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Treatment of gouty lumbar spinal stenosis: a case report and bioinformatics analysis

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Abstract

The case of Lumbar spinal stenosis (LSS) combined with tophi due to gout is rarely reported. In the course of our clinic work, we encountered a young male patient who was diagnosed with a history of gout for 5 years and was targeted as LSS combined with gouty tophi, and we would like to share this case. In addition, in order to further investigate the deep mechanism of LSS associated with gout, we obtained the intersecting genes of the two diseases based on a machine learning approach by obtaining the dataset GSE113212 related to LSS from the Gene Expression Omnibus (GEO) database, and the genes related to gout from the human gene database. We found that TGFB1, PPARG, and SAMRCC1 may be important biomarkers for treating of both diseases. From a clinical perspective, clinicians should be vigilant about the possibility of gouty lumbar spinal stenosis with tophi in young patients presenting with back pain, hyperuricemia, and elevated inflammatory markers. A combined surgical and pharmacological treatment plan has a favorable prognosis. Investigating the mechanisms of action of core genes may provide new insights for treatment, ultimately leading to the development of comprehensive and personalized diagnostic and therapeutic strategies.

Keywords Lumbar spinal stenosis, Gout, Gouty tophi, Data mining, Case report

Backgrounds

Gout is an inflammatory disease due to a disorder of purine metabolism and/or impaired excretion of uric acid, which results in the deposition of uric acid crystals [1]. Gouty tophi is mostly found in areas such as articular cartilage and periarticular tissues, and cause pain and other related symptoms. With the rapid development, gout prevalence is increasing yearly with the improvement of living standards [2]. Gouty tophi is most commonly found in the joints of the limbs, and over time, patients with advanced gout may develop persistent joint inflammation and peripheral tissue hyperplasia [3]. However, the development of gouty lumbar spinal stenosis is rarely reported, and the combination of intradermal gouty tophi is even rarer. Gouty lumbar spinal stenosis is difficult to diagnose and often requires intraoperative diagnosis and pathologic confirmation.

In recent years, as the rapid development of bioinformatics, the combination of proteomics, metabolomics, and biomarker analysis can provide valuable insights into disease diagnosis, prognosis, and therapeutic targets [4]. We admitted a young patient with gouty lumbar spinal stenosis combined with intracanalicular gouty tophi in 2023, who recovered well after surgical treatment. We retrospectively analyzed the case and analyzed the association of the two diseases, gout and lumbar spinal stenosis, from a bioinformatics perspective and suggested potential targets for treating both diseases simultaneously.

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Case presentation

A 26-year-old male patient presented with low back pain with intermittent claudication for 3 months. The patient's low back pain was intermittent and appeared when walking, and the number of feasible steps at the time of presentation was about 100 m. He had a 5-year history of previous gout and was taking oral febuxostat intermittently.

On examination, the patient was found to have positive percussion pain pressure and tenderness on both sides of the L4-5 spinous process and paravertebral region, and decreased skin sensation on the lateral side of the left thigh, the posterior lateral side of the left calf and the dorsum of the left foot. The straight leg raising test on the left lower limb was positive at 60°, and the Bragard's test was positive. The muscle strength of the left anterior tibialis muscle was grade IV. There were no obvious deformities in the limbs.

Lumbar spine X-ray showed: mild scoliosis of the lumbar spine; unevenly increased bone density in the L4-S1 appendages, narrowing and blurring of the intervertebral commissural space (Fig. 1a-b). Lumbar spine CT showed: narrowing of L1-5 lumbar facet joint space with erosion-like destruction (Fig. 1c). MRI enhancement of the lumbar spine showed: patchy abnormal signal on the left side of the spinal canal at the L4/5 level, and thickening and enhancement of the soft tissue in the accessory area at approximately the L4-S1 vertebral level (Fig. 1d-e). Laboratory tests included leukocytes 10.30×10^9/L, neutrophils 7.53×10^9/L, C-reactive protein 136 mg/L, erythrocyte sedimentation rate 41 mm/h, and blood uric acid 612 umol/L.

We performed L4-5 laminectomy decompression implant fusion internal fixation and gout stone cleaning. Intraoperatively, severe hyperplasia of the articular synovial joint was seen. After the laminectomy, an epidural white mass measuring about 3 cm*2 cm*2 cm was seen, which was tough and compressed the rural sac and the left nerve root of L5. The postoperative pathology report was the proliferation of fibrous tissue in the spinal

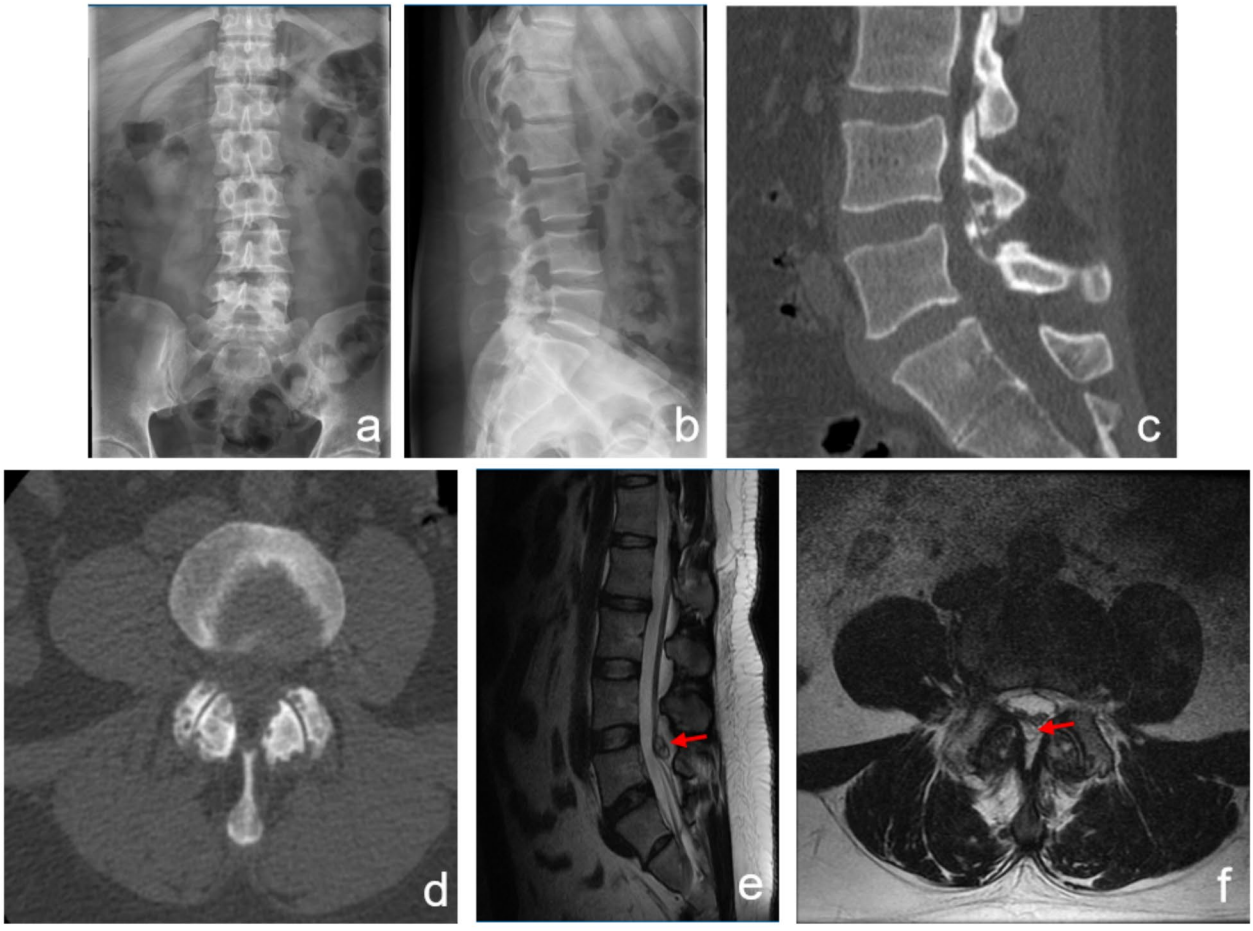


Fig. 1 The preoperative images showed lumbar joint stenosis, erosion and destruction, and significant compression of the gout stone at the L4/5 level of the spinal canal. **a**-**b**: lumbar spine joint stenosis with erosion and destruction. **c**-**d**: L1-5 small lumbar joint space narrowing with erosion-like destruction. **e**-**f**: left-sided patchy signal in the spinal canal at the L4/5 level with thickening of the surrounding tissue.The red arrow indicates gout

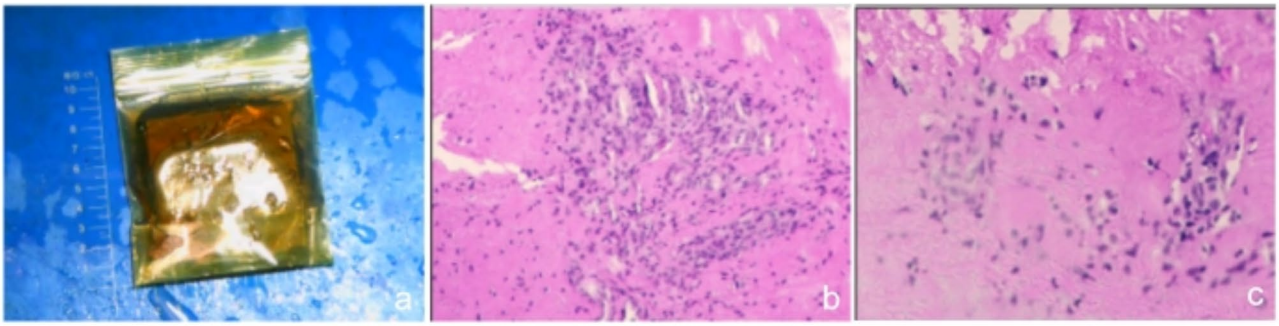


Fig. 2 Pathological findings: the vertebral mass was proliferating fibrous tissue, and the interstitial was seen to be infiltrated by a few lymphocytes and multinucleated giant cells

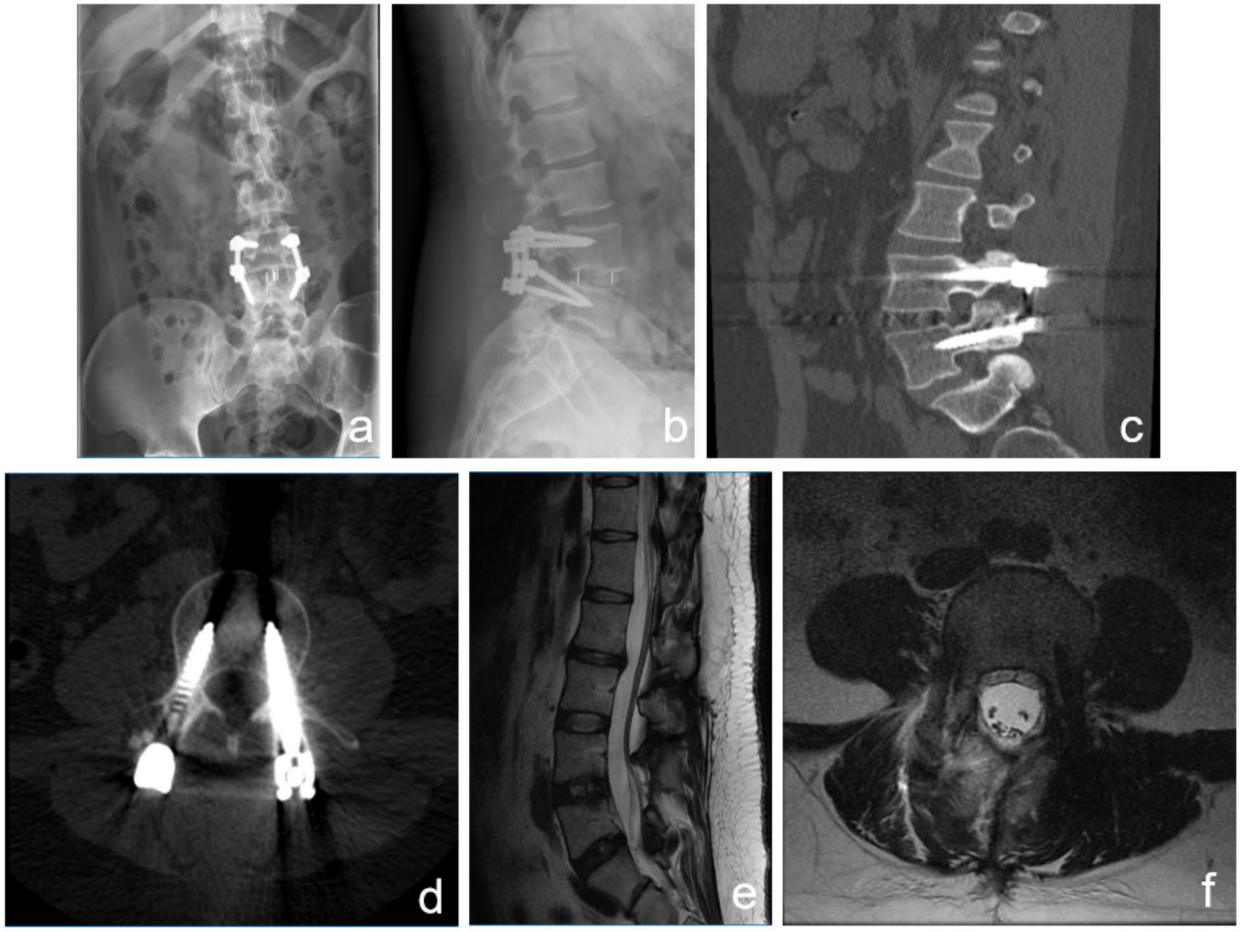


Fig. 3 Postoperative 3-month review results: **a**-**d**: lumbar spinal fusion and screw position are good; **e**-**f**: nerve compression is released and there was no recurrence of gout stone in the spinal canal

canal mass, and some lymphocytes and multinucleated giant cells' infiltration was seen in the interstitial, which showed an inflammatory reaction (Fig. 2). Postoperatively, the patient was given a low purine diet, antibiotics to prevent infection, glucocorticoid anti-inflammatory dehydration and other symptomatic treatment. After the operation, the patient's symptoms were significantly reduced, and the left side muscle strength was restored from grade IV to grade V. The patient was followed up for 3 months. After 3 months of follow-up, the symptoms completely disappeared. After reviewing the lumbar X-ray, CT and MRI, the surgical fusion was well fixed, and the gout stone did not recur (Fig. 3).

Bioinformatics mining

The major factor in lumbar spinal stenosis is the hypertrophy of the ligamentum flavum. To explore the link between the bioinformatics of the two diseases, lumbar spinal stenosis and gout, we obtained the dataset GSE113212 associated with ligamentum flavum from the Gene Expression Omnibus database (https://www.ncbi.nlm.nih.gov/). and searched for genes associated with ligamentum flavum from the Human Gene Database (https://www.genecards.org/) searched for gout-related genes with a score > 0.6. The two were taken to intersect and identify differentially expressed genes common to both diseases. We also performed GO gene ontology analysis, Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis, and gene set enrichment analysis, followed by a protein-protein interaction network constructed in the STRING database (https://cn.string-db.org/), to screen the genes with confidence > 0.9, and with disease genes obtained by LASSO to take the intersection and then finally obtained the key genes.

By intersecting and identifying the differential genes of the two diseases, 48 public differential genes were finally obtained (Fig. 4a-b), GO bioprocesses enriched in entries such as cell differentiation, cell proliferation, interleukin production, and RNAJIYI gene regulation; cellular composition (CC) enriched in entries such as regulation of the plasma membrane, RNA polymerase, and ATPase; and molecular function (MF) enriched in entries such as ligand receptor binding activity, cellular set factor activity and other entries (Fig. 4c-d). The shared targets were subjected to KEGG pathway enrichment analysis by R software, in which the top 30 pathways, the most significantly enriched pathways included the FoxO signaling pathway and the rheumatoid arthritis pathway (Fig. 4e). A Target-pathway analysis was performed on the FoxO signaling pathway, the rheumatoid arthritis

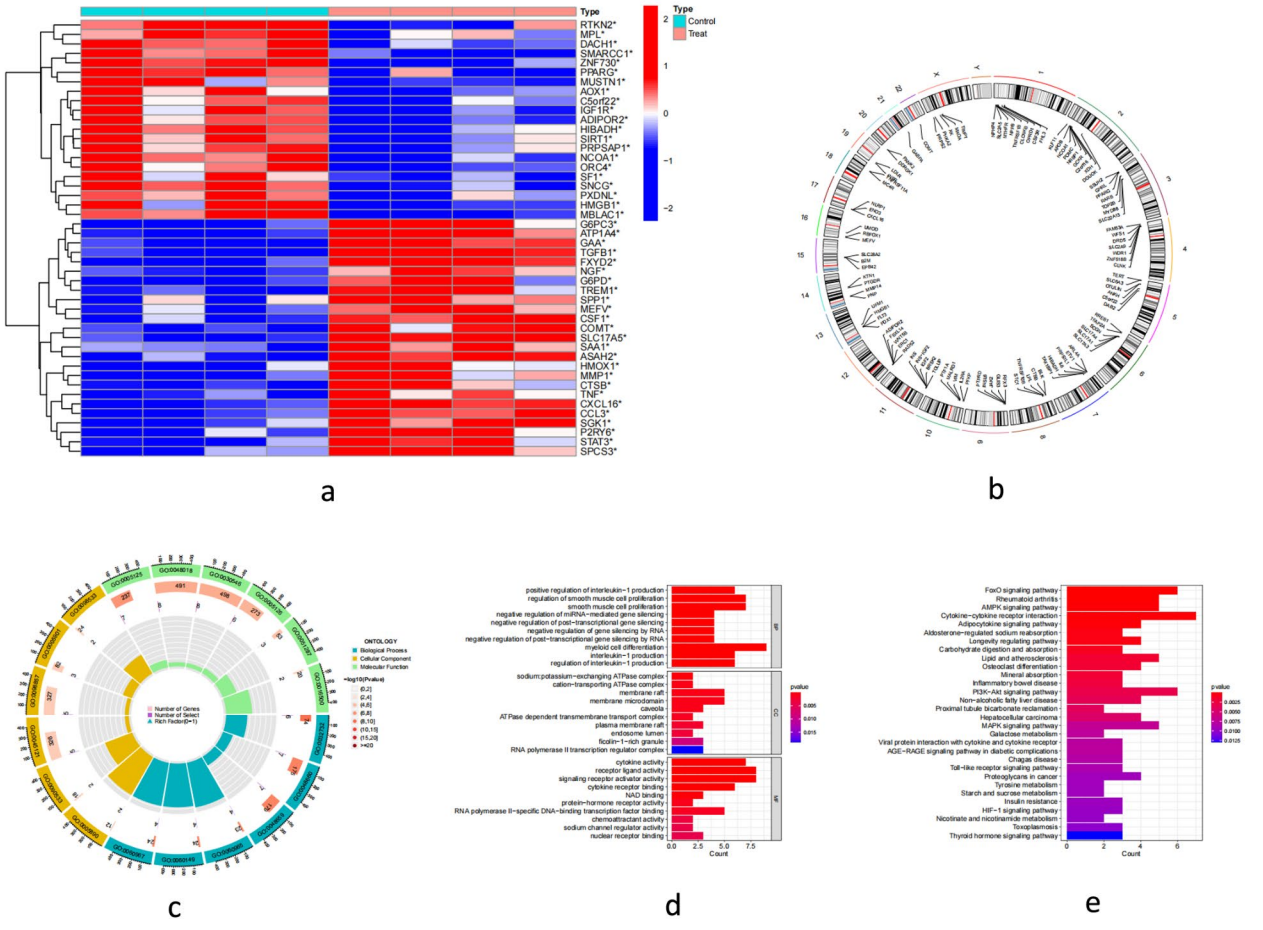


Fig. 4 **a**: heatmap of differential genes in gout-associated lumbar spinal stenosis; **b**: distribution of differential genes on human chromosomes; **c**-**d**: expression of molecular functions, cellular components, and biological processes in GO enrichment analysis (TOP 10); **e**: expression of KEGG pathway enrichment analysis (TOP 30); The numbers below represent the number of enriched genes as a percentage of the total number of entries, and the color corresponds to the color scale on the right side, representing the -Log10(P) value, the redder the color represents the higher degree of gene enrichment, the smaller the corresponding P value

pathway. (Fig. 5a-b). A total of 17 key genes with a confidence level of > 0.9 were screened by constructing a PPI network. 5 disease signature genes were obtained in the machine algorithm LASSO, and subsequently three key genes were finally obtained, namely, TGFB1, PPARG, and SAMRCC1. (Fig. 6). R and its related packages processed all of the aforementioned analyses. Thereby, we proposed a new strategy to treat two diseases simultaneously from the bioinformatics perspective.

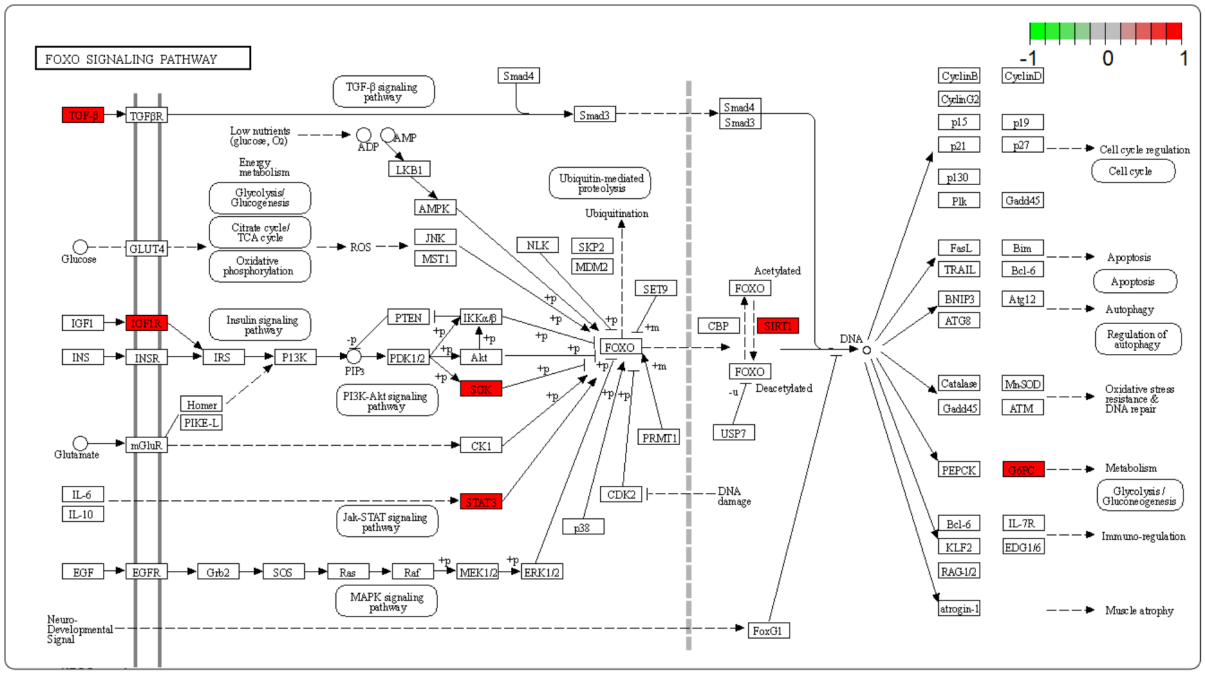
Discussion

Gout causes the deposition of urate crystals in the joints and surrounding structures, causing focal necrosis, periarticular granulation tissue proliferation and fibrosis to form gouty nodules. Gouty nodules rarely involve the spine, and the mechanism of spinal involvement has not yet been clarified, but an increase in blood uric acid is thought to increase the amount of uric acid in the cerebrospinal fluid, which can block the spinal canal or neural foramina [5]. We researched the incidence of sodium urate deposition in the spine and investigated whether gout or spinal urate deposition was associated with low back pain. The results found that gouty deposition of sodium urate was not significantly different between gouty patients and healthy individuals, but gouty patients had more back pain, which may be related to inflammation of the small joints of the lumbar spine [6]. Therefore, when gouty tophi in the lumbar spinal canal compress the nerves or spinal cord, low back pain and/or radiating pain to the lower extremities usually occurs. And as gout patients are getting younger, outpatient clinic encounters with young middle-aged patients with painful low back pain should be alert to the possibility of gout-induced pain and the need to differentiate it from herniated discs, infections, and tumors.

Patients with lumbar gout usually have a history of hyperuricemia or gout, as well as elevated markers of inflammation, such as elevated white blood cell counts, erythrocyte sedimentation rates, and C-reactive protein levels [7]. In this case, a 26-year-old male patient with low back pain and radiating pain to the left lower extremity had a history of gout, and his blood uric acid level, white blood cell count, and C-reactive protein level were all elevated. Therefore, when a patient with low back pain has a history of gout and elevated inflammatory markers, the possibility of spinal gout should be considered, even if the patient is young.

Early diagnosis of spinal gout is usually not possible due to atypical imaging manifestations on X-ray, CT, and MRI in patients with spinal gout.X-rays tend to be nonspecific, such as lumbar spine degeneration, osteophytes, and later, erosive bony changes can occur [8]. During CT examination, intra-articular and intrabony Gouty tophi of the spine can be scanned. Gouty tophi appear as medium- or high-density, irregularly shaped soft-tissue-like masses, and other manifestations include well-defined marginal sclerosis around the periphery of the bone [9]. MRI reveals that gouty tophi usually shows moderate or low signal at T1WI and either low or high signal changes at T2WI. Studies have shown that the reason for the low signal of Gouty tophi at T2WI may be related to the calcification of gouty tophi [10]. On enhanced scanning MRI, there may be homogeneous or heterogeneous enhancement signals around the gouty tophi [11]. In the case of this article, due to the destruction of vertebral bone and the increased density of the gouty tophi, the examination of plain CT or MRI can be easily confused with infection and human tumors, which in turn makes it difficult to make a definitive diagnosis of intraspinal gouty tophi. In recent years, dual-energy computed tomography (DECT) has demonstrated its unique clinical value in the study of tophi. Particularly, DECT has shown good effectiveness in monitoring the volume of tophi in patients with gout, with a positive correlation between the changes in urate volume measured by DECT and the improvement of the 20-item Tophus Impact Questionnaire (TIQ-20) [12]. Moreover, the application of DECT helps identify urate deposits in other parts of the body, indicating the systemic impact of gout, which provides new insights for clinical intervention [13]. Therefore, if clinically suspected, DECT can easily make a diagnosis of tophi. The versatility and efficiency of DECT have established it as an important modality in the imaging diagnosis of gout and other related diseases. Of course, histological examination remains an indispensable diagnostic method for confirming tophi .

It is thought that patients with acute attacks of lumbar gout, mostly accompanied by severe low back pain symptoms, if at this time you ignore the treatment of lowering uric acid and simple pain relief, often results in an unsatisfactory therapeutic effect, and delayed treatment can lead to the risk of paraplegia, so it should be diagnosed and treated as soon as possible [14]. An experiment has found that, Sodium urate crystals not only directly inhibit osteoblast viability, but also induce macrophages to release factors that promote osteoblast expression of bone-related factors and inflammatory mediators, thereby creating inflammation and causing a shift toward bone resorption; therefore, early intervention is warranted so that inflammation can be minimized and bone and osteoarticular destruction can be reduced [15]. Researchers regularly require intensive individualized medication management with a combination of uric acid-lowering therapy and anti-inflammatory drugs, which can hopefully lead to the gradual disappearance of urate crystals deposited in various parts of the spine, thus avoiding surgical treatment [16]. Given the symptoms of progressive spinal cord/nerve compression for the patient



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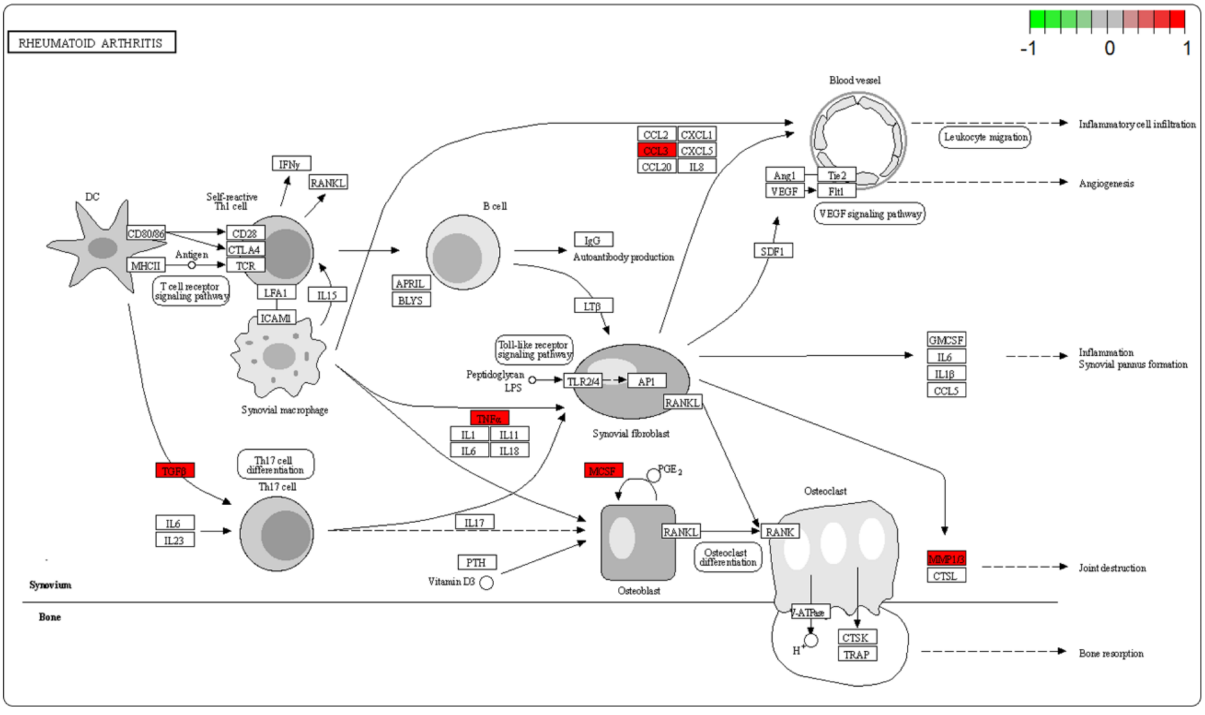

b

Fig. 5 **a**: the FoxO signaling pathway; **b**: the rheumatoid arthritis (RA) signaling pathway; Red markers in the figure stand for the represent potential targets of action for the treatment of gout combined with lumbar spinal stenosis(LSS)

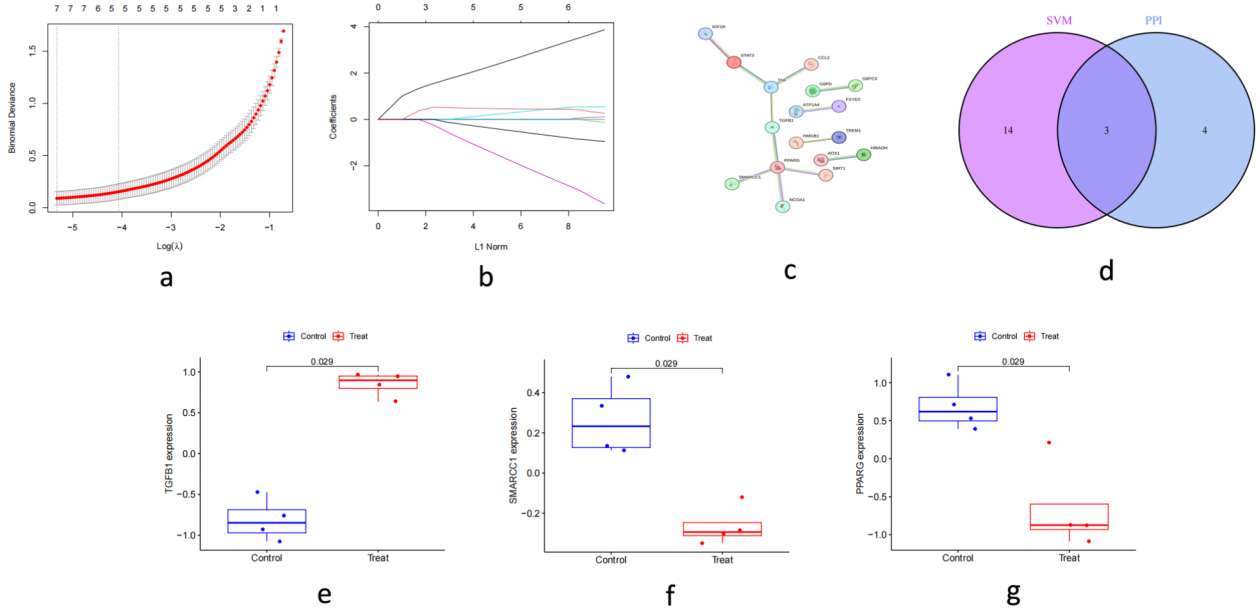

Fig. 6 **a**: trajectory of regression coefficients of LASSO model; **b**: variation process of the optimal penalty coefficient λ in the LASSO regression model; **c**: diagram of the reciprocal PPI network of the core genes of Gout-LSS; **d**: intersecting genes of the LASSO algorithm and the PPI network; **e**-**g**: differences in the expression of TGFB1, PPARG, and SMARCC1 in experimental groups and control groups

in this article, we opted for surgical intervention. Fortunately, satisfactory results were obtained after surgery. Therefore, patients with spinal gout must be diagnosed and treated early, with complete intraoperative excision of the gout stone and spinal nerve decompression. Postoperative combination of medications to treat gout and control uric acid can mostly lead to a better outcome.

Based on the development of bioinformatics, we explored the public intersecting genes related to lumbar spinal stenosis and gout, and then obtained the related differential genes and analyzed the expression of their genes in GO enrichment as well as KEGG signaling pathway. It was found that they were mainly enriched in the FoXO signaling pathway, the rheumatoid arthritis signaling pathway and so on; Li et al. investigated the regulatory mechanism of sodium urate (MSU)-induced inflammation in RAW264.7 macrophages by polyphenols (PSLP), which may be mediated by the HIF-1 signaling pathway, renal cell carcinoma, ErbB signaling pathway, and the FoxO signaling pathway [17]; it was reported that two patients with rheumatoid arthritis (RA) involving the lumbar spine also exhibited lumbar stenosis, and the RA patients recovered well after decompression with LSS surgery. Two patients with RA involving the lumbar spine were also reported to exhibit lumbar spinal stenosis, and patients with RA recovered well after surgical decompression of the LSS, and there was no increased risk of complications in patients with RA [18]。 Therefore, this rheumatoid arthritis signaling pathway suggests that gout patients causing lumbar spondylolisthesis may be caused by the rheumatoid arthritis pathway, but further validation is needed. The PPI results of our study suggest that there are several different target genes in gout and lumbar spinal stenosis. In this study, we used LASSO regression to screen from among the possible recurrence influences among the differential genes, and the intersection genes of the final screened genes with the genes in the PPI network resulted in three core genes: TGB1, PPARG, and SMARCC1. According to research, TGFB1 enhances the inflammatory response in joints by promoting the infiltration of inflammatory cells and the release of proinflammatory factors, leading to the onset of gout [19]. Additionally, PPARG, as a nuclear receptor, is involved in regulating lipid metabolism and inflammatory responses; its activation can suppress inflammation and improve the metabolic status of patients with gout [20]. The increased expression of SMARCC1 in gout-related cells may affect the progression of gout by regulating the expression of inflammatory factors and cellular proliferation [21]. We speculated that these three genes are playing similar roles in lumbar spinal stenosis caused by gout, but this needs further experimental proof.

Future research directions will focus on several key points. Firstly, functional validation of key genes is an important aspect. This study identified TGFB1, PPARG, and SAMRCC1 as potential key genes in gouty lumbar spinal stenosis through bioinformatics analysis, but experimental evidence is lacking. Therefore, subsequent

studies could conduct cellular experiments to clarify the specific mechanisms by which these genes influence disease progression at the cellular level. Secondly, investigation of upstream and downstream regulation of signaling pathways is also crucial. These key genes are known to be enriched in pathways such as the FoxO signaling pathway and rheumatoid arthritis pathway; thus, developing small molecule inhibitors or agonists to target these pathways could be an exploratory direction to impact disease progression. Lastly, optimization of treatment strategies cannot be overlooked. By achieving precise gene silencing or activation, combined with traditional treatment methods, we can develop personalized comprehensive treatment plans to enhance therapeutic efficacy.

Conclusion

In summary, we discussed and analyzed the cases that surgical treatment of intravertebral gouty tophi caused by gout can achieve better efficacy, and proposed a new strategy for the treatment of lumbar spinal stenosis caused by rejuvenated patients with gout from the perspective of bioinformatics, TGB1, PPARG, and SMARCC1 are important predictive targets for LSS associated with gout, but further research is still needed in the future.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12891-025-08273-z.

Supplementary Material 1: **Additional file**: Correlation analysis of GSE113212.

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Not applicable.

Author contributions
Xiao Zhang, Wenbo Gu and Haifeng Yuan proposed and designed this study. Xiao Zhang, Wenbo Gu, and Di Luo contributed to data collection and writing the manuscript. Haifeng Yuan, Xusheng Li and Xi Zhu revised the manuscript. All authors read and approved the final manuscript.

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Data availability
The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.the dataset GSE113212 associated with ligamentum flavum from the GEO database (https://www.ncbi.nlm.nih.gov//).

Declarations

Ethics approval and consent to participate
Informed consent was obtained from the participant and reviewed by the Ningxia Medical University General Hospital Ethics Council (Ethics number: KYLL-2023-0026).

Consent for publication
Consent for publication was obtained from the patients.

Competing interests
The authors declare no competing interests.

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