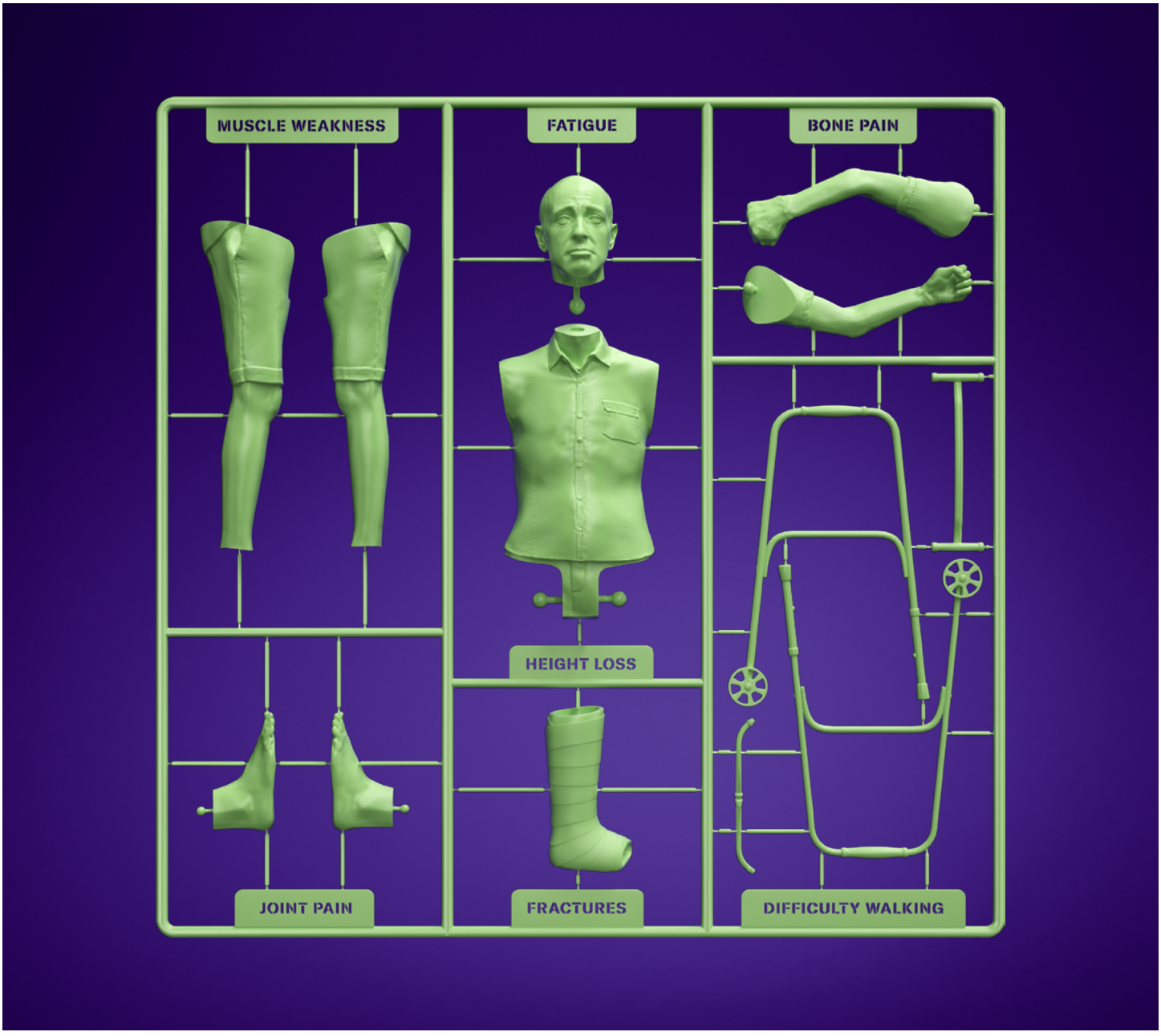
Connect the symptoms.

Is it tumor-induced osteomalacia (TIO)?

Learn about this underdiagnosed condition and how to help identify it[1-3]



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TIO: an underdiagnosed condition[1-3]

TIO is an acquired form of hypophosphatemia typically caused by benign phosphaturic mesenchymal tumors that produce excess fibroblast growth factor 23 (FGF23) hormone.[2,4] These tumors are[4]:

- Typically small and difficult to locate
- Located anywhere in the body–including within soft tissue and bone

FGF23 and TIO

Excess tumor-produced FGF23 in TIO disrupts phosphorus homeostasis, leading to renal phosphorus wasting and impaired active vitamin D (1,25[OH]$_2$D) synthesis, which ultimately results in chronic hypophosphatemia.[1,2]

Symptoms of TIO

Patients with TIO may experience various symptoms of osteomalacia and hypophosphatemia, including[2,4,5]:

Progressive musculoskeletal pain

Bone fractures that can lead to disability

Muscle weakness and loss of muscle mass

Fatigue

Gait abnormalities and difficulty walking

Height loss

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Common locations of TIO-causing tumors as seen in a review of 895 patient cases[6,a]:

Head/neck
25.7%

Upper limbs
6.9%

Trunk
9.7%

Pelvis
10.3%

Lower limbs
46.4%

Surgical removal of tumors that cause TIO can be curative. However, if tumors are unable to be localized or resected, the symptoms of TIO can continue to cause pain and weakness, impacting a patient's ability to move.[1]

[a]In a systematic clinical review of published cases that considered 5 regions for tumor localization.[6]

Actor portrayal

Symptoms of TIO are nonspecific, which may lead to misdiagnosis[4]

In a retrospective study, 95% (137/144) of patients were initially misdiagnosed[3]

Time from symptom onset to diagnosis can range from approximately 1 month to 42 years[6]

Delay in diagnosis can lead to physical deterioration, which may contribute to psychological impairment and depression.[7,8] In some cases, TIO symptoms may even be considered psychosomatic in the context of mental health conditions such as anxiety and depression.[9]

Actor portrayal

Other conditions that TIO is commonly misdiagnosed as include[3,10]:

- Intervertebral disc herniation
- Spondyloarthritis (including ankylosing spondylitis)
- Osteoporosis
- Rheumatoid arthritis
- Arthritis
- Bone metastases
- Connective tissue diseases
- Osteoarthritis
- Fibromyalgia syndrome
- Neuropsychiatric diseases

Due to the progressive nature of TIO, a delay in diagnosis and appropriate management may lead to severe osteomalacia and, ultimately, irreversible disability. Early intervention is critical to minimize the disease burden.[5]

Diagnosing TIO

Identifying TIO can involve assessing[1]:

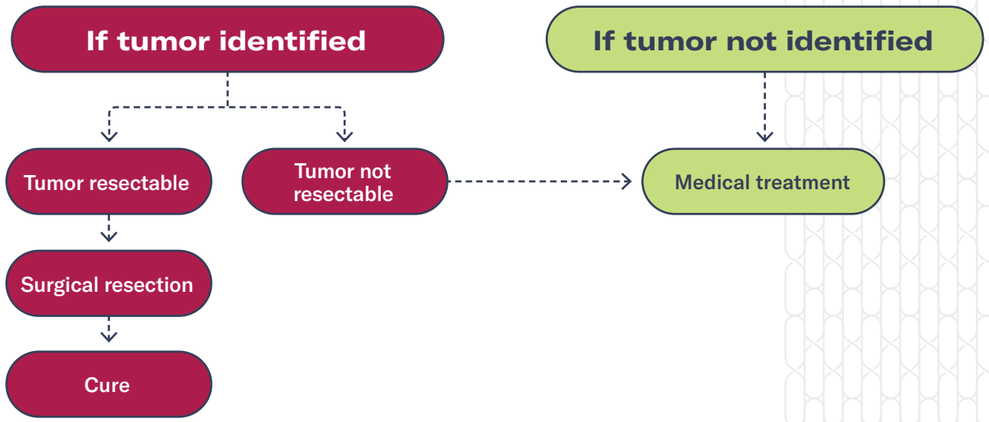
- Symptoms
- Family history
- Clinical signs
- Biochemical tests
- Genetic testing
- Functional and anatomical imaging

TIO is an underdiagnosed disease, with only approximately 1000 cases reported worldwide. Challenges in diagnosis and limited studies may hinder recognition of the disease.[2,3]

The diagnostic process for TIO[1]

Patient presenting with generalized musculoskeletal pain, muscle weakness, multiple fractures, and fatigue or palpable, localized mass

- Family and medical history, as well as physical examination
- Measure fasting serum phosphorus
- Biochemical workup, with or without genetic testing
- If clinical and biochemical suspicion of TIO, refer to a specialist center
- Functional and anatomical imaging



Biochemical findings in TIO[1]

Laboratory Test	TIO	Reference ranges (adults)[b]
Fasting serum phosphorus	↓ Down	2.5-4.5 mg/dL
Alkaline phosphatase	↑ Up	**Male:** 45-125 U/L **Female:** 35-100 U/L
$1,25(OH)_2D$	↓ Down or inappropriately normal	19.6-54.3 pg/mL
Intact FGF23[c]	↑ Up or inappropriately normal	11.7-48.6 pg/mL
Serum calcium	↓ Slightly down or normal	8.6-10.2 mg/dL
PTH	↑ Up or normal	12.0-65.0 pg/mL

PTH=parathyroid hormone.
[b]Reference ranges can vary based on laboratory, instrument used, and method of assessment; reference ranges for pediatric patients can differ from those of adult patients.[1]
[c]Results are assay-dependent.[1]

Genetic testing for mutations associated with hypophosphatemia can help exclude a diagnosis of genetic forms of FGF23-mediated phosphorus wasting disorders. Once TIO is biochemically confirmed, specialized imaging can help locate the tumor(s) prior to surgery.[1]

Kyowa Kirin, Inc. offers sponsored, no-charge genetic and FGF23 testing to patients who are being evaluated for a possible diagnosis of TIO.

Managing TIO

Complete surgical removal of tumors that cause TIO can be curative.[2]

Under certain conditions, tumors may not be localized or resectable. In such cases, medication is available to help patients manage TIO.[2]

With early diagnosis, you can help patients limit the progression of their TIO. Help them understand their condition and appropriate management options to improve their overall care.[5]

Suspect TIO?

Learn how genetic and FGF23 testing can help establish an accurate diagnosis for TIO[1]

Rule out genetic forms of hypophosphatemia[1]

Click here to learn about sponsored genetic testing[d]

Visit TIOLinkHCP.com to order an FGF23 testing kit

[d]See Terms of Use.

For questions regarding genetic testing or results, contact Invitae Client Services by emailing clientservices@invitae.com or calling 1-800-436-3037

For medical information and questions about the sponsored gene panel or the FGF23 test, contact Kyowa Kirin Medical Science Liaison (MSL) by emailing KyowaKirin-US@medinfodept.com

For help navigating diagnostic documentation required for payor coverage, contact Kyowa Kirin Cares by calling 1-833-552-2737 or visiting kyowakirincares.com

Terms of Use

Kyowa Kirin has partnered with Invitae Corp. and collaborated with Mayo Clinic Laboratories to offer sponsored, no-charge testing to patients who are being evaluated for a possible diagnosis of XLH or TIO. The Kyowa Kirin Sponsored Hypophosphatemia Program is intended to improve patient safety and quality of care by shortening the time to an accurate diagnosis, facilitate prompt confirmatory testing, and help patients with XLH and TIO meet payor coverage requirements. Use of or participation in the Kyowa Kirin Sponsored Hypophosphatemia Program does not create any obligation to use, prescribe, or recommend any Kyowa Kirin products or services. The Program is only available to patients that meet certain eligibility requirements and for whom the patient's health care provider has determined that testing is clinically appropriate. No patient or health care provider may seek reimbursement for testing or counseling services provided under the Kyowa Kirin Sponsored Hypophosphatemia Program from any third party, including but not limited to, any government health care programs.

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