014 [22]	Case report	67/F	South Korea	A palpable mass on the anterior neck	2 years	None	None	None	None	Thyroid gland	FNA	**US:** right thyroid 4.4 cm heterogeneous iso-echoic nodule; left thyroid 1.2 cm low-echoic nodule; no cervical lymphadenopathy; no distinct features of papillary carcinoma on imaging.
Suzuki et al., 2014 [23]	Case report	72/M	Japan	Routine checkup	N/A	Lung disease	None	None	N/A	Lung	Chest CT, PET-CT, transthoracic needle biopsy	**CT:** infiltrative shadow in right lower lobe with air bronchogram; **PET-CT:** SUV max 2.6; no lymphadenopathy or distant metastasis.

Table 1. Continued...

Author (yr)	Study design	Age (yr)/ Sex	Country of origin	Cause of presentation	Duration	Medical history	Surgical history	Family history of cancer	History of radiation exposure	Site of tumors	Initial diagnostic method	Imaging findings
Adnan et al., 2013 [24]	Case series	43/F	Israel	Thyroid follicular nodular disease	N/A	N/A	N/A	None	N/A	Thyroid gland	FNA	N/A
		44/F	Israel	Thyroid nodule	N/A	N/A	N/A	None	N/A	Thyroid gland	FNA	N/A
		77/F	Israel	Incidental thyroid nodule	N/A	Osteoporosis	N/A	None	None	Thyroid gland	FNA	**CT:** right thyroid nodule 1.63 cm; **US:** solid, hypervascular nodule.
Cornejo et al., 2013 [25]	Case report	84/M	United States	Pearly, nonpigmented papule on the chest	Not specified	Multiple actinic keratoses, basal cell carcinoma	N/A	N/A	N/A	Chest skin	Shave biopsy	N/A
Jang et al., 2012 [1]	Case report	70/F	South Korea	Abnormal uterine bleeding and abdominal pain	N/A	Hypertension	N/A	None	N/A	Uterus	Transvaginal US, pelvic CT	**Transvaginal US:** 9.2×5.9 cm mixed echogenic mass; **CT:** Large endometrial mass with myometrial invasion, omental nodules; **MRI:** Heterogeneous uterine mass with poor enhancement, peritumoral infiltration.
Rothschild et al., 2010 [26]	Case report	74/F	United States	Left flank pain	Not specified	Long history of recurrent UTIs and renal calculi	N/A	N/A	N/A	Left kidney	US, CT with contrast, MAG3 renal scan	**US:** enlarged left kidney with cystic areas and stones; **CT:** staghorn calculus, multiple cystic low-attenuation lesions replacing parenchyma, consistent with **XGP; MAG3** scan: non-functioning left kidney.
Terada, 2010 [27]	Case report	66/F	Japan	Cough; lung shadow detected on chest X-ray	N/A	N/A	N/A	N/A	N/A	Lung	Chest X-ray, CT, MRI, lung biopsy	**Chest X-ray:** abnormal shadow; **CT/MRI:** 3.5 cm mass in the right lower lobe, multiple lung metastases.

Table 1. Continued...

Author (yr)	Study design	Age (yr)/ Sex	Country of origin	Cause of presentation	Duration	Medical history	Surgical history	Family history of cancer	History of radiation exposure	Site of tumors	Initial diagnostic method	Imaging findings
Broughton et al., 2008 [28]	Case report	78/F	Belgium	Fever, painful left axillary swelling, nausea, loss of appetite, asthenia	2 weeks	Hypothyroidism, psoriasis, Diabetes mellitus	Hysterectomy, left breast tumor resection	N/A	N/A	Left axillary lymph nodes	FNA	**CT:** left axillary lymphadenopathy with surrounding soft tissue inflammation; **PET:** hot spots in the left axillary region, left breast, spleen, gastric fundus, left infraclavicular region.
Wang et al., 2008 [29]	Case report	62/M	United States	Vocal fatigue; nasopharyngeal mass	N/A	None	N/A	N/A	N/A	Nasopharynx	Videolaryngoscopy, biopsy, IHC, flow cytometry	**CT neck, chest, abdomen, pelvis:** negative for additional disease.
Rekhi et al., 2007 [30]	Case report	59/F	India	Enlarging neck mass with hoarseness of voice, dry cough, and increasing neck pain	5 years	None	N/A	N/A	None	Thyroid gland	FNA	**US:** 3 nodules (left lobe, mid/inferior pole, isthmus) with calcification and cystic areas; **CT:** heterogeneous left thyroid mass displacing strap muscles and vessels, multiple enlarged cervical nodes.
De Giorgi et al., 2005 [31]	Case report	38/F	Italy	Pigmented lesion on the hip	6 months	Cutaneous malignant melanoma	Previous melanoma excision	N/A	N/A	Hip skin	Clinical exam, dermoscopy, surgical excision	**Dermoscopy:** pigment network, regressive white area, punctiform vessels, blue-grey globules, pseudohorn cysts.
Badiali et al., 1987 [32]	Case report	63/M	Italy	Shortness of breath; occasional hemoptysis	1 month	Chronic bronchitis and emphysema; 48-year smoking history	None	N/A	None	Lung	Cytologic sputum exam, bronchoscopy	**Chest X-ray:** large lobulated upper lobe mass (6 cm), smaller peripheral lower lobe lesion (3 cm); **CT:** confirmed lesions; bone/liver scans negative.

CT: *Computed tomography;* ***FDG:*** *Fluorodeoxyglucose;* ***F:*** *Female;* ***FNA:*** *Fine needle aspiration;* ***GERD:*** *Gastroesophageal reflux disease;* ***GI:*** *Gastrointestinal;* ***IHC:*** *Immunohistochemistry;* ***M:*** *Male;* ***MAG3:*** *Mercaptoacetyltriglycine;* ***MRI:*** *Magnetic resonance imaging;* ***N/A:*** *Not applicable;* ***NMSC:*** *Non-melanoma skin cancers;* ***PET-CT:*** *Positron emission tomography–computed tomography;* ***SCC:*** *Squamous cell carcinoma;* ***SUV:*** *Standardized Uptake Value;* ***US:*** *Ultrasonography;* ***UTIs:*** *Urinary tract infections;* ***XGP:*** *Xanthogranulomatous Pyelonephritis;* ***yr:*** *Year;* ***DVT:*** *Deep vein thrombosis.*

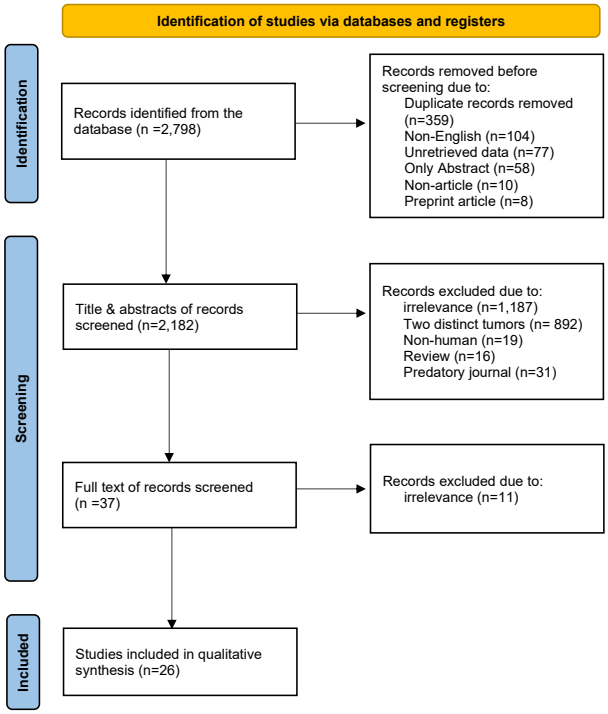

Figure 1. PRISMA flowchart detailing the identification, screening, eligibility, and inclusion of studies

4. Discussion

Terminological inconsistencies can lead to significant confusion, particularly when the term "double neoplasia" is used interchangeably across various clinical and pathological contexts. To minimize ambiguity, it is crucial to differentiate these entities based on both their anatomical location and the timing of their presentation [33]. Spagnolo and Heenan proposed specific diagnostic criteria for identifying collision tumors, emphasizing their dual origin. According to their definition, the two neoplastic components must arise from anatomically distinct topographic sites. At least partial separation should be evident between the components, enabling recognition of their independent origins, even in areas where the tumors are closely intermingled. Within the collision zone, transitional patterns may occur, ranging from areas of intimate admixture to regions displaying hybrid morphologies [34].

In contrast, synchronous tumors are defined as two or more independent primary malignancies diagnosed within a six-month period, whether they arise within the same organ or across separate anatomical locations. Metachronous tumors, on the other hand, are temporally separated, with the second tumor emerging more than six months after the first diagnosis. Meanwhile, composite, mixed, or heterologous tumors consist of histologically distinct cell populations within a single lesion, usually sharing a common molecular origin, as evidenced by clonal analyses that suggest derivation from a single progenitor mutation [33].

In this study, the term complex collision tumor was adopted to describe tumors composed of three or more histologically distinct neoplasms occurring within the same anatomical region without any intermixing. This subclassification represents a more advanced form of tumor heterogeneity, surpassing the traditional biphasic definition. Recognition of such complex entities holds clinical significance, as they often present diagnostic pitfalls and may necessitate individualized therapeutic strategies [5, 9, 10].

The pathogenesis of collision tumors remains incompletely understood, though multiple theories have been proposed. The most widely accepted explanation involves neoplastic heterogeneity, meaning that two or more different groups of tumor cells develop independently within the same area, resulting in separate but coexisting neoplasms [6]. Within this framework, Cornejo and Deng (2013) proposed several possible mechanisms. One is pure coincidence, as exemplified by the frequent co-occurrence of melanocytic nevus and basal cell carcinoma [25]. The second explanation is the field cancerization theory, which posits that chronically damaged tissue, such as sun-exposed skin or prior burn scars, has a predisposition for developing multiple distinct tumors in proximity. This is supported by the frequent occurrence of collision tumors in sun-damaged areas and in patients with conditions like xeroderma pigmentosum [6]. The third hypothesis, the interaction theory, suggests that one tumor may induce stromal or epithelial alterations in the surrounding tissue, thereby facilitating the emergence of a second tumor via paracrine signaling [6]. Alternative mechanisms not reliant on clonal divergence have also been proposed. Satter et al. described potential pathways such as hybrid tumor cell formation, aberrant immunophenotypic marker expression, stochastic genomic derepression, and dedifferentiation into a common stem-like precursor [35].

Despite these theoretical frameworks, the precise pathogenesis of complex collision tumors remains elusive. In a molecular study by Wang et al. (2008), fluorescence in situ hybridization and immunoglobulin gene rearrangement analyses revealed that two mantle cell lymphomas and a plasmacytoma were clonally unrelated, supporting the notion of a true collision event [29]. In contrast, Terada (2010) identified overlapping immunophenotypic features between adenocarcinoma and squamous cell carcinoma components of a lung scar carcinoma, suggesting divergent differentiation from a shared progenitor [27].

In this review of 28 complex collision tumors, 60.71% of patients were female, with a mean age of approximately 63.5 years. However, as patient age and sex were not stratified by tumor location in this study, these findings should be interpreted with caution. This apparent female predominance contrasts with most reports on dual-component collision tumors. For example, Schizas et al. (2024) reported that gastrointestinal collision tumors (n=53) predominantly affected males (81%) [4]. Conversely, Abdullah et al. (2024), in a systematic review of thyroid collision tumors (n = 122), observed a higher prevalence among females (71%) and a younger mean age of approximately 50 years [3].

Clinically, tumors in the current review presented with site-specific symptoms: thyroid lesions commonly appeared as nodules or neck masses, skin tumors as cutaneous lesions or plaques, esophageal tumors with dysphagia, renal tumors with flank pain, and uterine tumors with abnormal bleeding. These presentations are consistent with previous reports; thyroid collision tumors often present with neck swelling [3], while gastrointestinal collisions, such as those in the esophagus, typically cause obstructive symptoms [4]. All esophageal tripartite collisions in the present review presented as progressive dysphagia, mirroring the symptoms of dual-component gastrointestinal collisions.

Collision tumors are frequently diagnosed incidentally, as they often lack distinctive radiological or clinical features. Preoperative biopsies commonly sample only a single histological component, limiting diagnostic accuracy [4]. In this review, 78.57% of cases underwent an initial biopsy, while definitive diagnosis required surgical resection in 92.86% of cases. This highlights a significant diagnostic challenge, as limited tissue sampling may fail to reveal the complex and heterogeneous nature of these tumors. In the case reported by Suzuki et al. (2014), the biopsy initially indicated only chronic inflammation, whereas the final diagnosis following sur-

Table 2. Surgical Management and Histopathological Characterization of Reported Complex Collision Tumors

Author (yr)	Type of surgery performed	Collision tumor				Short HPE description			
		1st tumor	2nd tumor	3rd tumor	4th tumor	1st tumor	2nd tumor	3rd tumor	4th tumor
Luo et al., 2024 [5]	Thoracoscopic-laparoscopic partial esophagectomy with lymphadenectomy	Undifferentiated pleomorphic sarcoma	Adenoid cystic carcinoma	Squamous cell carcinoma	None	Storiform pattern, pleomorphic cells, myxoid degeneration. **IHC:** Vimentin+, CD68+, Desmin focal+, CD56+	Cribriform/tubular/ solid patterns, glandular and myoepithelial cells. **IHC:** CK5/6+, p63+, CD117+, EMA+, S100 weak focal+, SMA weak focal+	Confined to mucosa, incomplete keratinization, and intercellular bridges. **IHC:** CK+, CK5/6+, EMA+, P40+, p63+, BerEP4 focal+	N/A
Bahbahani et al., 2023 [9]	Radical left nephrectomy	Multilocular cystic clear cell renal cell carcinoma	Clear cell papillary renal cell carcinoma	Renal oncocytoma	Renomedullary interstitial cell tumor	Multilocular cystic tumor with thin fibrous septa and serous to gelatinous fluid. **IHC:** Not reported	Solid, hemorrhagic, cystic tumor in the medulla. **IHC:** Not reported	Well-demarcated, unencapsulated brown-tan nodule in cortex with pushing border. **IHC:** Not reported	Composed of stellate cells in loose fibrotic basophilic stroma with entrapped tubules. **IHC:** Not reported
Boukhannous et al., 2022 [10]	Radical right nephrectomy	Papillary Renal Cell Carcinoma	Chromophobe Renal Cell Carcinoma	Sarcomatoid dedifferentiation	None	Papillae of carcinomatous cells, moderate to marked nucleocytoplasmic atypia. **IHC:** CD10+, CK7+, vimentin+, pancytokeratin (weak +)	Large nests of cells with abundant cytoplasm and perinuclear halo. **IHC:** CK7+, CD117+, E-cadherin+	Sheets of atypical spindle/giant cells, high mitotic activity. **IHC:** Not reported.	N/A
Rose et al., 2021 [11]	Wedge excision, followed by re-excision	Squamous cell carcinoma	Basal cell carcinoma	Invasive nodular melanoma	None	Moderately differentiated (pT2). **IHC:** Not reported	Infiltrative (pT1). **IHC:** Not reported	Invasive nodular (pT3a), 2.8 mm Breslow thickness. **IHC:** Melan-A+; others not specified	N/A
Rupchandani et al., 2021 [12]	Excisional biopsy	Merkel cell carcinoma	Sebaceous carcinoma	Bowen's disease (Squamous cell carcinoma in situ)	None	Dermal nodules of small, round, blue cells. **IHC:** Not reported	Lobular architecture with sebaceous differentiation. **IHC:** Not reported	Full-thickness epidermal atypia (SCC in situ). **IHC:** Not reported	N/A

Table 2. Continued...

Author (yr)	Type of surgery performed	Collision tumor				Short HPE description			
		1st tumor	2nd tumor	3rd tumor	4th tumor	1st tumor	2nd tumor	3rd tumor	4th tumor
Hobbs et al., 2020 [14]	Mohs micrographic surgery followed by WLE and sentinel lymph node biopsy	Merkel cell carcinoma	Squamous cell carcinoma in situ	Basal cell carcinoma	None	Small blue cell tumor, neuroendocrine features, stippled chromatin, molding, high mitotic activity. **IHC:** TTF-1+, CK20−, synaptophysin+, CAM5.2+, AE1/AE3 (dot-like), neurofilament (rare +), chromogranin−	Intraepidermal atypia. **IHC:** CK5/6+	Peripheral palisading, retraction artifact. **IHC:** BerEP4+, chromogranin+, synaptophysin+, CK7 (some areas)	N/A
Lai et al., 2020 [15]	Robotic minimally invasive esophagectomy, gastric tube reconstruction, cervical esophagogastrostomy, feeding jejunostomy	Small cell carcinoma	Squamous cell carcinoma	Adenocarcinoma	None	Major component, poorly differentiated (G3), positive for insulinoma-associated one and CD56. **IHC:** insulinoma-associated 1+, CD56+, p40−	**IHC:** p40+	Morphology consistent with glandular origin. **IHC:** Not reported	N/A
Mizoguchi et al., 2020 [16]	Total abdominal hysterectomy with bilateral salpingo-oophorectomy	Low-grade endometrial stromal sarcoma	Uterine tumor resembling ovarian sex-cord tumor	Leiomyoma	None	CD10+, sex cord-like differentiation, necrosis, MI 20/10 HPF. **IHC:** CD10+	CD10−, cords of epithelioid/spindle cells, hyalinized stroma. **IHC:** CD10−; cyclin D1 negative	Spindle cells in fascicles, infarct-type necrosis. **IHC**: Not reported	N/A
Roshini et al., 2018 [17]	Right hemithyroidectomy followed by completion thyroidectomy	Not otherwise specified follicular-pattern carcinoma	Papillary thyroid carcinoma	Medullary thyroid carcinoma	None	Well-differentiated follicular pattern, capsular invasion. **IHC:** Not reported	Classical nuclear features in Hashimoto's background. **IHC:** Not reported	Oval-to-spindle cells with salt and pepper chromatin. **IHC:** Synaptophysin (3+, 90%), CEA (3+, 90%), Chromogranin (2+, 90%)	N/A

Table 2. Continued...

Author (yr)	Type of surgery performed	Collision tumor				Short HPE description			
		1st tumor	2nd tumor	3rd tumor	4th tumor	1st tumor	2nd tumor	3rd tumor	4th tumor
Schizas et al., 2017 [19]	Transthoracic total esophagectomy with standard lymphadenectomy	Small cell carcinoma (neuroendocrine)	Moderately differentiated adenocarcinoma	Signet ring cell carcinoma	None	Neuroendocrine appearance, upper lesion. **IHC:** Not reported	Moderately differentiated, enteric type. **IHC:** Not reported	Signet ring cell carcinoma: poorly cohesive adenocarcinoma, lower lesion. **IHC:** Not reported	N/A
Masuyama et al., 2016 [20]	Radical hysterectomy, bilateral adnexectomy, pelvic lymph node dissection	Endometrioid carcinoma	Undifferentiated carcinoma	Choriocarcinoma	None	G2, squamous differentiation, confined to the endometrium. **IHC:** Not reported	Invaded half of the myometrium. **IHC:** Not reported	Lymphovascular invasion, no endometrioid component. **IHC:** Not reported	N/A
Bloom et al., 2014 [21]	Shave biopsy	Eccrine poroma	Seborrheic keratosis	Viral wart	None	Bulbous aggregates of small squamous cells with eccrine ductal differentiation. **IHC:** Not reported	Horn pseudocysts, hypergranulosis, compact orthokeratosis with parakeratosis. **IHC:** Not reported	Papillated and polypoid lesion with crusting, spongiosis, and inflammatory infiltrate (neutrophils, plasma cells, lymphocytes). **IHC:** Not reported	N/A
Kim et al., 2014 [22]	Bilateral total thyroidectomy with central neck dissection	Follicular carcinoma	Papillary microcarcinoma	Medullary carcinoma	None	4.3 cm with capsular invasion. **IHC:** Not reported	0.3 cm microcarcinoma, papillary features. **IHC:** Not reported	0.8 cm, small round nuclei, positive calcitonin staining. **IHC:** calcitonin+	N/A
Suzuki et al., 2014 [23]	Right lower lobectomy with mediastinal lymph node dissection	Invasive mucinous adenocarcinoma	Invasive non-mucinous adenocarcinoma	Squamous cell carcinoma	None	Columnar, mucin-secreting cells with papillary invasion. **IHC:** Not reported	Invasive glandular growth. **IHC:** Not reported	Pseudostratified cells with keratinization and angular nuclei. **IHC:** Not reported	N/A
Adnan et al., 2013 [24]	Total thyroidectomy + right modified neck dissection	Medullary thyroid carcinoma	Papillary thyroid microcarcinoma	Follicular thyroid adenoma	None	Nests of oval cells. **IHC:** calcitonin+, thyroglobulin−	**IHC:** thyroglobulin+	microfollicular pattern. **IHC:** Not reported	N/A
	Total thyroidectomy + right modified neck dissection	Medullary thyroid carcinoma	Papillary thyroid microcarcinoma	Follicular thyroid adenoma	None	**IHC:** calcitonin+, chromogranin+, synaptophysin+, CEA (partial)+	Not reported	Not reported	N/A
	Right thyroidectomy and isthmectomy	Medullary thyroid carcinoma	Papillary thyroid microcarcinoma	Follicular thyroid adenoma	None	**IHC:** calcitonin+, CEA+, pankeratin+	Not reported	Not reported	N/A

Table 2. Continued...

Author (yr)	Type of surgery performed	Collision tumor				Short HPE description			
		1st tumor	2nd tumor	3rd tumor	4th tumor	1st tumor	2nd tumor	3rd tumor	4th tumor
Jang et al., 2012 [1]	Total hysterectomy, bilateral salpingo-oophorectomy, lymphadenectomy, omentectomy, appendectomy	Malignant mixed müllerian tumor	Papillary serous carcinoma	Endometrioid adenocarcinoma	None	Carcinomatous (glandular) and sarcomatous (spindle cell) components. **IHC:** p53+, CK+ (carcinoma), vimentin+ (sarcoma), MyoD1 focal+	Papillary growth, poorly differentiated, myometrial invasion. **IHC:** p53+, CK+, PR+, ER-	Glandular and solid patterns with squamous differentiation, confined to endometrium. **IHC:** p53+, CK+, ER-, PR-	N/A
Rothschild et al., 2010 [26]	Radical left nephrectomy	Squamous cell carcinoma	Osteogenic sarcoma	Xanthogranulomatous pyelonephritis	None	Moderately differentiated, keratinizing, with necrosis and angiolymphatic invasion. **IHC:** Not reported	High-grade spindle/polyhedral cells producing unmineralized osteoid. **IHC:** CD10+, pancytokeratin–, EMA–, SMA–, S100–, ALK-1–	Lipid-laden macrophages, foamy histiocytes, and abscess formation. **IHC:** Not reported	N/A
Terada, 2010 [27]	None; treated with chemotherapy only; autopsy performed after death	Adenocarcinoma	Squamous cell carcinoma	Small cell carcinoma	None	Irregular glands with atypical cells and desmoplastic stroma. **IHC:** CK7+, CK8+, CK18+, CK19+, EMA+, CEA+, PDGFRA+	Keratinizing nests with intercellular bridges; merged with adenocarcinoma. **IHC:** CK5/6+, CK7+, CK8+, EMA+, CEA+, PDGFRA+	Small hyperchromatic cells with nuclear molding; distinct and separate. **IHC:** CK18+, chromogranin+, synaptophysin+, CD56+, PDGFRA+	N/A
Broughton et al., 2008 [28]	Left upper-inner quadrantectomy and axillary lymph node dissection	Infiltrating lobular carcinoma (from breast cancer)	Scleronodular Hodgkin's disease	Tuberculous lymphadenitis	None	Cohesive sheets of tumor cells (metastasis in the lymph node). **IHC:** ER+, Cerb2 (HER2) -	Reed-Sternberg cells in hyperplastic cortex/para-cortex. **IHC:** Not reported	Caseous necrosis, granulomas with epithelioid and Langhans giant cells. **IHC:** Not reported	N/A
Wang et al., 2008 [29]	Biopsy only	Mantle cell lymphoma (IgM+ phenotype)	Mantle cell lymphoma (IgA+ phenotype)	Extramedullary plasmacytoma	None	Sheets of small- to medium-sized lymphoid cells with slightly irregular nuclear contours and scant cytoplasm. **IHC:** CD20+, CD5+, cyclin D1+, IgM+	Similar morphology to the IgM+ MCL, but a distinct population based on immunophenotyping. **IHC:** CD20+, CD5+, cyclin D1+, IgA+	Composed of mature-appearing plasma cells arranged in sheets. **IHC:** CD138+, CD20−, IgG+, κ+, λ−, cyclin D1−	N/A

Table 2. Continued...

Author (yr)	Type of surgery performed	Collision tumor				Short HPE description			
		1st tumor	2nd tumor	3rd tumor	4th tumor	1st tumor	2nd tumor	3rd tumor	4th tumor
De Giorgi et al., 2005 [31]	Surgical excision	Melanocytic compound naevus	Nodular basal cell carcinoma	Seborrhoeic keratosis	None	Nests of pigmented melanocytes without significant atypia. **IHC:** Not reported	Basaloid cells with peripheral palisading, clefts between the tumor and stroma. **IHC:** Not reported	Pigmented basaloid cell proliferation, small keratin-filled cysts. **IHC:** Not reported	N/A
Badiali et al., 1987 [32]	Right upper lobectomy, atypical resection of RLL, total right pneumonectomy	Squamous cell carcinoma	Small cell carcinoma	Adenocarcinoma	None	Moderately differentiated; keratinization; intercellular bridges. **IHC:** Not reported	Typical intermediate type; high nuclear-cytoplasmic ratio. **IHC:** Grimelius stain +	Well-differentiated, mucin-secreting cells; glandular formation. **IHC:** Not reported	N/A

IHC: *Immunohistochemistry;* ***N/A:*** *Not applicable;* ***WLE:*** *Wide local excision;* ***yr:*** *Year;* ***HPE:*** *Histopathological examination;* ***SCC:*** *Squamous cell carcinoma;* ***PTC:*** *Papillary thyroid carcinoma;* ***MCL:*** *Mantle cell lymphoma.* ***RLL:*** *Right lower lobe*

Table 3. Clinical outcomes and follow-up data

Author (yr)	Lymph node metastasis	Organ metastasis	Adjuvant therapies	Postoperative complications	Follow-up duration	Recurrence	Status at last follow-up
Luo et al., 2024 [5]	Yes, the middle esophageal lymph node	N/A	None	N/A	101 months	None	Alive, no recurrence or metastasis
Bahbahani et al., 2023 [9]	None	None	None	Elevated creatinine/eGFR drop	1 week	None	Alive with stable disease
Boukhannous et al., 2022 [10]	Yes, ipsilateral hilar lymphadenopathy	Lungs	Sunitinib	N/A	1 year	None	Alive with stable disease
Rose et al., 2021 [11]	N/A	N/A	None	N/A	Ongoing at the time of the report	N/A	Alive, on regular follow-up
Rupchandani et al., 2021 [12]	Yes, extensive nodal disease in the right axilla and subpectoral region	None	Palliative radiotherapy	N/A	43 days	Local recurrence at the distal forearm wound site before radiotherapy	Deceased
Toyoshima et al., 2021 [13]	Yes, bilateral cervical levels II–V, extracapsular invasion	Lungs and liver	RAI therapy (206 mCi); external-beam radiotherapy; sorafenib	Developed respiratory failure; tracheostomy required	12 months	Local, lymph node, and distant (lung and liver)	Deceased

Table 3. Continued...

Author (yr)	Lymph node metastasis	Organ metastasis	Adjuvant therapies	Postoperative complications	Follow-up duration	Recurrence	Status at last follow-up
Hobbs et al., 2020 [14]	Yes, positive sentinel lymph node biopsy	None	N/A	N/A	N/A	N/A	Alive, under evaluation.
Lai et al., 2020 [15]	Yes, pericardial lymph nodes	Esophagus	Concurrent chemoradiation therapy with etoposide and cisplatin	N/A	N/A	N/A	Alive, under treatment
Mizoguchi et al., 2020 [16]	None	None	None	N/A	6 months	None	Alive and disease-free
Roshini et al., 2018 [17]	N/A	N/A	N/A	N/A	N/A	N/A	Alive, on regular follow-up
Liu et al., 2017 [18]	Yes, axillary lymph nodes	Adrenal gland, bone, left supraclavicular region, lung hila	Aromatase inhibitor	N/A	10 months	Progression of metastatic disease	Deceased
Schizas et al., 2017 [19]	Yes, the Gastrohepatic ligament lymph node	Liver	Cisplatin and etoposide	N/A	6 months	Multiple liver metastases	Alive, undergoing definitive chemotherapy
Masuyama et al., 2016 [20]	Yes, the left external iliac lymph node	None	6 cycles paclitaxel/carboplatin + 5 cycles methotrexate	N/A	1 year	N/A	Alive and disease-free
Bloom et al., 2014 [21]	None	None	None	N/A	N/A	N/A	N/A
Kim et al., 2014 [22]	None	None	RAI (130 mCi)	N/A	7 months	None	Alive and disease-free
Suzuki et al., 2014 [23]	None	N/A	None	N/A	12 months	N/A	Alive and disease-free
Adnan et al., 2013 [24]	None	None	RAI (I-131, 100 mCi)	N/A	1 year	None	Alive and disease-free
	None	None	RAI (I-131, 100 mCi)	N/A	N/A	None	Alive and disease-free
	None	None	None	N/A	N/A	None	Alive and disease-free

Table 3. Continued...

Author (yr)	Lymph node metastasis	Organ metastasis	Adjuvant therapies	Postoperative complications	Follow-up duration	Recurrence	Status at last follow-up
Cornejo et al., 2013 [25]	N/A	N/A	None	N/A	6 months	None	Alive and disease-free
Jang et al., 2012 [1]	Yes, pelvic and para-aortic lymph nodes	Omentum, serosa of the sigmoid colon	Intraperitoneal chemotherapy (paclitaxel); systemic chemotherapy (paclitaxel, epirubicin, carboplatin); radiation therapy	N/A	8 years	None	Alive and disease-free
Rothschild et al., 2010 [26]	None	N/A	N/A	N/A	N/A	N/A	Alive
Terada, 2010 [27]	Yes, systemic lymph nodes are positive for all three components	Lungs, pleura, brain, bones, liver	Chemotherapy	N/A	7 months (from diagnosis to death)	N/A	Deceased
Broughton et al., 2008 [28]	Yes, nodes positive for breast carcinoma	N/A	Tamoxifen (for breast cancer), six cycles ABVD chemotherapy (for Hodgkin's), 9-month anti-TB (isoniazid, rifampicin, ethambutol)	Progressive anemia	N/A	N/A	Alive with stable disease
Wang et al., 2008 [29]	N/A	Bone marrow	Radiotherapy to the nasopharynx (50 Gy in 25 fractions)	N/A	15 months	None	Alive
Rekhi et al., 2007 [30]	Yes	N/A	RAI ablation (195 mCi)	N/A	Ongoing at the time of the report	N/A	Alive, on regular follow-up
De Giorgi et al., 2005 [31]	None	None	None	N/A	N/A	N/A	Alive and disease-free
Badiali et al., 1987 [32]	None	None	None	Empyema	<1 month	N/A	Deceased

ABVD: *Adriamycin (doxorubicin),* ***Bleomycin,*** *Vinblastine,* ***and*** *Dacarbazine;* ***eGFR:*** *Estimated glomerular filtration rate;* ***GY:*** *Gray;* ***mCi:*** *Millicuries;* ***RAI:*** *Radioactive iodine;* ***TB:*** *Tuberculosis;* ***yr:*** *Year;* ***N/A:*** *Not available*

Table 4. Types of Tumors Constituting the Reported Complex Collision Neoplasms

Type of tumors	Frequency (%)
Papillary thyroid carcinoma (all variants)	9 (32.14%)
Squamous cell carcinoma	8 (28.57%)
Adenocarcinoma (all subtypes)	7 (25.0%)
Endometrioid adenocarcinoma	1 (3.57%)
Invasive mucinous adenocarcinoma	1 (3.57%)
Invasive non-mucinous adenocarcinoma	1 (3.57%)
Others	4 (14.28%)
Medullary thyroid carcinoma	6 (21.43%)
Small cell carcinoma	4 (14.28%)
Basal cell carcinoma	3 (10.71%)
Follicular thyroid adenoma	3 (10.71%)
Merkel cell carcinoma	2 (7.14%)
Seborrheic keratosis	2 (7.14%)
Bowen's disease (Squamous cell carcinoma in situ)	2 (7.14%)
Adenoid cystic carcinoma	1 (3.57%)
Adrenal adenoma	1 (3.57%)
Choriocarcinoma	1 (3.57%)
Chromophobe renal cell carcinoma	1 (3.57%)
Clear cell papillary renal cell carcinoma	1 (3.57%)
Eccrine poroma	1 (3.57%)

Table 4. Continued...

Type of tumors	Frequency (%)
Endometrioid carcinoma	1 (3.57%)
Extramedullary plasmacytoma	1 (3.57%)
Follicular carcinoma	1 (3.57%)
Infiltrating lobular carcinoma	1 (3.57%)
Invasive nodular melanoma	1 (3.57%)
Leiomyoma	1 (3.57%)
Low-grade endometrial stromal sarcoma	1 (3.57%)
Malignant mixed müllerian tumor	1 (3.57%)
Mantle cell lymphoma (IgA+ phenotype)	1 (3.57%)
Mantle cell lymphoma (IgM+ phenotype)	1 (3.57%)
Melanocytic compound naevus	1 (3.57%)
Melanoma	1 (3.57%)
Metastatic breast carcinoma	1 (3.57%)
Multilocular cystic clear cell renal cell carcinoma	1 (3.57%)
Myelolipoma	1 (3.57%)
Nodular basal cell carcinoma	1 (3.57%)
Not otherwise specified follicular-pattern carcinoma	1 (3.57%)
Osteogenic sarcoma	1 (3.57%)
Papillary Renal Cell Carcinoma	1 (3.57%)
Papillary serous carcinoma	1 (3.57%)
Renal oncocytoma	1 (3.57%)
Poorly differentiated thyroid carcinoma	1 (3.57%)
Renomedullary interstitial cell tumor	1 (3.57%)
Sarcomatoid dedifferentiation	1 (3.57%)
Scleronodular Hodgkin's disease	1 (3.57%)
Sebaceous carcinoma	1 (3.57%)
Signet ring cell carcinoma	1 (3.57%)
Tuberculous lymphadenitis	1 (3.57%)
Undifferentiated carcinoma	1 (3.57%)
Undifferentiated pleomorphic sarcoma	1 (3.57%)
Uterine tumor resembling ovarian sex-cord tumor	1 (3.57%)
Viral wart	1 (3.57%)
Widely invasive oncocytic carcinoma	1 (3.57%)
Xanthogranulomatous pyelonephritis	1 (3.57%)

Table 5. Summary of Clinical Features, Diagnosis, Treatment, And Outcomes

Parameters	
Age (mean ± SD)	63.46 ± 14.00 years
Sex	**Frequency (%)**
Female	17 (60.71%)
Male	11 (39.29%)
Tumor site/Presentations[a]	
Thyroid	**7 (25.0%)**
Thyroid nodule	3 (42.86%)
Neck mass	2 (28.57%)
Neck pain	2 (28.57%)
Dry cough	1 (14.28%)
Dysphagia	1 (14.28%)
Hoarseness	1 (14.28%)
Thyroid follicular nodular disease	1 (14.28%)
Neck swelling	1 (14.28%)
Skin	**5 (17.86%)**
Lesion	3 (60.0%)
Nonpigmented papule	1 (20.0%)
Red-brown plaque	1 (20.0%)
Esophagus	**3 (10.71%)**
Dysphagia	3 (100.0%)
Epigastric pain	1 (33.33%)
Weight loss	1 (33.33%)
Kidney	**3 (10.71%)**
Flank pain	2 (66.66%)
Routine checkup	1 (33.33%)
Lung	**3 (10.71%)**
Cough	1 (33.33%)
Hemoptysis	1 (33.33%)
Routine checkup	1 (33.33%)
Shortness of breath	1 (33.33%)
Uterus	**3 (10.71%)**
Abnormal uterine bleeding	2 (66.66%)
Abdominal pain	1 (33.33%)

Table 5. Continued...

Parameters	
Anemia	1 (33.33%)
Genital bleeding	1 (33.33%)
Adrenal gland	**1 (3.57%)**
Abdominal fullness	1 (100.0%)
Back pain	1 (100.0%)
Chest pain	1 (100.0%)
Chills	1 (100.0%)
Fever	1 (100.0%)
Lymph nodes	**1 (3.57%)**
Fever	1 (100.0%)
Axillary swelling	1 (100.0%)
Nausea	1 (100.0%)
Loss of appetite	1 (100.0%)
Asthenia	1 (100.0%)
Ear	**1 (3.57%)**
Ulcerated keratotic lesion	1 (100.0%)
Upper respiratory tract	**1 (3.57%)**
Vocal fatigue	1 (100.0%)
Nasopharyngeal mass	1 (100.0%)
Initial diagnostic methods[b]	
Biopsy	21 (75.0%)
CT scan	9 (32.14%)
Ultrasound	7 (25.0%)
Clinical examination	4 (14.28%)
MRI	4 (14.28%)
PET-CT	3 (10.71%)
Others	13 (46.43%)
Type of intervention	
Surgical	26 (92.86%)
Non-surgical	2 (7.14%)
Types of complex collision tumors	
Triple collision tumor	26 (92.86%)
Quadruple collision tumor	2 (7.14%)
Lymph node metastasis	
Yes	13 (46.43%)
No	11 (39.28%)
N/A	4 (14.28%)
Organ metastasis[c]	
Yes	8 (28.57%)
Lungs	4 (50.0%)
Liver	3 (37.50%)
Bone	2 (25.0%)
Adrenal gland	1 (12.50%)
Bone marrow	1 (12.50%)
Brain	1 (12.50%)
Esophagus	1 (12.50%)
Omentum	1 (12.50%)
Pleura	1 (12.50%)
Sigmoid colon	1 (12.50%)
Supraclavicular region	1 (12.50%)
No	12 (42.86%)
N/A	8 (28.57%)
Adjuvant therapies[d]	
Yes	15 (53.57%)
Radiotherapy	9 (60%)
Chemotherapy	5 (33.33%)
Hormonal therapy	2 (13.33%)
Targeted therapy	2 (13.33%)
Anti-TB therapy	1 (6.66%)
Chemoradiotherapy	1 (6.66%)
No	10 (35.71%)
N/A	3 (10.71%)
Recurrence	
Yes	4 (14.28%)
No	11 (39.29%)
N/A	13 (46.43%)
Status at last follow-up	
Alive	22 (78.57%)
Deceased	5 (17.86%)
N/A	1 (3.57%)

(a): *Some patients had more than one presenting symptom;* ***(b):*** *Some patients underwent more than one initial diagnostic method;* ***(c):*** *Some patients had metastases involving multiple organs;* ***(d):*** *Some patients received more than one type of adjuvant therapy;* ***TB:*** *Tuberculosis;* ***CT scan:*** *Computed tomography scan;* ***FNA:*** *Fine needle aspiration;* ***MRI:*** *Magnetic resonance imaging;* ***PET-CT:*** *Positron emission tomography–computed tomography;* ***N/A:*** *Not applicable;* ***SD:*** *Standard deviation.*

gery revealed a triple-component lung tumor composed of squamous cell carcinoma, invasive mucinous adenocarcinoma, and invasive non-mucinous adenocarcinoma [23]. Similarly, Thomas et al. (2021) found that in thyroid collision tumors, preoperative imaging failed to detect the smaller component in 60% of cases, and fine-needle aspiration cytology identified only the medullary element in all evaluated patients [36]. Luo et al. (2024) also reported that esophageal tripartite collisions were not suspected prior to surgery, as biopsies detected only one histological type and imaging revealed no distinguishing features [5].

Histopathologically, the most commonly observed components in complex collision tumors were papillary thyroid carcinoma (32.14%), squamous cell carcinoma (28.57%), adenocarcinoma (25.0%), medullary thyroid carcinoma (21.43%), and small cell carcinoma (14.28%). These findings align with reports in the literature. Toyoshima et al. (2021) described an aggressive thyroid tumor comprising widely invasive oncocytic carcinoma, classical and hobnail variants of papillary carcinoma, and poorly differentiated carcinoma [13]. Similarly, Kim et al. (2014) and Rekhi et al. (2007) reported combinations involving medullary, follicular, and papillary components [22, 30]. Tumors incorporating small cell carcinoma tended to exhibit particularly aggressive clinical courses, as noted in cases by Schizas et al. (2017) and Terada (2010), in-

volving small cell carcinoma in conjunction with adenocarcinoma and squamous cell carcinoma in the esophagus and lung, respectively [19, 27].

Anatomically, dual collision tumors are most frequently reported in the liver, stomach, adrenal glands, ovaries, lungs, kidneys, and colon [3]. In contrast, the present study found that complex collision tumors most commonly involved the thyroid gland (25%), followed by the skin (17.86%), with the esophagus, lung, kidney, and uterus each accounting for approximately 10.71% of cases. The marked predominance of thyroid involvement may reflect the gland's intrinsic predisposition to multiple neoplastic transformations arising from its follicular, parafollicular, and oncocytic cell lineages [3]. Although less frequent, cutaneous complex collision tumors present considerable diagnostic challenges. Rupchandani et al. (2021) and Hobbs et al. (2020) reported triple skin tumors combining Merkel cell carcinoma, basal or sebaceous carcinoma, and Bowen's disease (in situ squamous cell carcinoma). Such lesions often mimic benign dermatologic conditions, increasing the risk of misdiagnosis unless thoroughly sampled and supported by immunohistochemical evaluation [12, 14].

Adjuvant therapy, including radiation and chemotherapy, was administered in over half of the cases (53.6%), reflecting the heterogeneity of tumor types. Despite these interventions, the recurrence rate was 14.28%, and the mortality rate approached 17.86%, highlighting the clinical severity of these tumors. Schizas et al. (2024) reported that among gastrointestinal collision tumors, several patients experienced early recurrence or metastasis (7.55%), and an equal proportion died within months of surgery, indicating the aggressive nature of certain tumor components [4]. Bladder collision tumors appear particularly concerning; a literature review by Omar et al. (2025) found that approximately 60% of cases were associated with recurrence or mortality [37]. Similarly, Luo et al. (2024) observed that most esophageal tripartite tumors exhibited rapid disease progression, with several patients dying within 1 to 14 months [5].

This study has several limitations, primarily stemming from the nature of the available literature, which consisted solely of case reports due to the rarity of the condition. As a result, quantitative statistical analysis was not possible. Furthermore, the limited number of cases and the variability in data reporting across the included reports may have introduced bias into the review's findings. Despite a comprehensive search strategy using predefined keywords, it is also possible that some relevant studies were unintentionally missed.

5. Conclusion

Complex collision tumors represent rare and histologically diverse entities with significant diagnostic and therapeutic implications. They are most frequently found in the thyroid and skin. Accurate diagnosis typically requires comprehensive histopathological and immunohistochemical analysis of the entire lesion. Recognition of these entities is critical to guide appropriate management and improve patient outcomes.

Declarations

Conflicts of interest: The authors have no conflicts of interest to disclose.

Ethical approval: Not applicable.

Consent for participation: Not applicable.

Consent for publication: Not applicable

Funding: The present study received no financial support.

Acknowledgments: None to be declared.

Authors' contributions: D.A: contribution to the conceptualization of the study, performing the literature search, data extraction, and methodological assessment, and drafting the initial version of the manuscript, including the preparation of the diagram and tables. M.A.A: contribution to the conceptualization and supervision of the study, validating the methodological quality and interpreting the data, critically revising the manuscript for important intellectual content. Both authors approved the final version of the manuscript for submission.

Use of AI: ChatGPT-4.5 was used to assist with language refinement and improve the overall clarity of the manuscript. All content was thoroughly reviewed and approved by the authors, who bear full responsibility for the final version.

Data availability statement: Data are available from the corresponding author upon reasonable request.

References

1. Jang KS, Lee WM, Kim YJ, Cho SH. Collision of three histologically distinct endometrial cancers of the uterus. Journal of Korean Medical Science. 2012;**27(1)**:89-92. https://doi.org/10.3346/jkms.2012.27.1.89
2. Mayer R. Beitrag zur Verstandigung uber die Namengebung in der Geschwulstlehre. Zentralbl Allg Pathol. 1919;**30**:291-6. https://doi.org/10.1159/000514395
3. Abdullah AM, Qaradakhy AJ, Ali RM, Ali RM, Mahmood YM, Omar SS et al. Thyroid Collision Tumors: A Systematic Review. Barw Med J. 2024;**2(3)**:44-56. https://doi.org/10.58742/bmj.v2i2.94
4. Schizas D, Katsaros I, Michalinos A, Damaskos C, Garmpis N, Ntomi V et al. Collision tumors of the gastrointestinal tract: a systematic review of the literature. Anticancer Research. 2018;**38(11)**:6047-57. https://doi.org/10.21873/anticanres.12955
5. Luo S, Tian X, Xu T, Wang J. A unique tripartite collision tumor of the esophagus: a case report and literature review. Frontiers in Oncology. 2024;**14**:1497154. https://doi.org/10.3389/fonc.2024.1497154
6. Bulte CA, Hoegler KM, Khachemoune A. Collision tumors: a review of their types, pathogenesis, and diagnostic challenges. Dermatologic Therapy. 2020;**33(6)**:e14236. https://doi.org/10.1111/dth.14236
7. Bhangoo MS, Zhou JY, Ali SM, Madison R, Schrock AB, Costantini C. Objective response to mTOR inhibition in a metastatic collision tumor of the liver composed of melanoma and adenocarcinoma with TSC1 loss: a case report. BMC Cancer. 2017;**17**:1-5. https://doi.org/10.1186/s12885-017-3167-y
8. Abdullah HO, Abdalla BA, Kakamad FH, Ahmed JO, Baba HO, Hassan MN, et al. Predatory publishing lists: a review on the ongoing battle against fraudulent actions. Barw Med J. 2024;**2(2)**:26-30. https://doi.org/10.58742/bmj.v2i2.91
9. Bahbahani B, Khan RN, Ahmed I, Al-Rabiy FN, Baqer M, Al-Terki A. Rare renaissance: Quadruple synchronous renal cell tumors in one kidney–A case report. Urology Case Reports. 2023;**51**:102574. https://doi.org/10.1016/j.eucr.2023.102574
10. Boukhannous I, El Moudane A, Mokhtari M, Chennoufi M, Miry A, Barki A. Acute pyelonephritis revealing a rare renal collision tumor of papillary and chromophobe cell carcinoma with sarcomatoid features. Oxford Medical Case Reports. 2022;**2022(5)**:omac048. https://doi.org/10.1093/omcr/omac048
11. Rose A, Thomson SE, Melly L, Arkoulis N. Three skin cancers in one: an extremely rare collision tumour. BMJ Case Reports. 2021;**14(6)**:e240271. https://doi.org/10.1136/bcr-2020-240271
12. Rupchandani R, Umar T, Walsh S. Collision tumor: Merkel cell carcinoma and sebaceous carcinoma overlying Bowen's disease. Our Dermatol Online. 2021;**12(3)**:277-279. https://doi.org/10.7241/ourd.20213.10
13. Toyoshima MT, Domingues RB, Soares IC, Danilovic DL, Amorim LC, Cavalcante ER et al. Thyroid collision tumor containing oncocytic carcinoma, classical and hobnail variants of papillary carcinoma, and areas of poorly differentiated carcinoma. Archives of Endocrinology and Metabolism. 2021;**65(4)**:495-9. https://doi.org/10.20945/2359-3997000000389
14. Hobbs MM, Geers TE, Brown TS, Malone JC. Triple collision tumor comprising Merkel cell carcinoma with an unusual immunophenotype, squamous cell carcinoma in situ, and basal cell carcinoma. Journal of Cutaneous Pathology. 2020;**47(8)**:764-7. https://doi.org/10.1111/cup.13698
15. Lai JI, Yeh YC, Chen MH. A Rare Case of Colliding Cancer of the Esoph-

agus with Small Cell Neuroendocrine, Squamous, and Adenocarcinoma Components. Journal of Cancer Research and Practice. 2020;**7(1)**:34-7. https://doi.org/10.4103/JCRP.JCRP_21_19
16. Mizoguchi C, Matsumoto H, Nasu K, Kai K, Arakane M, Narahara H. Collision tumour of endometrial stromal sarcoma, uterine tumour resembling ovarian sexcord tumour, and leiomyoma. Eur. J. Gynaecol. Oncol. 2020;**7(1)**:34-37. https://www.ejgo.net/articles/10.31083/j.ejgo.2020.04.3936
17. Roshini AP, Ramesh R, Rajalakshmi T. HATRICK—Synchronous Triple Primary Tumors of Thyroid. Indian Journal of Surgical Oncology. 2018;**9**:592-4. https://doi.org/10.1007/s13193-018-0772-4
18. Liu D, Kumar SA. An exceedingly rare adrenal collision tumor: adrenal adenoma–metastatic breast cancer–myelolipoma. Journal of Community Hospital Internal Medicine Perspectives. 2017;**7(4)**:241-4. https://doi.org/10.1080/20009666.2017.1362315
19. Schizas D, Michalinos A, Alexandrou P, Moris D, Baliou E, Tsilimigras D, Throupis T, Liakakos T. A unique tripartite collision tumor of the esophagus: A case report. Medicine. 2017;**96(49)**:e8784. https://doi.org/10.1097/md.0000000000008784
20. Masuyama H, Haraga J, Nishida T, Ogawa C, Kusumoto T, Nakamura K et al. Three histologically distinct cancers of the uterine corpus: A case report and review of the literature. Molecular and Clinical Oncology. 2016;**4(4)**:563-6. https://doi.org/10.3892/mco.2016.770
21. Bloom BS, Kamino H, Hale CS, Pomeranz MK. Collision tumor of eccrine poroma, seborrheic keratosis, and a viral wart. Dermatology Online Journal. 2014;**20(12)**:13030-qt8tm0r9b9. https://doi.org/10.5070/D32012025065
22. Kim KJ, Hong SW, Kim SM, Lee YS, Chang HS, Park CS. Synchronous occurrence of papillary, follicular, and medullary carcinoma in the same thyroid gland. Korean Journal of Endocrine Surgery. 2014;**14(3)**:167-70. http://doi.org/10.0000/kjes.2014.14.3.167
23. Suzuki S, Ohtsuka T, Hato T, Kamiyama I, Goto T, Kohno M et al. Primary pulmonary collision tumor with three components in the underlying interstitial lung disease. Thoracic Cancer. 2014;**5(5)**:460-2. https://doi.org/10.1111/1759-7714.12110
24. Adnan Z, Arad E, Dana J, Shendler Y, Baron E. Simultaneous occurrence of medullary and papillary thyroid microcarcinomas: a case series and review of the literature. Journal of Medical Case Reports. 2013;**7**:1-5. https://doi.org/10.1186/1752-1947-7-26
25. Cornejo KM, Deng AC. Malignant melanoma within squamous cell carcinoma and basal cell carcinoma: is it a combined or collision tumor?—A case report and review of the literature. The American Journal of Dermatopathology. 2013;**35(2)**:226-34. https://doi.org/10.1097/dad.0b013e3182545e27
26. Rothschild J, Bhatt S, Dogra VS. Renal collision tumor in association with xanthogranulomatous pyelonephritis. Journal of Clinical Imaging Science. 2010;**1(1)**:9. https://doi.org/10.4103/2156-7514.75263
27. Terada T. Primary pulmonary combined scar carcinoma composed of adenocarcinoma, squamous cell carcinoma, and small cell carcinoma: An autopsy case and literature review. Respiratory Medicine CME. 2010;**3(4)**:246-51. https://doi.org/10.1016/j.rmedc.2009.10.002
28. Broughton A, Galant C, Hainaut P. Simultaneous occurrence of metastatic breast cancer, Hodgkin's disease and tuberculous lymphadenitis in homolateral axillary lymph nodes–a case report. Acta Clinica Belgica. 2008;**63(6)**:391-3. https://doi.org/10.1179/acb.2008.080
29. Wang HY, Karandikar N, Payne D, Maleki A, Schultz BA, Collins R, et al. A 3-way collision tumor of the upper respiratory tract: a composite of 2 immunophenotypically distinct mantle cell lymphomas and a plasmacytoma. Human pathology. 2008;**39(5)**:781-7. https://doi.org/10.1016/j.humpath.2007.08.023
30. Rekhi B, Badhe RR, Desouza MA, Chaukar D, D'Cruz AK, Arya S et al. A unique RET EXON 11 (G691S) polymorphism in an Indian patient with a collision tumor of the thyroid. Diagnostic Pathology. 2007;**2**:39 . https://doi.org/10.1186/1746-1596-2-39
31. De Giorgi V, Massi D, Sestini S, Alfaioli B, Carelli G, Carli P. Cutaneous collision tumour (melanocytic naevus, basal cell carcinoma, seborrhoeic keratosis): a clinical, dermoscopic and pathological case report. British Journal of Dermatology. 2005;**152(4)**:787-90. https://doi.org/10.1111/j.1365-2133.2005.06448.x
32. Badiali P, Alloisio M, Lombardi L. Synchronous triple carcinoma of the lung in one patient. Tumori Journal. 1987;**73(5)**:525-9. https://doi.org/10.1177/030089168707300518
33. Lazureanu DC, Anderco D, Dema S, Jurescu A, Cornea R, Vita O et al. Collision Tumors of the Colon and Peritoneum: Signet-Ring Cell Carcinoma and Granular Cell Tumor. Life. 2023;**13(12)**:2263. https://doi.org/10.3390/life13122263
34. Spagnolo DV, Heenan PJ. Collision carcinoma at the esophagogastric junction: report of two cases. Cancer. 1980;**46(12)**:2702-8. https://doi.org/10.1002/1097-0142(19801215)46:12<2702::AID-CNCR2820461228>3.0.CO;2-M
35. Satter EK, Metcalf J, Lountzis N, Elston DM. Tumors composed of malignant epithelial and melanocytic populations: a case series and review of the literature. Journal of Cutaneous Pathology. 2009;**36(2)**:211-9. https://doi.org/10.1111/j.1600-0560.2008.01000.x
36. Thomas A, Mittal N, Rane SU, Bal M, Patil A, Ankathi SK et al. Papillary and medullary thyroid carcinomas presenting as collision tumors: a case series of 21 cases at a tertiary care cancer center. Head and Neck Pathology. 2021;**15**:1137-46. https://doi.org/10.1007/s12105-021-01323-7
37. Omar SS, Fakhralddin SS, Ali RM, Abdullah AM, Tahir SH, Muhammed BO et al. Urinary bladder collision tumors: A case report and literature review. Medicine International. 2025;**5(3)**:26. https://doi.org/10.3892/mi.2025.225