Immunoglobulin G4-related disease (IgG4-RD)

Immunoglobulin G4-related disease (IgG4-RD) is a chronic, systemic, fibroinflammatory disorder that can affect virtually any organ. It is characterized histologically by a dense lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis.

Histopathological Features

- Dense lymphoplasmacytic infiltrate
- Storiform fibrosis
- Obliterative phlebitis
- IgG4+ plasma cells >10/high-power field (HPF)
- IgG4+/IgG+ cell ratio >40%

Frequently Involved Organs

- Pancreas → Autoimmune pancreatitis (type 1)
- Biliary tract → IgG4-related sclerosing cholangitis
- Salivary and lacrimal glands → Mikulicz's disease
- Retroperitoneum → Retroperitoneal fibrosis
- Kidneys → Tubulointerstitial nephritis
- Lungs → Inflammatory pseudotumor
- Orbit → IgG4-related ophthalmic disease
- CNS → Hypertrophic pachymeningitis

Clinical Features

- Painless swelling or mass-like lesions
- Organ dysfunction depending on site
- Constitutional symptoms (rare): weight loss, low-grade fever

Diagnosis

- Clinical suspicion based on organ involvement
- Imaging showing mass or enlargement
- Histopathology confirming IgG4-RD criteria
- Immunohistochemistry: IgG4+ plasma cells and IgG4+/IgG+ ratio
- Serum IgG4 levels (elevated in ~60–70%)

Treatment

- First-line: Glucocorticoids (e.g., prednisolone)
- Steroid-sparing agents: azathioprine, mycophenolate mofetil
- Refractory cases: Rituximab

Differential Diagnosis

- Lymphoma
- Sarcoidosis
- Granulomatosis with polyangiitis (Wegener)
- Infectious or neoplastic diseases

Case reports

Zeng et al. present a case report of a man in his 30s with IgG4-related ophthalmic disease (IgG4-ROD) and an orbital hemangioma, claiming extreme rarity of this co-occurrence [1)].

While interesting, the manuscript never explains why this coexistence matters pathophysiologically or therapeutically—other than as a curiosity. Without a rationale for clinical relevance, the reader is left wondering: so what?

 2. Diagnostic Flimsiness The diagnosis of IgG4-related disease—a notoriously tricky entity requiring a combination of histopathological, serological, and imaging criteria—is asserted without rigorous justification:

No detailed histopathological scoring (e.g., IgG4+/IgG+ plasma cell ratio).

No mention of serum IgG4 level thresholds or systemic involvement.

Vague description of fibrosis or phlebitis. → In essence: They label it IgG4-ROD without ticking the diagnostic boxes.

 3. Orbital Hemangioma = Red Herring The coexistence with an orbital hemangioma is presented as if it's a new syndrome. But:

Orbital hemangiomas are common vascular lesions.

There is no mechanistic link proposed between the two conditions.

No compelling imaging or immunohistochemistry tying both pathologies together.

It reads like a case of a guy with two things in the same place, not a true overlap syndrome.

 4. Therapeutic Vagueness They describe treatment with glucocorticoids (as per IgG4 disease protocols), but:

No response curve.

No discussion of tapering, resistance, or follow-up.

No exploration of whether the hemangioma itself required any intervention.

It ends up looking like a missed opportunity to inform on management nuances of these lesions in tandem.

 5. Formatting & Style Deficiencies The writing is uncritical and descriptive, lacking reflection.

References are outdated or scant.

Figures (if any) are not described in a way that adds value.

 Bottom Line This is a classic case report written for the sake of publishing a rare association—without analysis, insight, or educational depth. Its contribution to clinical practice is minimal, and its diagnostic reasoning is more decorative than robust.

Final diagnosis: Case report syndrome—benign but self-limiting

1)

Zeng H, Peng X, He W. Immunoglobulin G4-related ophthalmic disease with orbital deep hemangioma: A case report. J Int Med Res. 2025 Jun;53(6):3000605251345239. doi: 10.1177/03000605251345239. Epub 2025 Jun 10. PMID: 40494658.