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Navigating the Diagnostic Labyrinth: A Narrative Review of Atypical Pelvic Pain Syndromes at the Intersection of Gynecologic Oncology, Chronic Infection, and Odontogenic Referred Pain

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Abstract

Background: Atypical pelvic pain presents a profound diagnostic challenge, often masking serious underlying pathology across disparate anatomical systems. The convergence of gynecologic malignancies, chronic pelvic inflammatory disease (PID), and referred pain from advanced odontogenic infections creates a clinical triad requiring sophisticated multidisciplinary differentiation.

Aim: This narrative review synthesizes current evidence to construct an integrated diagnostic pathway for atypical pelvic pain, emphasizing the collaborative roles of gynecologic oncology, infectious diseases, internal medicine, dentistry, radiology, laboratory medicine, nursing, and administrative support.

Methods: A comprehensive search of PubMed, Scopus, CINAHL, and Cochrane databases was conducted for English-language articles published between 2010 and 2024. Search terms included "pelvic pain differential diagnosis," "gynecologic cancer masquerade," "chronic pelvic inflammatory disease," "odontogenic referred pain," "multidisciplinary pain assessment," combined with specific disciplines.

Results: The review delineates distinct yet overlapping clinical presentations, biomarker profiles, and imaging findings for ovarian/endometrial malignancies, chronic PID, and maxillofacial pain referral. Key discriminators include nuanced symptom patterns (cyclic vs. constant, positional relationships), inflammatory markers (CA-125, CRP, PVL), and cross-sectional imaging characteristics.

Conclusion: Atypical pelvic pain demands a paradigm shift from sequential specialty consultation to synchronous, coordinated multidisciplinary evaluation. Implementing structured diagnostic algorithms with clear referral triggers can reduce time-to-diagnosis, optimize resource use, and improve patient outcomes. Future directions include developing integrated clinics and shared decision-support tools.

Keywords: chronic pelvic pain, diagnostic odyssey, multidisciplinary diagnosis, gynecologic cancer, odontogenic pain.

Introduction

Pelvic pain represents one of the most common yet diagnostically formidable presentations in clinical medicine, accounting for approximately 10% of outpatient gynecology visits and a significant portion of chronic pain referrals (Ahangari, 2014). While often attributed to benign gynecologic or musculoskeletal causes, a subset of patients present with atypical pelvic pain—pain that is persistent, refractory to initial treatments, and accompanied by unusual symptom constellations that defy straightforward categorization. Within this

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challenging subset lies a critical diagnostic triad: occult gynecologic malignancies, chronic pelvic inflammatory disease (PID), and referred pain from advanced odontogenic infections. These conditions, originating from embryologically distinct but neurologically interconnected regions, can produce remarkably similar pain patterns, creating a perfect storm for diagnostic error and delay (Bittelbrunn et al., 2023).

The consequences of misdiagnosis are substantial. For gynecologic cancers, particularly ovarian and endometrial malignancies, diagnostic delay remains a primary contributor to advanced-stage presentation and associated mortality (Mahoney & Pierce, 2022). Chronic PID, often a sequela of inadequately treated acute infection, leads to persistent inflammation, tubal damage, infertility, and chronic pain syndromes that are both debilitating and challenging to treat (Paavonen et al., 2021). Perhaps most counterintuitive is the phenomenon of odontogenic referred pain, where infections or pathology in the maxillofacial region refer pain along the trigeminal nerve and its cervical connections to the lower abdomen and pelvis, a phenomenon supported by convergent nociceptive pathways in the spinal cord dorsal horn (Šedý et al., 2022). This referral pattern is frequently overlooked, leading to extensive, negative gynecologic and gastroenterological workups.

Traditional diagnostic approaches, characterized by sequential referrals from primary care to gynecology to gastroenterology, are fundamentally inadequate for this complex differential (Comelli et al., 2023). They operate on a "ruling out" paradigm within specialty silos, wasting time and resources while the patient's condition potentially progresses. This review argues for a synchronous, integrated diagnostic model led by internal medicine as the coordinating discipline, actively engaging gynecologic oncology, infectious disease, dentistry, radiology, laboratory medicine, nursing, and administrative support from the outset. By synthesizing literature from 2010 to 2024, this narrative review will: 1) delineate the clinical, biomarker, and imaging profiles of each condition; 2) analyze the neuroanatomical basis for pain referral; 3) map a collaborative diagnostic algorithm; and 4) define the essential roles of each team member in navigating this diagnostic labyrinth to achieve accurate, timely diagnosis and appropriate management.

Deciphering the Pain Language

The first step in differentiation lies in meticulous history-taking that transcends organ-specific questioning to capture the nuanced "language" of the pain. While overlap exists, distinctive patterns can guide the diagnostic trajectory.

Gynecologic Malignancies

Pain from ovarian or endometrial cancer is often insidious. It may present as a constant, dull, deep pelvic ache or pressure, frequently described as a "bloating" sensation that is worse after meals (Funston et al., 2020). Positional relationships are key: pain exacerbated by specific movements or positions (e.g., bending, intercourse) may suggest a fixed pelvic mass. Associated "red flag" symptoms include abnormal uterine bleeding (particularly postmenopausal), rapid satiety, unexplained weight loss, and changes in bowel or bladder habits. Pain is typically non-cyclic but may be perceived as such if it fluctuates in intensity. A family history of breast, ovarian, or colorectal cancer significantly elevates suspicion (Watanabe et al., 2022).

Chronic Pelvic Inflammatory Disease

Pain from chronic PID is often described as a bilateral, chronic ache, frequently exacerbated during or after menstruation and coitus. It is commonly accompanied by a history of acute PID episodes (although up to 70% may be subclinical), sexually transmitted infections, or invasive gynecologic procedures (Mitchell & Prabhu, 2013). Patients may report persistent vaginal discharge, dyspareunia, and low-grade fever. The pain is inflammatory in character—constant and aching—with potential acute exacerbations. A critical differentiating factor is the temporal link to menstrual cycles and sexual activity, and the presence of mucopurulent cervical discharge on examination (Brunham et al., 2015).

Odontogenic Referred Pain

This is the great masquerader. Pain typically originates from chronic apical periodontitis, impacted third molars, or osteomyelitis of the jaw. The referred pelvic pain is often unilateral, deep, and poorly localized. Patients may describe a constant, burning, or aching sensation in the lower abdomen or pelvis without clear gynecologic or gastrointestinal triggers (Shinoda et al., 2021). Crucial clues include a concurrent or recent history of ipsilateral toothache, facial pain, earache, or temporal headache. The patient may have undergone extensive dental work or have known untreated caries. Pain may be exacerbated by chewing or changes in head position, a finding seldom sought in pelvic pain evaluations (Lavigne & Sessle, 2016). The lack of pelvic organ-related symptom triggers is a pivotal negative finding (Table 1). Figure 1 illustrates a parallel, multidisciplinary diagnostic algorithm for patients presenting with atypical pelvic pain. Initial assessment incorporates comprehensive history-taking, pelvic examination, inflammatory and tumor biomarkers (e.g., CRP, CA-125), and multimodal imaging.

Table 1: Clinical Differentiation of Atypical Pelvic Pain Syndromes

Clinical Feature	Gynecologic Malignancy	Chronic Pelvic Inflammatory Disease	Odontogenic Referred Pain

Pain Quality	Dull ache, pressure, "bloating," constant.	Bilateral ache, cramping, inflammatory.	Deep, burning, aching; poorly localized.
Key Aggravating Factors	Position (bending), meals, intercourse.	Menstruation, sexual intercourse.	Chewing, head movement, stress.
Associated Symptoms	Abnormal uterine bleeding, early satiety, weight change, urinary/bowel changes.	Chronic discharge, dyspareunia, infertility, low-grade fever.	Tooth sensitivity, facial/ear pain, temporal headache, jaw stiffness.
Temporal Pattern	Progressive, constant.	Cyclic exacerbation, history of acute PID or STI.	Constant with fluctuations; may correlate with dental disease activity.
Critical History Element	Family history of BRCA-related cancers.	History of STI, multiple partners, prior PID, IUD use.	Recent dental work, untreated caries, poor oral health.
Physical Exam Findings	Palpable adnexal/uterine mass, nodularity in cul-de-sac.	Cervical motion tenderness, uterine/adnexal tenderness, mucopurulent discharge.	Dental caries, percussion-sensitive tooth, sinus tract, jaw swelling.

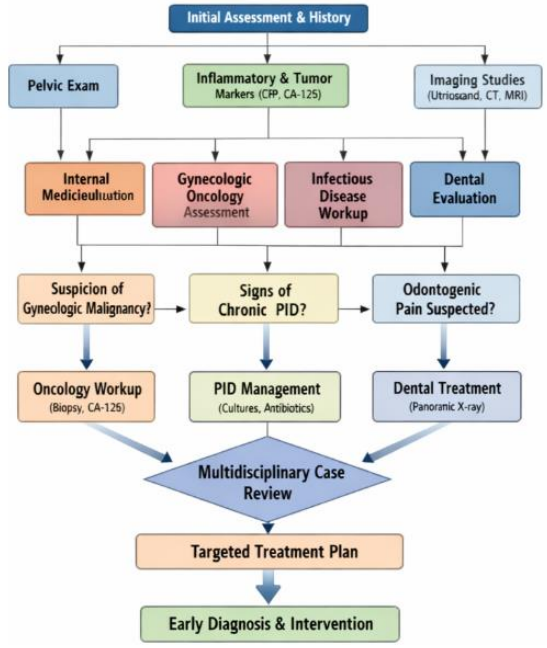

Figure 1. Integrated Multidisciplinary Diagnostic Pathway for Atypical Pelvic Pain

The Diagnostic Arsenal of Biomarkers, Imaging, and Specialized Tests

Once clinical suspicion is raised, a coordinated investigative strategy leveraging laboratory and imaging expertise is paramount.

Clinical Laboratory Medicine

The laboratory provides the first objective discriminators. For gynecologic oncology, serum CA-125 remains the cornerstone biomarker for epithelial ovarian cancer, though it is nonspecific and elevated in numerous benign conditions, including endometriosis and PID (Grossman et al., 2018). HE4, used in the ROMA algorithm, offers better specificity, especially in premenopausal women (Moore et al., 2019). For endometrial cancer, no reliable serum biomarker exists, though CA-125 may be elevated in advanced disease. In contrast, chronic PID evaluation relies on markers of persistent inflammation: a persistent elevation of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) is common. Microscopy of cervical discharge showing >10 polymorphonuclear leukocytes per high-power field supports infection, while NAAT testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* is essential, even in chronic stages (Workowski & Bachmann, 2022). For odontogenic sources, there are no specific serum markers, but a panoramic radiograph (panorex) or cone-beam CT ordered by dentistry is the definitive test.

Diagnostic and Interventional Radiology

Imaging is the spatial roadmap. Transvaginal ultrasound (TVUS) is the first-line modality for gynecologic structures, identifying ovarian morphology, solid components, and vascularity suggestive of malignancy (Sayasneh et al., 2016). For chronic PID, ultrasound may show hydrosalpinx, pyosalpinx, or tubo-ovarian complex. However, cross-sectional imaging is often required. Pelvic MRI excels in characterizing indeterminate adnexal masses, detecting myometrial invasion in endometrial cancer, and identifying deep infiltrating endometriosis that can mimic chronic PID (Thomassin-Naggara et al., 2020). CT of the abdomen and pelvis is superior for detecting lymphadenopathy, omental caking, and upper abdominal disease in ovarian cancer, and can also identify complicated appendicitis or diverticulitis. Critically, when odontogenic referral is suspected, imaging must extend cephalad. A panoramic radiograph or cone-beam CT of the jaws, interpreted by a dentist or oral radiologist, can reveal periapical radiolucencies, impacted teeth, or bony erosions confirming a dental source (Farman & Scarfe, 2018).

The Role of Endoscopy and Biopsy

When imaging is equivocal, direct visualization and histopathology provide the answer. Diagnostic laparoscopy allows direct inspection of the pelvis, peritoneal surfaces, and biopsy of suspicious

lesions. It is the gold standard for diagnosing peritoneal tuberculosis or disseminated carcinomatosis (Agarwal & Lim, 2019). For endometrial assessment, hysteroscopy with biopsy is definitive. In the dental realm, periapical testing (cold, electric pulp testing) of suspect teeth by an endodontist can confirm pulpal necrosis, the most common source of referred pain.

Neuroanatomical Basis of Referred Pain: The Convergence-Projection Theory

Understanding why a toothache can manifest as pelvic pain is fundamental to accepting this diagnostic possibility. The phenomenon is explained by the convergence-projection theory. Afferent pain fibers from visceral structures (e.g., uterus, ovaries) and somatic structures (e.g., teeth, facial skin) converge on the same second-order neurons in the dorsal horn of the spinal cord and trigeminal nucleus (Sessle, 2021). The brain, having more experience localizing somatic pain, misinterprets the visceral input as originating from the somatic region.

The trigeminal nerve (cranial nerve V), which innervates the teeth and face, has extensive connections with the upper cervical spinal nerves (C1-C3) via the trigeminocervical nucleus. These cervical connections, in turn, synapse with neurons receiving input from thoracic and lumbar dermatomes, including those supplying the pelvis (Baron et al., 2013). This creates a neurological bridge allowing nociceptive signals from maxillofacial structures to be perceived in distant pelvic regions. This pathway underscores why a comprehensive review of systems must include craniofacial and dental health in any unexplained chronic pelvic pain evaluation. Figure 2 demonstrates the convergence–projection mechanism underlying referred pelvic pain originating from odontogenic pathology.

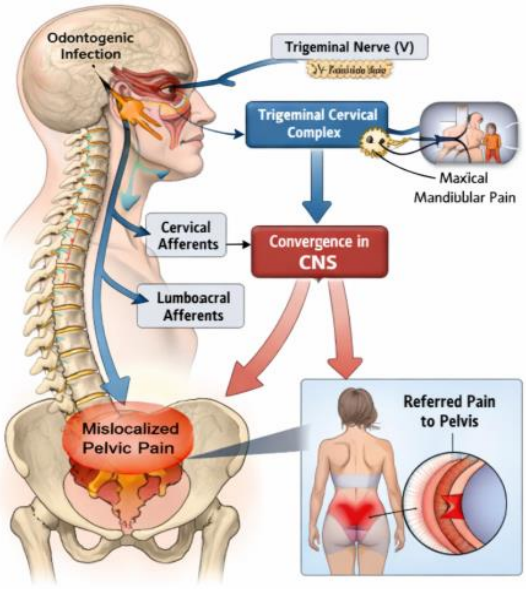

Figure 2. Neuroanatomical Mechanism of Odontogenic Referred Pelvic Pain

The Integrated Diagnostic Pathway

An effective diagnostic strategy for atypical pelvic pain necessitates a fundamental departure from traditional linear referral models. Instead of a sequential process where one specialty "rules out" its domain before passing the patient to the next, a coordinated, parallel investigation must be initiated from the outset. This paradigm shift positions the primary care provider—typically in internal medicine or general practice—as the essential diagnostic quarterback. This clinician assumes responsibility for maintaining a broad differential, orchestrating simultaneous evaluations, and integrating disparate data streams into a coherent diagnostic picture. This role is critical to prevent premature diagnostic closure within a single specialty silo and to ensure all potential etiologies are pursued with appropriate urgency (Agrawal & Kolli, 2019).

The pathway begins with the comprehensive initial assessment, jointly led by the primary care physician and the nurse. The physician conducts a holistic history that explicitly explores gynecologic, infectious, *and* dental domains, actively seeking red flags for malignancy, chronic infection, and craniofacial pathology (Caetano et al., 2022). Concurrently, nursing performs a detailed assessment of the multidimensional pain experience, including its characteristics, impact on function, and associated psychosocial burden. Based on this evaluation, simultaneous diagnostic orders are generated to expedite the workup. These typically include (1) pelvic imaging (transvaginal ultrasound) and initial laboratory studies (complete blood count, inflammatory markers like C-reactive protein, and tumor markers such as CA-125/HE4 if clinically indicated), and (2) a panoramic dental radiograph if any historical clues (e.g., unexplained facial pain, poor oral health) or risk factors are present. The medical secretary or care coordinator is instrumental in this phase, scheduling these disparate appointments to occur in close temporal proximity, thereby compressing the diagnostic timeline and reducing patient anxiety (Silow-Carroll et al., 2012; Almutairi et al., 2024).

Parallel specialty consultation is activated based on the initial findings. Rather than waiting for one consultant's conclusion, referrals are made concurrently to the relevant specialties based on specific triggers (Goldthorpe et al., 2018). A consultation with a gynecologic oncologist is prompted by an abnormal pelvic exam, a significant family history of relevant cancers, suspicious ultrasound findings (e.g., a complex ovarian mass or thickened endometrium), or elevated tumor markers. An infectious disease or specialized gynecology consult is triggered by signs of persistent inflammation, such as elevated inflammatory markers, mucopurulent cervical discharge, or a compelling history of sexually transmitted infection or prior pelvic

inflammatory disease (Shroff, 2023). A dental or orofacial pain consult—with an endodontist or oral medicine specialist familiar with pain referral patterns—is initiated either by positive findings on the panoramic radiograph, strong historical clues, or as a deliberate "rule-out" in cases where the medical workup remains negative. This parallel approach ensures that all diagnostic avenues are explored without delay (Erdogan et al., 2022).

For patients who remain undiagnosed after initial parallel consultations, a multidisciplinary case conference and definitive testing are convened. This formal multidisciplinary team (MDT) meeting brings together the primary care internist, gynecologic oncologist, infectious disease specialist, consulting dentist or oral surgeon, radiologist, and often a pathologist. All available data—clinical history, imaging, and laboratory results—are reviewed collectively. The combined expertise of the group allows for a nuanced discussion of the likeliest diagnosis and the most appropriate, highest-yield definitive test (Stewart et al., 2019). A consensus decision is reached on whether to proceed with procedures such as diagnostic laparoscopy with biopsy, hysteroscopy with endometrial biopsy, or advanced endodontic testing and possible apical surgery. The nursing team plays a vital role in this phase, coordinating patient education, managing expectations, and preparing the patient for the agreed-upon invasive diagnostic procedure (Luther et al., 2019).

Finally, diagnosis, treatment initiation, and follow-up coordination commence once a definitive diagnosis is established. The relevant specialist (e.g., the oncologist, infectious disease expert, or oral surgeon) assumes lead responsibility for disease-specific treatment. However, the coordinating role of the primary care physician and the nurse does not end (Parker et al., 2020). They remain pivotal in managing comorbid conditions, ensuring smooth transitions between treatments—such as coordinating a course of antibiotic therapy for chronic pelvic inflammatory disease before planned cancer surgery—and providing continuous patient advocacy. The medical secretary or administrator continues to be essential, managing the complex scheduling of multidisciplinary follow-up appointments, surveillance tests, and ongoing care coordination (Pradeep et al., 2023). This integrated four-phase pathway, from initial suspicion through to resolution and follow-up, represents a systematic, patient-centered framework designed to dismantle the diagnostic odyssey and deliver timely, accurate care (Table 2).

Table 2: The Multidisciplinary Team (MDT) Roles in Atypical Pelvic Pain Diagnosis

Team Member	Primary Diagnostic Role	Key Collaborative Actions	Critical Contribution
Internal Medicine	Diagnostic quarterback; holistic history; initial test selection; comorbidity management.	Convenes MDT; integrates data from all specialties; refers in parallel.	Maintains broad differential; prevents premature closure.
Clinical Nursing	Comprehensive pain/symptom assessment; psychosocial evaluation; patient education.	Acts as patient advocate; communicates patient-reported outcomes to team; coordinates care transitions.	Provides nuanced pain characterization; identifies functional impact.
Gynecologic Oncology	Expert pelvic exam; interpretation of gynecologic imaging; surgical diagnosis & management.	Provides risk assessment based on family history/exam; performs diagnostic laparoscopy/hysterectomy.	Differentiates benign from malignant masses; provides definitive surgical diagnosis.
Infectious Disease	Interpretation of infectious markers; management of chronic/atypical PID; STI expertise.	Guides antibiotic selection for chronic infection; rules out TB or actinomycosis.	Identifies subtle signs of chronic infection; manages complex antibiotic regimens.
Dentistry (Endodontist/Oral Surgeon)	Comprehensive dental/orofacial exam; interpretation of dental imaging; periapical testing.	Rules in/out odontogenic source; performs definitive dental treatment.	Solves the "masquerade" diagnosis; prevents unnecessary medical/surgical interventions.

Radiology	Performance & interpretation of ultrasound, CT, MRI, panoramic radiographs.	Provides specific imaging protocols for each suspicion; participates in MDT review.	Identifies characteristic findings across anatomical domains; suggests next imaging step.
Clinical Laboratory	Analysis of tumor markers (CA-125, HE4), inflammatory markers (CRP, ESR), microbiology.	Provides rapid turnaround and clinical correlation for biomarker results.	Supplies objective data to differentiate inflammatory vs. neoplastic processes.
Medical Secretary/Administrator	Coordinates multi-specialty appointments, imaging, and MDT scheduling.	Ensures minimal delay between consultations and tests; manages patient communication loop.	Enables the parallel workup model; reduces system-based diagnostic delay.

Challenges and Barriers to Implementation

Despite its logic, this integrated model faces significant barriers. Specialty silos and territoriality can hinder open collaboration and data sharing. Reimbursement structures often do not support parallel consultations or MDT meetings without an established diagnosis. There is a profound knowledge gap among medical professionals regarding odontogenic referred pain, often dismissed as improbable. Access to dental consultants within a medical framework is limited, and dental insurance is typically separate from medical insurance, creating financial barriers for patients. Furthermore, the time-intensive nature of coordinating multiple specialists can be daunting in busy clinical settings without dedicated administrative support.

Future Directions and Conclusion

To overcome these barriers, healthcare systems must innovate. The establishment of "Undiagnosed Pelvic Pain" clinics with embedded internists, gynecologists, and teleconsultation access to dentistry and infectious disease would provide a structural solution (Troncon et al., 2023). Integrated electronic health records that allow easy sharing of imaging and lab results across medical and dental domains are essential. Professional education must include cross-disciplinary training on pain referral patterns in medical, nursing, and dental curricula.

Developing and validating a standardized diagnostic algorithm—similar to those for chest pain or acute abdominal pain—for chronic pelvic pain could guide primary care providers. This algorithm would explicitly include dental imaging as a branch point. Research should focus on prospectively evaluating the yield and cost-effectiveness of this parallel, integrated approach compared to traditional sequential referral.

In conclusion, atypical pelvic pain at the intersection of oncology, chronic infection, and odontogenic referral represents a classic example of a problem that no single specialty can solve alone. The convergent neuroanatomy of pain demands a corresponding convergence of clinical expertise. By moving from a sequential, exclusionary model to a synchronous, integrative one—led by internal medicine and actively involving laboratory, radiology, nursing, administrative, gynecologic, infectious disease, and dental specialists—we can dismantle the diagnostic labyrinth. This approach promises to shorten the diagnostic odyssey, reduce patient suffering, allocate resources more efficiently, and ultimately, improve outcomes for this challenging patient population. The pelvic pain may be atypical, but our diagnostic approach must become systematically routine.

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