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Clinical Diagnosis and Management of Reptile Tumors with Emphasis on Chromatophoroma in Leopard Geckos

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ABSTRACT

Reptile neoplasia is increasingly recognized in clinical practice; however, available evidence remains limited and is largely derived from case reports and small retrospective studies. Among these, pigment cell tumors (chromatophoromas) are of particular interest due to their variable presentation and species-specific associations, especially in leopard geckos. This review summarizes current knowledge on the epidemiology, etiology, clinical presentation, diagnosis, and management of reptile tumors, with an emphasis on chromatophoromas. Diagnostic approaches, including imaging, histopathology, and immunohistochemistry, are outlined with consideration of their applicability and limitations in reptiles. Management strategies are discussed with a focus on surgical excision as the primary intervention, while other therapies are interpreted in the context of limited evidence. Recent findings related to SPINT1-associated chromatophoroma in leopard geckos are presented as a species- and morph-specific observation. Molecular mechanisms described in other species are included as comparative references but should be interpreted with caution. Overall, this review provides a clinically oriented summary of current evidence and highlights existing gaps that warrant further investigation.

1. INTRODUCTION

Reptiles are increasingly maintained as companion animals, and clinical reports of neoplastic diseases in these species have gradually increased [1]. Compared with domestic mammals, however, reptile oncology remains less well characterized, and much of the available information is derived from individual case reports, small retrospective studies [2], and diagnostic pathology submissions [3].

Reptile tumors may involve multiple organ systems, including the integumentary, gastrointestinal, reproductive, hematopoietic, musculoskeletal, and respiratory systems [4]. Among these, pigment cell tumors, also known as chromatophoromas, are clinically important because they may present as visible cutaneous

masses and may be associated with species- or morph-specific predispositions [2]. Leopard geckos, particularly Lemon Frost morph animals, have received increasing attention because of reported associations between iridophoroma development and SPINT1-related biology [5].

This review provides an overview of reptile tumors, with a focused discussion of chromatophoromas in leopard geckos. The aim is to summarize current evidence on clinical presentation, diagnosis, differential diagnosis, and management, while clearly distinguishing reptile-supported findings from comparative or hypothetical mechanisms derived from mammalian oncology.

2. OVERVIEW OF REPTILE NEOPLASIA

2.1. Epidemiology

Neoplastic diseases have been reported in a wide range of reptile taxa, including lizards, snakes, turtles, tortoises, and crocodilians [4]. Reported tumor prevalence varies across studies and may be influenced by species, age, sex, husbandry conditions, diagnostic access, and sampling bias [2]. Therefore, statements regarding tumor frequency should be interpreted cautiously [1, 3, 5], particularly when based on retrospective pathology submissions rather than population-level surveillance.

Earlier retrospective studies suggested differences in tumor occurrence among reptile groups [6]; however, contemporary data remain insufficient to establish definitive taxon-wide prevalence rankings. In clinical practice, tumors are commonly reported in captive reptiles, especially in long-lived species and animals receiving prolonged veterinary care [3]. In leopard geckos, increased attention has been given to pigment cell tumors, but reported high incidence is most clearly associated with specific morphs, such as Lemon Frost animals, rather than the species as a whole [5].

2.2. Etiology and Risk Factors

The etiology of reptile tumors is likely multifactorial. Proposed contributing factors include genetic predisposition, age, captive breeding practices, viral infection, ultraviolet exposure, chronic inflammation, hormonal influences, and environmental or husbandry-related stressors. However, direct causal evidence remains limited for many tumor types [7].

Genetic factors may contribute to tumor susceptibility in selected reptile lineages. In leopard geckos, SPINT1-associated alterations have been linked to iridophoroma development in the Lemon Frost morph [5]. This finding should be interpreted as a morph-specific observation rather than a general mechanism for all leopard gecko tumors.

Exogenous factors may also play a role. Viral-associated tumors have been reported in reptiles, suggesting a potential contribution of infectious agents in some cases [6]. Ultraviolet radiation has been discussed as a possible contributing factor in selected cutaneous neoplasms, although direct evidence in reptiles remains limited [8]. Because reptile species differ markedly in anatomy, physiology, ecology, and husbandry requirements, risk factors should be evaluated in a species-specific context.

3. CLINICAL PRESENTATION AND DIAGNOSIS

3.1. Clinical Signs

Clinical signs of reptile tumors are variable and depend on tumor type, location, size, growth rate, and degree of local invasion or metastasis [9]. Common clinical findings include localized swelling, visible masses, changes in skin color or scale morphology, ulceration, bleeding, weight loss, reduced appetite, lethargy, impaired locomotion, respiratory difficulty, gastrointestinal signs, ocular abnormalities, and neurological signs [10].

Cutaneous tumors may be easier to recognize than internal neoplasms because they often present as raised, pigmented, ulcerated, or irregular lesions. However, not all raised or pigmented lesions are neoplastic [11, 12]. Therefore, suspicious lesions should be evaluated using an integrated diagnostic approach rather

than clinical appearance alone.

3.2. Diagnostic Approaches

Diagnosis of reptile tumors generally requires a combination of physical examination, imaging, cytology, biopsy, histopathology, and, when available, immunohistochemistry [4]. Blood biochemical testing may provide supportive information, particularly when systemic disease, organ dysfunction, or metabolic disturbance is suspected, but it is rarely diagnostic on its own.

Imaging methods such as radiography, ultrasonography, computed tomography, and magnetic resonance imaging may help define tumor location, size, tissue involvement, and possible metastasis [13]. Radiography is useful for skeletal involvement and gross internal masses, whereas ultrasonography may assist in evaluating soft tissue and coelomic lesions [14]. CT and MRI can provide more detailed anatomical information, especially for complex or deep-seated tumors, although access and cost may limit their routine use in reptile practice.

Histopathology remains central to the definitive diagnosis of reptile tumors [15]. Biopsy or surgical excision allows assessment of tumor architecture, cellular morphology, mitotic activity, local invasion, and surgical margins [10]. Representative histopathological features of chromatophoromas are illustrated in **Figure 1**.

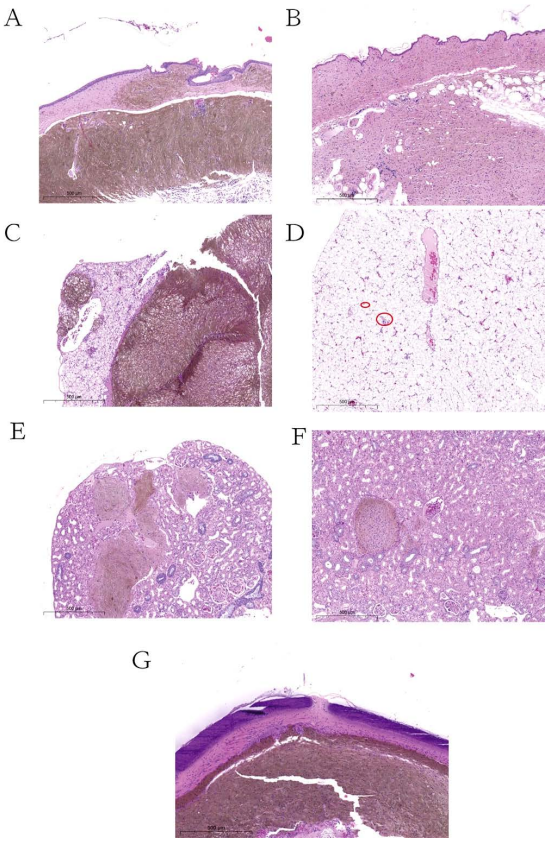

Figure 1. Histopathological features of chromatophoroma in a leopard gecko. (A) (B) Cutaneous iridophoroma showing dermal infiltration by neoplastic pigment cells. (C) (D) Liver tissue showing clusters of tumor cells. (E) (F) Renal tissue showing tumor cell infiltration. (G) Ocular tissue showing pigment cell proliferation.

Immunohistochemistry can provide additional diagnostic support, particularly in poorly differentiated or amelanotic tumors. Markers such as Melan-A and S100 have been successfully applied in reptile diagnostic pathology; however, species-specific validation remains limited and immunoreactivity may vary among studies [16]. Cytological evaluation may also aid preliminary assessment in selected cases, with representative features shown in **Figure 2**.

Diagnostic and prognostic criteria derived from human melanoma, including dermoscopic patterns, lymph-node staging, and cure-rate estimates, should not be directly applied to reptiles unless supported by reptile-specific evidence.

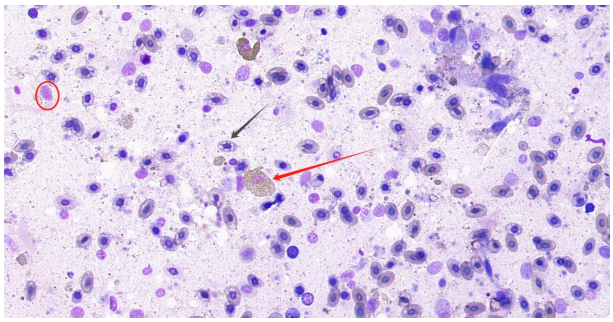

Figure 2. Cytological features of chromatophoroma. Black arrow: nucleated erythrocyte. Red arrow: iridophoroma cell containing pigment granules. Circle: lymphocyte.

3.3. Differential Diagnosis of Pigmented or Raised Skin Lesions

Pigmented or raised skin lesions in reptiles should be differentiated from both neoplastic and non-neoplastic conditions [17]. Important differential diagnoses include abscesses, granulomas, traumatic lesions, cysts, inflammatory nodules, infectious dermatitis, parasitic lesions, hematomas, epithelial tumors, mesenchymal tumors, and pigment cell tumors [18].

Because reptiles may form firm caseous abscesses and chronic inflammatory masses [19], clinical appearance alone may be misleading. Cytology, biopsy, microbial testing, and histopathology are often required to distinguish chromatophoroma from inflammatory or infectious mimics [20].

4. MANAGEMENT STRATEGIES

4.1. Surgical Management

Surgical excision remains the primary treatment for many localized reptile tumors [21], especially when lesions are accessible and complete removal is feasible [22]. Early intervention may improve local control, reduce complications, and allow histopathological assessment of margins.

However, treatment outcome depends on tumor type, anatomical location, completeness of excision, biological behavior, and the presence or absence of metastasis. Broad cure-rate claims should be avoided unless supported by species-specific outcome data. In reptiles, published evidence is often limited to case reports or small case series, making general prognostic statements difficult [2].

4.2. Non-Surgical and Adjunctive Therapies

Non-surgical treatments, including chemotherapy, radiotherapy, electrochemotherapy, cryotherapy, laser therapy, and photodynamic therapy, have been reported in selected reptile cases [23]. Their use should be considered case by case because evidence remains limited and responses may vary by species, tumor type, dose, and route of administration.

Chemotherapy protocols in reptiles are often adapted from mammalian veterinary oncology, but differences in metabolism, thermoregulation, renal physiology, and drug tolerance require caution [2]. Intralesional therapy may be considered for selected localized tumors but is unlikely to control systemic or metastatic disease [24]. Radiotherapy and electrochemotherapy may provide local control in specific cases [25], but standardized protocols for reptiles are not well established [26]. In other oncology settings, drug-delivery technologies and cell-death-based approaches have been explored to improve local targeting and overcome treatment resistance [27, 28]; however, these strategies remain conceptual references for reptile oncology rather than current clinical options.

4.3. Clinical Decision Framework

Management should begin with tumor staging and assessment of resectability [9]. A practical clinical framework is outlined in **Table 1** and should be adapted to species, tumor type, available facilities, and welfare considerations.

Table 1. Reported therapeutic approaches and outcomes in reptile tumors.

Species	Disease Type	Chemotherapy Protocol	Outcome
Pogona vitticeps	Lymphoblastic leukemia	Lomustine + Methylprednisolone + Marbofloxacin	Transient clinical improvement, rapid deterioration within days, death [29]
Furcifer pardalis	Cutaneous squamous-cell carcinoma	Carboplatin sustained-release microspheres	Good local tumor control [30]
Tiliqua scincoides	Lingual squamous-cell carcinoma	Surgical excision; chemotherapy (if any) not disclosed	Uneventful post-operative recovery [23]
Iguana iguana	Metastatic granulosa-cell tumor	Carboplatin 10 mg/kg q3wk intracoelomic	Transient improvement followed by recurrence [31]

5. INTEGUMENTARY TUMORS AND CHROMATOPHOROMAS

5.1. Integumentary Tumors in Reptiles

The integument is a common site for clinically visible lesions in reptiles [21]. Integumentary tumors may include epithelial tumors, mesenchymal tumors, round-cell tumors, and pigment cell tumors [32]. Because external lesions are often detected by owners or clinicians, they provide an important opportunity for early diagnosis.

Pigment cell tumors are especially relevant in reptiles because reptilian skin contains diverse pigment-producing cells [33]. Unlike mammals, reptiles may possess melanophores, iridophores, xanthophores, and other chromatophores [34], which contribute to their complex coloration. Neoplastic transformation of these pigment cells gives rise to chromatophoromas [35, 36].

5.2. Definition and Classification of Chromatophoromas

Chromatophoromas are tumors derived from pigment cells. They are classified according to the predominant pigment cell lineage involved [11, 12]. Melanophoromas arise from melanophores, iridophoromas from iridophores, and xanthophoromas from xanthophores. Mixed chromatophoromas may contain more than one pigment cell type.

Melanophoromas commonly contain dark brown to black pigment. Iridophoromas may appear pale, white, yellow, or reflective and may contain birefringent pigment granules. Xanthophoromas are associated with yellow to orange pigmentation [37]. However, gross appearance alone is not sufficient for diagnosis;

and histopathological confirmation is required [10].

5.3. Clinical and Pathological Features of Chromatophoromas

Chromatophoromas typically present as cutaneous or subcutaneous masses with variable pigmentation, including dark, pale, or yellow-orange coloration depending on the predominant pigment cell type [12]. Lesions may appear as nodules, plaques, or infiltrative masses and may occasionally ulcerate [6]. Clinical presentation varies among species and tumor subtypes.

Histopathologically, chromatophoromas are composed of neoplastic pigment cells showing variable morphology, including spindle-shaped, epithelioid, or pleomorphic cells. Pigmentation may range from abundant to minimal or absent, particularly in amelanotic variants [16]. Mitotic activity, cellular atypia, and local invasion may vary and are not yet standardized prognostic indicators in reptiles. In some cases, metastasis to internal organs has been reported, although available data remain limited [38].

The biological behavior of chromatophoromas appears variable among reptile species and tumor subtypes. Some lesions may remain localized, whereas others have been reported to show local invasion or metastasis to internal organs [21]. Nevertheless, standardized prognostic criteria for reptile chromatophoromas have not been established, and parameters such as mitotic count, cellular atypia, local invasion, and metastasis should be interpreted cautiously due to the limited number of reported cases [39].

Immunohistochemistry may support the diagnosis of chromatophoromas, particularly in poorly differentiated or amelanotic tumors. Markers such as Melan-A and S100 have been applied in reptile pigment cell tumors [35, 36], but antibody cross-reactivity, staining consistency, and species-specific validation remain important limitations [40]. Therefore, immunohistochemical findings should be interpreted together with gross appearance, cytology, histopathology, pigment characteristics, and tissue distribution rather than used as standalone diagnostic criteria [41]. The main characteristics of chromatophoroma subtypes are summarized in **Table 2**.

Table 2. Key features of chromatophoroma subtypes in reptiles.

Type of Pigment Cell	Originating Pigment Cell	Common Presentation	Malignant potential	Cytological features
Melanoma	Melanocytes	skin, which can affect the eyes, ears, and the brain	Dark pigment, varied shapes, nuclei with distinct nucleoli [42].	Benign or Malignant
Iridophoroma	Iridophores	White nodules in the skin	Spindle cells with limited pleomorphism and birefringent golden to olive-green granules under polarized light.	Benign or Malignant
Xanthophoroma	Xanthophores	skin	Cells contain deep orange pigment, with intracellular lipid pigments.	Benign, linked to hereditary lipidosis, may cause neurologic impairment.
Mixed Chromatophoromas	pigment cell	N/A	N/A	Benign or Malignant

6. SPINT1-ASSOCIATED CHROMATOPHOROMA IN LEOPARD GECKOS

The Lemon Frost morph of the leopard gecko has been associated with a high frequency of iridophoroma

development [43]. Current evidence supports an association between SPINT1-related genetic alteration and pigment cell tumor predisposition in this morph [43]. This represents an important example of a morph-specific tumor phenotype in reptile oncology [41].

SPINT1 is involved in epithelial and cellular regulatory processes in other species, and studies in mammalian or fish models may provide comparative biological context. However, molecular pathways such as SPINT1-AS1 regulation [44], HGF/c-Met signaling, receptor tyrosine kinase activity [45], and melanoma-associated prognostic mechanisms should not be presented as established reptile mechanisms unless directly demonstrated in reptile studies [46].

Overall, SPINT1-associated chromatophoroma in Lemon Frost leopard geckos should be interpreted as a valuable morph-specific observation and a potential comparative model for pigment cell tumor biology [41]. At present, however, available evidence does not support the use of SPINT1-related pathways as validated prognostic or therapeutic targets in reptile oncology [30, 47]. Further studies are needed to clarify the molecular mechanisms, diagnostic value, and clinical significance of SPINT1-associated tumorigenesis in reptiles.

7. DISCUSSION

Reptile oncology remains an emerging field with important diagnostic and therapeutic challenges. Current evidence is limited by small sample sizes, species diversity, incomplete follow-up, and the frequent use of diagnostic criteria adapted from mammalian medicine. These limitations are particularly relevant for pigment cell tumors, where terminology, classification, immunohistochemical interpretation, and prognostic assessment may vary among reports.

For clinicians, early recognition of suspicious lesions, appropriate biopsy, histopathological confirmation, and metastasis screening are central to case management. Surgical excision remains the mainstay of treatment for localized tumors, but adjunctive therapies may be considered in selected cases [24]. Because standardized treatment protocols are lacking, each case should be managed according to tumor behavior, anatomical site, patient condition, and available evidence.

For researchers, chromatophoromas in leopard geckos provide a useful model for studying pigment cell biology and morph-associated tumor predisposition [41]. However, future studies should prioritize reptile-specific validation of molecular markers, diagnostic criteria, treatment outcomes, and prognostic indicators. Studies in other tumor systems also illustrate how molecular biomarkers may be evaluated for tumor proliferation, invasion, and prognosis, but comparable reptile-specific biomarker frameworks remain lacking [48].

8. CONCLUSIONS

Reptile tumors are increasingly recognized in clinical practice, but current knowledge remains limited and uneven across species. Diagnosis should rely on integrated clinical assessment, imaging, histopathology, and selected immunohistochemical markers. For pigmented or raised skin lesions, differential diagnosis is essential because inflammatory, infectious, cystic, and other neoplastic lesions may mimic chromatophoromas.

Surgical excision remains the primary treatment for localized reptile tumors, while non-surgical therapies should be interpreted cautiously due to limited evidence. SPINT1-associated chromatophoroma in Lemon Frost leopard geckos represents an important morph-specific observation and may support future studies in reptile comparative oncology. Further reptile-focused research is needed to improve diagnostic accuracy, therapeutic decision-making, and prognostic assessment.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this paper.

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